18445: Genetic Bases for Resistance and Immunity to Avian Diseases

Status: Draft

Duration 10/01/2017 to 09/30/2022
Admin Advisors:
NIFA Reps:

Statement of Issues and Justification

a) The Ongoing Need for this Work, as indicated by stakeholders

The US per capita poultry (chickens, turkeys) consumption equals the combined per capita consumption of both beef and pork. The consumption of poultry worldwide has steadily increased since 1960. Given the high feed efficiency of poultry, this food source represents one of the most economically- and environmentally-sustainable means to provide protein to the growing human population. United Nations projects the 2050 world population to be 9.7 billion people up from the 7.3 billion people in 2015. Poultry breeders and producers seek to provide consumers with a wholesome product with higher production efficiency and lower production cost to meet this ever-increasing demand.

Disease remains a major issue for the poultry industry. Economic losses due to morbidity, poor performance, and mortality are significant with the added threat that some bacterial and viral zoonotic pathogens can cause human illness or death. While advances have been made in controlling many poultry pathogens, the impact of diseases is one major impediment for sustained productivity. The total disease impact on poultry production not only includes losses due to mortality, decreased meat and egg production, and condemnations at processing, but encompasses the increased costs in prevention (i.e. vaccinations, biosecurity, and eradication programs for exotic diseases). Moreover, with a major focus on antibiotic free (ABF) production, understanding and optimizing immune function has become of paramount importance to maintaining sustainable levels of production.

This project aligns with the producers' goal of the judicious antibiotic use in poultry meat and egg production, since healthier birds will reduce the events in which these drugs are necessary. The use of pharmacological agents (e.g., antibiotics) to treat disease poses its own challenges to animal production, the environment, as well as the wellbeing of poultry and the consumer.

Protection of poultry flocks against endemic and exotic diseases is a priority for meat and egg

producers. The 2015 outbreak of highly-pathogenic avian influenza (HPAI) in the U.S. (Washington, Wisconsin, Minnesota, and Iowa) and subsequent smaller outbreaks in Montana, Tennessee, Alabama, Kentucky and Georgia, remind us of the vulnerability of these systems. In addition, consumer preferences are also driving commercial production systems to be more open (free range), elevating the risk for exotic disease introduction. The U.S. Poultry and Egg Association defines 28 critical needs for controlling disease and ensuring food safety in poultry. These needs include a focus on prevention of diseases, while decreasing the use of antibiotics, pesticides and anti-parasitic drugs.

This project addresses the genetic bases of disease resistance and immunity in poultry, as well as mechanistic understanding of innate and adaptive immune processes; issues having fundamental importance. Primary stakeholders (the most immediate users of these data, reagents, and tools generated in this project) are poultry breeding, vaccine, and allied animal health industries. Their frequent participation in the annual Technical Committee meetings, and their many collaborative research with the members, clearly indicate the high value that stakeholders ascribe to this project.

b) The Essential Nature of this Project

This work is essential to advance disease prevention and control strategies that ensure a sustainable poultry industry with increased production for a growing world population. Genetic variability is inherent within populations of species and is a product of natural selection. This project addresses the important issues of genetic bases of resistance and immunity to diseases in poultry providing stakeholders with a better understanding of genetic variability within their stocks in order to produce future populations with sustainable, desired traits. Disease resistance as a genetic trait is very multifaceted. Sometimes one or a few genes, such as the major histocompatibility complex, affect disease responses. Other instances are more complex with many contributory genes, making heritability low, and difficult to improve by traditional genetic selection methods. Although there is a chicken genome sequence, much remains to be learned about loci that are naturally polymorphic and about the functional outcomes of interactions among polymorphic loci that are increasingly under directed selection. We will also be able to better understand immune responses to common poultry pathogens through this project. This information is crucial in order to strategize novel preventative strategies, which in some cases can be cross protective. Disease is one of the major limiting factors in large-scale and small-scale poultry production. Shifts toward managing birds in less-controlled environments, and reduction of antibiotics use in animal production are exacerbating disease issues. Currently pathologies that seemed to be controlled are recurring thereby disrupting commercial production. This project addresses the important issues of environmental and physiologic factors that regulate or affect immune system development, optimal immune function and disease resistance in poultry. If this work is not done, disease will increase, production efficiency will decrease, food safety will be greatly compromised, and as a result export markets will be closed. This project also addresses the need for development of methods, reagents and specialized genetic stocks to be able to assess, monitor and modulate immune system development, patterning and function. In contrast to biomedical model species, such as mice, few of the reagents needed for poultry research are commercially available. If immune development is not monitored, immune responses to vaccine

and disease organisms could deteriorate, thereby increasing morbidity and mortality. Understanding immune system development as affected by genetic and environmental factors will find direct application in the breeding poultry stocks that have improved health and effective responses to vaccination. These improvements will contain production costs.

c) The Technical Feasibility of This Project

The NE-1334 Technical Committee collectively possesses a spectrum of scientific expertise to execute the collaborative research essential for the future of poultry production. Their a range of expertise encompasses many disciplines; including: immunology, infectious diseases, genetics, genomics, virology, kinomics, poultry medicine, physiology, nutrition, biochemistry, microbiology, and molecular biology. The work is technically feasible as it is rooted in methodologies that have been demonstrated as successful when used in other species, most notably human medicine. In the past decade, next generation sequencing, gene editing and many highly sophisticated methods have become now available to examine the expression and interactions of genes important in disease resistance. The techniques can be readily applied in investigations of disease especially in genetically defined experimental lines. The researchers work on the leading-edge of science, have demonstrated their expertise with the requisite infrastructure to successfully complete the described work, if sufficient financial support is made available.

d) Advantages for doing the work as a multistate effort (The Essential Collaborative Nature of this Project)

Conducting this work as a multistate project offers the advantage of pooling and sharing resources to address critical scientific questions. The members of the NE-1334 committee are well-established scientists conducting research in a range of disciplines to examine disease resistance at all levels. In addition, participants have unique skills or specialized resources such as genetic stocks and poultry-specific reagents that are needed to conduct the work. The multistate effort is required for the synergistic and collaborative conduct of research that is based upon the combination of biological materials (experimental lines of birds, antibodies, cell lines, pathogen stocks), facilities, equipment and expertise from multiple stations. No single station possesses all of these to address the major scientific issues for the project. Conducting this work as a multistate effort allows for the greatest efficiency of resource use from 27 independent laboratories from 17 U.S. states [AL (1), AR (1), CA (6), DE (1), GA (1), IA (1), IN (1), MD (1), MI (USDA-ADOL, 1), MO (1), NC (2) , NY (1), OH (1), TX (1), VA (1), WI (1), WV (1)], and 2 other countries [Canada (2, ON, PEI) and the Netherlands (2, NL)] in the current NE-1334 group of scientists - each addressing complementary aspects of the problem. The truly essential, cooperative, multidisciplinary nature of the project is illustrated by the many joint-authored publications among participating stations. Between 2015 and 2016, the NE-1334 project members have produced 119 refereed publications and 145 abstracts many of which feature joint authorship among multiple stations. The extensive expertise of the NE-1334 Technical Committee members and collaborators is also very clearly illustrated by the members' contributions to books such as Avian Immunology (published in 2013) co-edited by a NE-1334 member plus authorship in 7 of the 22 chapters plus one of the two appendices. In addition, contributions of NE-1334 Technical Committee members and collaborators have been recognized by the Poultry Science Association (PSA) and the American Association of Avian Pathologists: PSA Early Achievement Award for Research, Hy-Line

International Poultry Science Research Award, Embrex Fundamental Science Award, Evonik Degussa Award for Achievement in Poultry Science, Novus International, Inc. Teaching Award, two US Poultry Distinguished Poultry Industry career recognitions, Induction as Poultry Science Association Fellow and Bayer Snoeyenbos New Investigator Award.

e) Outcomes and Impacts of this Project

Impacts are expected to include but not be limited to: a better understanding of polymorphic loci and the consequence of selection on poultry health and production; new breeding strategies to produce more robust, disease resistant lines of poultry; improved efficacy of vaccines and other pharmaceutical agents; new vaccine programs for controlling existing as well as emerging diseases; a better comprehension of immune responses to specific antigens and a better fundamental understanding of how the avian immune system functions. These impacts aid future scientists by facilitating prevention or control strategies for current issues plus new problems that will arise. Improved disease resistance and enhanced prevention strategies will boost production efficiency, animal health and hence welfare. Reduced antibiotic use and improved poultry product safety will have favorable consumer reception. Much new knowledge in the basic and translational sciences, as well as, reagents and tools generated by this project, will constitute valuable resources to the stakeholders.

Related, Current and Previous Work

Objectives

Methods

Measurement of Progress and Results

Outputs

Outcomes or Projected Impacts

Milestones

Outreach Plan

Organization/Governance

Literature Cited

Land Grant Participating States/Institutions

Non Land Grant Participating States/Institutions

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
Grand Total:	**0**	**0**	**0**

Program/KA	Total FTE
Grand FTE Total:	**0**

NEtemp1833: NE-1333: Biological Improvement of Chestnut through Technologies that Address Management of the Species, its Pathogens and Pests

Status: Draft

Duration 10/01/2017 to 09/30/2022
Admin Advisors:
NIFA Reps:

Statement of Issues and Justification

NE-1333: Biological Improvement of Chestnut through Technologies that Address Management of the Species, its Pathogens and Pests

Status: Draft

Duration: 10/01/2017 - 09/30/2022

Administrative Advisor: Bradley Hillman

NIFA Reps:

Statement of Issues and Justification

Chestnut blight, incited by *Cryphonectria parasitica* (Murr.) Barr, devastated the American chestnut tree (*Castanea dentata* (Borkh.) Marsh) in the first half of the 20th century, killing approximately 4 billion dominant and codominant trees in the hardwood forests of the eastern United States. Prior to blight, the tree had many uses, producing sawtimber, poles, posts, fence rails, cord wood for fuel, paper and tannin extraction, and nuts for humans, livestock and wildlife. It also can be characterized as a member of our charismatic megaflora; many people mourn its loss and participate in citizen-science projects to restore it. Restoration of the American chestnut would be a beacon of light and hope shown by science in the face of continuing environmental degradation due to the advent of industrial and now postindustrial economies and the accompanying influx of exotic pests.

The United States Department of Agriculture (U.S.D.A.), in cooperation with state and private agencies, began work in the 1910s to restore the chestnut tree after recognition it would be destroyed by blight. As part of their work, exotic species of *Castanea* were introduced, which has resulted in a nascent orchard industry in numerous states from coast to coast in the U.S. Although the aggregate production of edible chestnuts is still too small to be tallied separately by the U.S.D.A., in 2015, the United States had 919 farms producing chestnuts on more than 3,700 acres. The states with the most chestnut acreage were Michigan, Florida, California, Oregon, Virginia, and Iowa. Most of those trees are not afflicted by blight, but are affected by other pests, which need management, and cultivation techniques for the trees are required. Moreover, infrastructure to process and market chestnuts needs further development. NE-1333 members have done research to address these needs and formulated extension recommendations.

The NE-1333 project and its predecessors have been the central organization coordinating chestnut research since 1983. Members span numerous disciplines in plant sciences, and the annual meeting provides an opportunity for members to be exposed to this diversity. NE-1333 has provided a forum for new and established researchers to develop collaborative relationships and to share resources and expertise. NE-1333 meetings are well attended, and about 30 presentations are typically made by participants each year. International visitors and collaborators are often included in these presentations, and two international symposia have been organized and hosted by NE-1333. Numerous multi-state and international research efforts have been undertaken by NE-1333 members. The project was initiated to explore the diversity of hypoviruses and their efficacy for controlling blight on American chestnut at different locations in its natural range. That original goal persists, but range-wide studies additionally include breeding and evaluation of disease-resistant progeny as well as studies of orchard chestnuts for nut production. An additional activity requiring a multistate effort has been development of genomic tools for *Castanea*.

The NE-1333 project comprises three objectives: 1) develop and evaluate disease-resistant chestnuts for food and fiber through traditional and molecular approaches that incorporate knowledge of the chestnut genome; 2) evaluate biological approaches for controlling chestnut blight from the ecological to the molecular level by utilizing knowledge of the fungal and hypovirus genomes to investigate the mechanisms that regulate virulence and hypovirulence in C. parasitica; and 3) investigate chestnut reestablishment in orchard and forest settings with special consideration of the current and historical knowledge of the species and its interaction with other pests and pathogens.

Objective 1: Develop and evaluate disease-resistant chestnuts for food and fiber through traditional

and molecular approaches that incorporate knowledge of the chestnut genome.

Two diseases of particular interest are chestnut blight and Phytophthora root rot. Resistance is being addressed on the one hand through breeding, supported by genetic mapping and development of genomic selection as well as metabolomic analysis to facilitate selection; and on the other hand, by transformation, including both trans- and cis-genetic approaches. Development of genomic tools, including an assembled sequence, supports both breeding and genetic engineering approaches.

Blight resistance has been backcrossed from Chinese into American chestnut. Seed orchards with an aggregate inbreeding effective population size (Nei) of about 50 have been producing progeny since 2006. The Nei is predicted to increase to 300 as satellite breeding programs in 14 states progress. The satellite programs have progressed to planting seedling seed orchards. Selection for blight resistance within the two original seed orchards is still incomplete. It is expected to be complete in 5-10 years. Once selection is complete, blight resistance is predicted from analysis of orchard progeny tests to be midway between Chinese and American chestnut. Forest progeny tests were installed beginning in 2009; they have not matured enough to evaluate the severity of naturally occurring blight. However, growth rates of families overlapped with that of families of American chestnut, and were significantly better than growth rates of Chinese chestnut families.

Resistance to Phytophthora root rot (PRR), incited by *P. cinnamomi,* occurs in lines derived from one source of blight resistance. Heritability of resistance to PRR is high enough that it should be possible to fix it while retaining Nei and blight resistance.

Techniques were developed to regenerate chestnut plants from embryo cultures, which was a significant accomplishment for this difficult-to-root hardwood. A gene from wheat encoding oxalate oxidase conferred blight resistance on plantlets when transformed into American chestnut. Transformant events are being propagated to tree size for further characterization of blight resistance and for increase into American and backcross chestnut populations. The oxalate oxidase gene is heritable. Regulatory approval is being sought to release genetically transformed trees into the wild. A thorough pipeline has been developed for producing trees from embryonic cultures.

Integrated physical and genetic maps of Chinese chestnut were prepared and blight resistance mapped to three QTLs in a small set of Chinese x American F2 progeny. Several candidate genes for bight resistance from the QTLs have been transformed into American chestnut but no plantlets have been evaluated for blight resistance yet. Multiple QTLs for PRR resistance have been detected using Restriction site-Associated DNA Sequencing (RAD-Seq), although they need further characterization. That characterization may resolve the discrepancy between the number of QTLs predicted from mapping and the single factor of high heritability predicted by classical analysis. Blight resistance is also being characterized by RAD-Seq and sequence capture. Genomic selection, including selection for major QTLs for blight resistance, may be extremely helpful in speeding up selection in seed orchards, which currently requires progeny tests in addition to phenotypic testing. That selection may also be facilitated by more rapid screens for blight resistance and by metabolomic analyses.

Version 2 of the *Castanea* genome sequence has the 5,745 largest scaffolds anchored to the integrated genetic-physical map to produce a set of 12 pseudo-chromosome sequences, representing the 12 linkage groups and providing 798 Mbp (98%) of genome coverage. Predicted gene positions have been transferred over to the pseudo-chromosomes, as well as the previously assembled blight-resistance-QTL sequences. Long-read PACBio sequence is being used for further validation of sequence and for gap closing. To test the value of the chestnut reference genome for use in genetic variation studies and in Genome-Wide-Selection in breeding programs, 10X depth sequence data were produced for 21 *Castanea* genotypes.

Objective 2: Evaluate biological approaches for controlling chestnut blight from the ecological to the molecular level by utilizing knowledge of the fungal and hypovirus genomes to investigate the mechanisms that regulate virulence and hypovirulence in *C. parasitica*.

Chestnut blight appears to have been controlled by naturally occurring hypoviruses on*C. sativa* in Europe but not on *C. dentata* in North America, except in specialized settings. Research by NE-1333 members and their European colleagues contributed to the view that control in North America was hampered by the much larger number of strains of *C. parasitica* in different vegetative compatibility groups than occurred in Europe. Other factors hampering control in North America

versus Europe may have been greater competition from other hardwood species and greater susceptibility to blight in *C. dentata.*

The RNA sequence of an hypovirus was first determined by members of NE-1333, and a number of species of virus were found based on sequence analysis. Viruses in families other than the Hypoviridae, including mitochondrial plasmids, were found infecting *C. parasitica,* some associated with reduced virulence and biocontrol. Transformation of *C. parasitica* with cDNA of Cryphonectria hypovirus 1 resulted in transmission of the DNA in ascospores and regeneration of RNA viruses in progeny. This completed Koch's Postulates for the hypovirus. Unfortunately, while transformed fungus strains could produce progeny that infected adjacent chestnut trees with hypovirus-containing *C. parasitica,* disease remission did not occur.

Strain Ep155 of *C. parasitica* was crossed with a European strain and six vegetative compatibility loci, known as Vic genes, were genetically mapped in the progeny. The DNA of strain Ep155 of *C. parasitica* was sequenced and the European strain resequenced. The six Vic genes were identified and a "super donor" strain prepared with five inactivated Vic genes (four Vic genes were knocked out). The super donor strain should be able to transmit hypoviruses to strains with any combination of Vic genes. The strain is being tested in the forest for disease control.

Strain Ep155 has very high pathogenicity. It is used to screen chestnut trees for blight resistance in combination with a virulent strain of low pathogenicity known as SG2-3. The two strains were crossed and 96 progeny evaluated for pathogenicity. It is hoped that the progeny can be resequenced and QTLs for pathogenicity identified by knockout. This should help lead to further understanding of mechanisms of pathogenicity in the fungus. The mechanisms of virulence reduction by hypoviruses in the fungus also remain an active area of investigation, as do other aspects of virus activity in the fungus. Reannotation of the fungus genome is almost complete, which should facilitate transcriptomics analyses and the above studies.

Objective 3: Investigate chestnut reestablishment in orchard and forest settings with special consideration of the current and historical knowledge of the species and its interaction with other pests and pathogens.

In addition to the activities discussed under Objectives 1 and 2 above, research is ongoing on gall wasp, silvics, juvenile *versus* adult chestnut blight resistance, genetic variation in American chestnut, and integrating resistance with hypovirulence to control blight, *inter alia*.

It has been found that introduced and native parasites of the gall wasp control the pest after the first few years of infestation. Despite a plant quarantine, Michigan is now in the third year of gall-wasp infestation. While nut harvests are markedly decreased during those first few years of infestation, insecticidal treatments also would destroy the parasites, so the recommendation is to NOT spray insecticides to control gall wasp. Dispersal of parasites is recommended, but none are being produced currently. There have been efforts to bring parasite-infested boughs to new areas of infestation, to introduce parasites earlier. There is variation between cultivars in their susceptibility to gall wasp.

In general, silvicultural evaluations of American chestnut in several states have found that it is a very rapid grower, frequently much faster than oak and walnut. Chestnut growth varies with site, like most hardwoods, so it is not faster than oak and walnut on all sites. Earlier research found that exotic chestnut species do not grow well in native forests, unlike American chestnut. This finding was part of the motivation leading to the proposal to backcross resistance from exotic into American chestnut.

The results of inoculating young seedlings of the three chestnut species in China do not match up with blight severity on mature specimens of the three species in China; this result needs more detailed experimental evaluation. Low levels of blight resistance occur in a few American chestnut trees. Intercrossing of these to enhance that resistance has been pursued for a long time. In combination with hypoviruses, impressive levels of blight control have been observed on some pure American chestnut with low levels of resistance. The hypothesis that hypoviruses coupled with resistance in backcross progenies will diminish blight severity is being evaluated.

NE-1333 members collectively published 15 peer-reviewed articles, 3 Ph.D. Dissertations, 1 book chapter, and 6 abstracts in 2015-2016. These are typical statistics for the past 5 years, with the

number of refereed publication being on the low end of the range. Members are renowned for their work on chestnut, *Cryphonectria,* and fungal viruses. Venues for presentations include the Plant and Animal Genome Conference, the American Phytopathological Society, the Mycological Society of America, the Ecological Society of America, the Society of American Foresters, various venues of the International Union of Forest Research Organizations, The American Chestnut Foundation, Encyclopedia Britannica, International Plant Protection Congress, the Entomological Society of America, the American Society for Virology. The results of research have been extended to growers, especially in Michigan, and to volunteer citizen scientists guided by the American Chestnut Foundation and the American Chestnut Cooperators' Foundation.

In recognition of these successes, NE-1333 received the ESS Excellence in Multistate Research award in 2010 (NE-1333 was then known as NE-1033). NE-1333 has met the milestones detailed in the project description and will continue to work on similar collaborative projects in the next 5 years. Data generated under the auspices of the NE-1333 project have been used by members to gain intramural and extramural funding for all aspects of chestnut biology and restoration.

In summary, the NE-1333 project is a productive group of collaborators that has provided new and meaningful information to all clients interested in chestnut biology and restoration, from the bench scientist to the professional orchardist and to the individual volunteer grower of chestnut for restoration. In the next 5 years, we will continue to pursue collaborative projects under our 3 stated objectives. This will lead to increased production of chestnuts in orchards and will further restoration of the iconic American chestnut. Great progress has been achieved toward restoration and continued research efforts are needed to guide it to completion.

Related, Current and Previous Work

Objectives

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Literature Cited

Land Grant Participating States/Institutions

Non Land Grant Participating States/Institutions

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
Grand Total:	**0**	**0**	**0**

Program/KA	Total FTE
Grand FTE Total:	**0**

18443: Sustaining Herbaria as Key Resources for Addressing Agricultural and Environmental Issues

Status: Draft

Duration 10/01/2018 to 09/30/2023
Admin Advisors:
NIFA Reps:

Statement of Issues and Justification

NEED AS DEFINED BY STAKEHOLDERS. The management and use of natural resources are key to successful agriculture in a densely populated world. Because plants are the essential natural resource, basic plant biology is key to the future prosperity of the human population. In the same way that basic medical researchers seek clinical solutions to fundamental challenges in human health care, plant biologists seek to provide the insights that make it possible to feed, clothe, and shelter our ever-larger population in spite of intensifying environmental concerns. To paraphrase the organizers of the AAAS Plant Biology Symposium in February of 2013, fundamental discoveries and sophisticated research in the plant sciences will provide novel strategies and practical solutions or mitigations to some of the major global challenges that face future generations. Major problems plant biologists can address include natural-resource sustainability, food security, renewable energy, and human health and well-being. Though plants are essential to human survival, some plants—such as weeds and invasive species—interfere with human priorities, such as agricultural production and the conservation of natural resources. Hence, we are all stakeholders when it comes to seeking new understanding of the distribution and interactions of the native and introduced plant species in the United States.

In the last twenty years, there has been an explosive increase in the use of biological collections for ecological and environmental research (Pyke and Ehrlich, 2007; Heberling et al., 2017), including research addressing key agricultural issues. With the launch of web portals such as iDigBio for access to online data and images of plant and animal collections in American museums and herbaria, an entirely novel way for researchers to deploy data from these collections for solutions to agriculture-related problems has emerged. Within this terrain, the dried plant specimens in the herbaria of Land-Grant Universities stand as a key research resource for addressing problems such as invasive species, pollinator availability, protection of genetic diversity among wild relatives of domesticated species, and overall sustainability of biological diversity.

Herbaria document wild plant diversity over time and across space, providing the basis for insights into changes in plant distribution and frequency. Herbaria also provide a permanent physical resource for assessing genetic diversity in plant species, because DNA extraction from the collections remains a tractable option for, at a minimum, over a century. Documented changes in distribution, interpreted in the light of the distribution of genetic diversity, lead to insights into the changing roles of plants on the earth’s surface and the significance of genetic diversity in these

changes.

Land-Grant Institution herbaria have played an important role in the inauguration of what we call virtual herbaria. These vast arrays of digitized images and collection data generated from physical specimens and integrated across the herbaria form the basis for large-scale inquiries into biodiversity and conservation issues. Access to these data has expedited new research on plant species demographics, current and predicted distributions of species, and changes in the timing of flowering and fruiting (Daru et al., 2017).

IMPORTANCE OF THE WORK. A challenge that plant biologists face in developing virtual herbaria as research tools is that biases in collections data are limiting their utility (Daru et al., 2017). Our research program will address this key problem through developing protocols for promoting the reduction of bias in the addition of new collections to the herbaria. In this proposal, we outline a program shared across at least 12 herbaria at Land Grant institutions, that will enhance the quality and thus the utility of the collections with the overall goal in the context of the Hatch Multistate Program of improving the security of farm and forest products and protecting the natural resource base and the environment. The approach is to enhance the quality of online information representing the diversity of plant collections in Land-Grant Institution herbaria for better access to data on geographic distribution, temporal change in distribution, and genetic diversity. Easier access to ***enhanced data*** will provide the basis for **promoting the application of these data** to research projects at the individual herbaria leading to improving the security of farm and forest products and safeguarding the natural-resource base and environment.

ADVANTAGES OF A MULTISTATE APPROACH. Herbarium Curators at two NERA-region land-grant institutions, the University of New Hampshire and Rutgers, have agreed to co-sponsor this proposal with us at the University of Vermont.

Advantages of a multistate approach are threefold: 1) Funding will lead to substantially expanded resources for problem-solving, because the collection at each institution is a unique assembly of specimens from diverse geographical locations gathered over time, BUT no one collection alone provides a sufficient record of plant distributions; uniting the resources across herbaria overcomes this limitation. 2. The collaborating herbaria will work to provide integrated high-quality data and images from across as many herbaria as possible for the solution of local environmental and food-security problems relevant to the individual state experiment stations. 3. The solutions to these problems can be addressed in the light of genetic data obtainable from the relevant plant collections across the broader community of herbaria.

TECHNICAL FEASIBILITY: All the Land-Grant Institution Herbaria who have communicated an interest in this multistate proposal are developing their databases and images using the state-of-the-art open-source software package Symbiota (Gries et al., 2014) and are already sharing their digital data and images via portals such as iDigBio and JSTOR plants. Thus, the proposed community of participants in this activity are fully prepared to work together to develop solutions to problems encountered in the development of the proposed agenda for this multistate program. In

addition, the participants are already part of a research community participating in the annual meetings of the Botanical Society of America, making for the kind of excellent communication we see as central to the success of this multistate program.

CONSEQUENCES OF FAILURE TO IMPLEMENT A MULTISTATE GRANT FOR HERBARIA
Without integration of the herbaria at Land-grant Institutions into a network including closely collaborating colleagues, each contributing to a globally available database of plant distribution and ecological data, member institutions will continue to be hindered in their efforts to provide high-quality, integrated information to stakeholders by their isolation from other institutions. The absence of communication will have its greatest impact on the rate at which land-grant herbaria implement and expand their programs in support of environmental quality and agricultural security, because sharing of expertise and experience between institutions is an efficient way to increase the rate at which institutions implement change.

There are two goals for the Land-Grant University Herbaria participating in this multistate project, each with a set of objectives ldetailed below.

- The first goal is **enhancing the quality** of the on-line data derived from the herbaria through funding for substantial improvements.
- The second is **promoting the application** of these data by the experiment-station faculty to research thatprotects human health and the environment and enhances the natural resource base and the environment.

Related, Current and Previous Work

In 2008, the Western Association of Agricultural Experiment Station Directors approved the WDC 12 project, for Integrating Access to Information from Herbaria. This project brought together more than 40 representatives from herbaria across the country at the BOTANY 2008 conference. The group unanimously supported the creation of a “US Virtual Herbarium” (USVH), to provide, through collaboration with regional networks, a single portal accessing information in the nation's herbaria. A Hatch Multistate Proposal was approved to inaugurate a coordinating committee with representatives from herbaria and the bioinformatics community to expedite the development of the portal. This multistate grant, WERA1015: *Developing the US National Virtual Herbarium [USVH]*, has had the overall goal of supporting Agricultural Experiment Stations by increasing the information available about plants that contribute to or impact the US agriculture industry through more efficient access to the wealth of information that resides in herbaria.

In fact, the United States Virtual Herbarium (USVH) as such never became a reality. At the 2014 meeting, the USVH Coordinating Committee decided to work with iDigBio (the NSF-funded national aggregator for non-federal herbaria) to develop a national vascular plant network, thus accomplishing the original goal envisioned for the USVH. Nonetheless, the WERA 1015 coordinating committee played an important role in developing land-grant institution herbaria as resources.

Impact of Previous Work

The number of herbaria sharing their specimen data via the web has increased dramatically during the lifetime of the USVH Multistate Coordinating Committee.

Many of these herbaria have made their data available through regional networks that enable users to draw on information from multiple herbaria with a single query.

Some portals were already available at the outset, and more have come on-line since WERA1015's inception. Prominent among these portals are

1, the Global Biodiversity Information Facility (https://www.gbif.org/) with over 800 million records

2. iDigBio (https://www.idigbio.org/portal), with over 100 million records

3. national networks for four taxonomic groups (lichens, bryophytes, macrofungi, and macroalgae).

4. regional portals, such as

   the Consortium of Northeastern Herbaria (http://portal.neherbaria.org/portal/),

   the Consortium of California Herbaria (http://ucjeps.berkeley.edu/consortium/), and

   the North American Network of Small Herbaria (http://nansh.org/portal/) house significant data and images of plant specimens relevant to Experiment Station goals.

Importantly, several networks have made it possible to contribute data without installing and maintaining a local specimen database. Thus, smaller, locally focused herbaria have started to contribute. In the process, undergraduates from many herbaria have become involved in digitization, contributing to the concepts and tools and knowledge they take with them after graduation. Working together on digitization has increased interaction among those in charge of herbaria and is leading to new collaborations in development of educational resources and research tools. Finally, software has been developed that makes capturing and sharing specimen data much easier and more efficient than when the project began.

Overall, the number of U.S. herbaria contributing to a US-based herbarium network as of FY 2016 was 371, somewhat more than 50%. The number of herbarium records in U.S.-based herbarium networks was 21,685,093

Thus, through a remarkable series of successes with funding opportunities, the community of United States herbaria, notably including those at Land-grant Institutions, have made real progress towards an integrated virtual herbarium, that is an on-line combined digital and image resource representing the combined collecting resources assembled North American botanists over the last 200 years.

Land-grant institution herbaria who have indicated that they are interested in participating the new Hatch Multistate Proposal that we are requesting to write, the following activity has been reported (institution, correspondents, number of specimens on portals). Total specimens on line, 1.7 million. All of these institutions have used Symbiota to develop their databases.

University of California, Berkeley—Brent Mishler: 299,567 specimens

Colorado State University—Mark Simmons: 65,777 specimens

Iowa State University—Lynn Clark and Deb Lewis: 92,122 specimens

Louisiana State University—Meredith Blackwell: 210,419 specimens

Michigan State University—Alan Prather: 111,633 specimens

North Carolina State University—Marc Cubeta: 6,806 specimens

Oregon State University—Aaron Liston and Melanie Link-Preez: 184,354 specimens

Rutgers University—Lena Struwe: 67,053 specimens

University of Minnesota—George Weiblen: 223,541 specimens

University of New Hampshire—Chris Neefus and Janet Sullivan: 173,002 specimens

University of Vermont—Dave Barrington and Michael Sundue: 105,410 specimens

Utah State University—Paul Wolf and Mary Barkworth: 166,587 specimens

The Current Situation for Land-Grant Institution Herbaria

The challenge that the community of U.S. herbaria now face is to overcome the following problems:

1. We do not have all of our current collections digitized and made available on portals.
2. The data and images now available on the web are incomplete. Some records consist of just an image, some of an image plus minimal information, some have all the information on the specimen label but no image. In 2016, the number of herbarium records with latitude and longitude data in US-based herbarium networks was 8,138,176, i.e. 37%, and the number of records with accompanying images in US-based herbarium network is 9,962,412, i.e. 46%.
3. The geographic data are incomplete, inconsistent, and imprecise. We do not yet have a culture of requiring consistent, high-quality georeferencing of specimen data in our herbaria.
4. We do not have a financial plan in place for the inclusion of new collections in these on-line databases.
5. We do not consistently represent plant collections with on-line digital resources using best standards for the use of scientific names and other nomenclature issues.
6. The herbarium community has yet to integrate the on-line data fully into a single universally searchable database.

Objectives

1. Enhancing Quality 1. improve the utility of existing collection data—by extracting expanded data, especially habitat data, from specimens, and improved georeferencing
2. Enhancing Quality 2: participate in the building and sharing of new tools for processing and analyzing virtual data—e.g. expanding OCR transcription of label data, optimizing searches for previously digitized duplicates, leveraging citizen science participation (see Ellwood et al, 2017 for recommendations).
3. Enhancing Quality 3. digitize new accessions to expedite the inclusion of new Land Grant Herbaria collections in virtual-herbarium-based research
4. Enhancing Quality 4. improve quality of data for new collections—encouraging and vetting new accessions with bias in mind (see Daru et al., 2017 for a digest of the problems to be solved)
5. Promoting Application 1. identify the ecological and temporal factors that determine species distributions.
6. Promoting Application 2. predict areas to which an introduced species will spread or additional populations of a native species be found (e.g. Meyerson and Mooney, 2007).
7. Promoting Application 3. explore the potential distribution of insect pests to the distribution of their crop-species targets and wild relatives.
8. Promoting Application 4. predict the potential for spread of genetically modified plants into related wild populations in the same geographic region
9. Promoting Application 5. assess areas of great genetic diversity in a geographic context relative to indications of over-harvesting for non-timber forest products (e.g. Koenemann et al., 2011; Nualart et al. 2017)
10. Promoting Application 6. identify areas of critical importance for native pollinators (e.g. Tobler et al., 2007; Maldonado, 2015).
11. Promoting Application 7. Identify best wild species to use in establishing riparian buffer zones for flood control and water quality improvement (as explored in Shultz et al. 2004i
12. Promoting Application 8. stabilize the ecological context for agriculture through the planning of agricultural buffer plant communities (see Altieri (1999)

Methods

- The principal goal of the this Multistate Grant is to enable the member herbaria to reach the goals for the digitization of data that provide answers to the identified key questions relating to agricultural and environmental issues, as articulated in our objectives. The methods articulated here, following from the goal of ***enhancing quality***, are shared by all the institutions.

The methods for ***promoting application*** all lead to enabling the success of the specific research projects defined as local priorities at the land-grant institutions served by the herbaria.

METHODS: ENHANCING QUALITY

1. Funding of Collections Digitization at the Member Institutions
2. Incorporating citizen-science and iNaturalist activity into transcription and recording of specimen records
3. Organizing of meetings by the Steering Committee for this Multistate Grant with the goal of expediting progress in

Improving OCR processing of images through providing routes to participation in OCR hackathons.

Seeking a way to have a full thesaurus of names available at all times

Improving retrieval and incorporation of data from duplicates specimens at other institutions

Promoting the development of a single on-line research environment in which to access all collection information

Participating in on-line and institutional meetings of existing collections-oriented communities, e.g.

1. iDigBio https://www.idigbio.org/
2. The Society for the Preservation of Natural History Collections http://www.spnhc.org/2/what-spnhc-does

METHODS: PROMOTING APPLICATION

Organizing meetings by the Steering Committee for this Multistate Grant with the goal of

1. exchanging ideas for sustaining and enhancing the natural resource base and the environment.
2. communicating local research priorities among the collaborating institutions and beyond into the herbarium community at large with the goal of integrating the research agendas into a common program.

Measurement of Progress and Results

Outputs

- 1. Improved records for existing collections, including added images and data
- 2. inclusion of new collections in the online databases
- 3. reduction of bias in newly accessioned collections in land-grant herbaria

Outcomes or Projected Impacts

- enhanced application of herbarium data to natural-resources, agricultural, and environmental problems

Milestones

(**2018**):organization of lang-grant herbarium community, definition of specific goals

(**2018**):development of plans for on-line data improvement, including OCR data transfer,improving latin-name consistency, linking data on duplicate specimens

(**2019**):plan approaches to improving full integration of national datasets

(**2018**):enter and upload data from existing and new collections, continuing for the length of the project

(**2020**):implement plans to support research applications at member land-grant herbaria

(**2019**):Develop communication among land-grant institution herbaria with the goal of facilitating the development of local projects that promote the application of digital data to relevant solutions

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Outreach Plan

We consider the best form of outreach to be direct participation by stakeholders in research activities. Participation of “citizen scientists” in the gathering of data have demonstrably invigorated the digitization of biological collections (Ellwood et al, 2017). Involvement of citizen scientists also increases awareness biodiversity and biological collections, advances STEM literacy, increases public support for biological collections, and builds sustainability for digitization activities. To this end, we will support land grant institutions with the resources needed to host offsite and onsite digitization events where citizen scientists transcribe specimen labels using Symbiota’s crowdsourcing module. These events have the capacity to reach a broad audience, both at the home institutions and via the web. At the inaugural WeDigBio event, thousands of participating citizen scientists transcribed 30,000 specimen labels at 25 events over four days. Similar successful events have already been implemented by some of the participating land grant institutions as well, demonstrating their value and feasibility.

Organization/Governance

At the outset there will be a steering committee formed by the curators of the participating land grant institutions that have indicated interest in collaborating on this project (listed above under *Impact of Previous Work*). The steering committee will develop a permanent governance plan that incorporates a plan for including the broader community of United States herbaria. The University of Vermont will provide administrative support as well as the administrative advisor for the project.

Literature Cited

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Land Grant Participating States/Institutions

VT

Non Land Grant Participating States/Institutions

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Barrington, David S	Yes	Vermont - University of Vermont		136	2499	1060	0.00	0.00	0.00	0	0

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
136-2499-1060	0	0	0
Grand Total:	**0.00**	**0.00**	**0.00**

Program/KA	Total FTE
0	0
Grand FTE Total:	**0**

NECC_TEMP1702: Establishment of a Formal Structure for the Minor Use Animal Drug Program

Status: Under Review

Duration 10/01/2017 to 09/30/2022
Admin Advisors: [Margaret E. Smith]
NIFA Reps:

Statement of Issues and Justification

Globalization of food markets has allowed countries with less stringent animal drug approval requirements to dominate U.S. sheep, goat, farmed shrimp and fish, venison, honey and game bird production industries. At the same time, the growing concern in the U.S. over antibiotic resistance in human health and the use of antibiotics in food producing animals threatens to eliminate or severely curtail antimicrobial use in veterinary medicine. In April of 2013, the Center for Disease Control and Prevention (CDC) released their report entitled, “Antibiotic Resistance Threats in the United States 2013”. With respect to the issue of antibiotic use in food animals, the CDC report concluded “Because of the link between antibiotic use in food-producing animals and the occurrence of antibiotic-resistant infections in humans, antibiotics should be used in food-producing animals only under veterinary oversight and only to manage and treat infectious diseases, not to promote growth.” Since the release of this report, efforts have grown to sharply eliminate any use of antibiotics in animals without veterinary oversight. There appears little doubt that the next several years will introduce a new era of antimicrobial use in veterinary medicine. The Minor Use Animal Drug Program is the only national program designed and organized to address the issues of the prudent use of antibiotics, anthelmintics and production drugs in minor species of food- and fiber-producing animals, and for minor uses in major animal species.

The following issues require a formal structure for the Minor Use Animal Drug Program (MUADP):

1. The termination of the NRSP-7 program has left 88 Investigational New Animal Drug Applications (INADAs) filed at the Food and Drug Administration Center for Veterinary Medicine (FDA/CVM) scheduled to terminate for lack of sponsor. Loss of these INADAs will result (1) in a collective loss of work estimated in excess of $5 million dollars and (2) loss of stakeholder incentive to provide support for the Program.

2. The MUADP has received a $250,000 grant from Animal and Plant Health Inspection Service (APHIS) for continued research on ivermectin blocks for cattle tick fever as well as chlortetracycline and meloxicam for sheep.

3. Dr. Sonny Ramaswamy, director of the National Institute of Food and Agriculture (NIFA), has proposed a tactical science initiative within NIFA merging the Minor Crop Pest Management Program (IR-4/NRSP4), Food Animal Residue Avoidance Program (FARD), and Minor Use Animal Drug Program (MUADP) into a single funding entity.

Objectives

1. Provide the formal structure necessary to maintain the 88 INADAs held in the name of the MUADP.
2. Continue APHIA funded research on cattle fever tick and sheep drug approvals.
3. Interact with NIFA in the establishment of a tactical science program that includes Minor Crop Pest Management, Food Animal Residue Avoidance Program and Minor Use Animal Drug Program to be included in the new Farm Bill and supported by NIFA.

Procedures and Activities

1. Continue research on cattle fever tick and ASI drug requests under APHIS funding. Complete report on research conducted to date is included in Attachments.

2. Teleconference and meet with NIFA associates to address the development of a tactical science initiative and formation of a unified Regulatory Systems Support Program that would include Minor Crop Pest Management, Food Animal Residue Avoidance Program and the Minor Use Animal Drug Program. An abbreviated summary (two pages from a total of 15 pages) from NIFA entitled, “Call to Conversation on Tactical Sciences for Protection of the U.S. Agricultural Enterprise” hosted by the University of Maryland College of Agriculture and Natural Resources on February 15 and 16, 2017 is included in the Attachments.

Expected Outcomes and Impacts

- Objective 1: The establishment of a formal structure for the MUADP will prevent the loss of the 88 INADAs filed at the FDA/CVM scheduled to terminate for lack of sponsor.
- Objective 2: A summary of the APHIS funded research is provided as Attachment #1. This quarterly report has been submitted to APHIS. The Program expects continued support from APHIS based upon progress in critical areas of stakeholder need.
- Objective 3: Input and assistance provided to NIFA on the logistics of merging the Minor Crop Pest Management Program, Food Animal Residue Avoidance Program and Minor Use Animal Drug Program into a single funding entity with a consolidated regulatory support system, that can provide research ensuring the safety and diversity of agricultural products. Comments: Both Drs. John G. Babish, National Coordinator MUADP and Meg Oeller, DVM, Director, Office of Minor Use & Minor Species Animal Drug Development, attended the Call to Conversation on Tactical Sciences for Protection of the U.S. Agricultural Enterprise, hosted by the University of Maryland College of Agriculture and Natural Resources on February 15 and 16, 2017 in support of the MUADP. At the Call to Conversation, participants agreed that current investments in tactical sciences are not sufficient to address growing challenges posed by the threats to our nation’s food supply. The group identified several major forces that are likely to impact the security of the U.S. agriculture and food system enterprise in the coming years, and agreed that a major initiative to protect the biosecurity of our nation’s food systems by raising the stature and increased support for tactical sciences is timely, necessary, and worthwhile. To continue the momentum generated by the conversation, a working group of key, representative stakeholders was formed to provide recommendations for strengthening the tactical science portfolio. As nominated by Dr. Babish, Dr. Oeller was selected to represent Minor Animal Drug interests in the working group. This select subset of stakeholders will be asked to: 1) Develop a vision for a robust, coordinated framework of tactical science capabilities that will ensure the biosecurity of the U.S. food and agricultural system; 2) Develop an aspirational outcome that will strengthen tactical science capabilities in the United States; and 3) Develop a communication strategy that effectively conveys the importance of tactical sciences to relevant audiences. Ideally, the efforts of this working group will result in a national initiative to strengthen tactical science programs and enhanced protection of the U.S. food and agricultural system from existing and emerging threats.

Educational Plan

Organization/Governance

The recommended Standard Governance for multistate research activities include the election of a Chair, a Chair-elect, and a Secretary. All officers are to be elected for at least two-year terms to provide continuity. Administrative guidance will be provided by an assigned Administrative Advisor and a NIFA Representative.

Literature Cited

USDA NIFA. 2017. Report of Call to Conversation on Tactical Sciences for Protection of the U.S. Agricultural Enterprise. 15-16 February 2017, University of Maryland College of Agriculture and Natural Resources, College Park MD. 15 pp.

Land Grant Participating States/Institutions

IA

Non Land Grant Participating States/Institutions

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Griffith, R.W.	Yes	Iowa - Iowa State University	1,2,3	311	3910	1180	0.10	0.00	0.00	0	0

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
311-3910-1180	0.1	0	0
Grand Total:	**0.10**	**0.00**	**0.00**

Program/KA	Total FTE
0	0
Grand FTE Total:	**0**

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1702: Establishment of a Formal Structure for the Minor Use Animal Drug Program

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Excellent**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Excellent**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Excellent**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation
Approve/continue with revision (provide specific recommendations in Comments below).
Comments:
This group has a long history of success providing needed research for veterinarians and livestock owners to make rational decisions on medication usage and make needed medications available for minor species. Now more than ever, with heightened awareness of responsible stewardship of antimicrobials and pain management (as examples) the work of NRSP7 and its projects are needed to help sustain food animal production in minor species.

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1702: Establishment of a Formal Structure for the Minor Use Animal Drug Program

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Excellent**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Excellent**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Excellent**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation
Approve/continue with normal revision.
Comments:
There is an acute need for a formal structure supporting the MUADP. The authors of this proposal has clearly described this need in the document I have reviewed. The authors are to the best of my knowledge more than qualified to lead these research efforts that will increase the availability of drugs for minor use and minor species.

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1702: Establishment of a Formal Structure for the Minor Use Animal Drug Program

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Excellent**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Excellent**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Excellent**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation
Approve/continue with normal revision.
Comments:
The project has been very beneficial to numerous minor species in the past and continuation of the program is still a high priority.

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1702: Establishment of a Formal Structure for the Minor Use Animal Drug Program

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Excellent**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Excellent**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Excellent**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation
Approve/continue with normal revision.
Comments:
This approach has the potential to efficiently improve the health of animals and the safety and quality of food through coordinated research activities.

NECC_TEMP1700: Equine Clinical Studies

Status: Under Review

Duration 10/01/2017 to 09/30/2022
Admin Advisors:
NIFA Reps:

Statement of Issues and Justification

The North Eastern United States is home to a strong equine industry, supported by equine research programs in veterinary colleges, and the animal and/or veterinary science departments of public universities. Increased collaboration and pooling of resources between basic scientists, teaching hospital clinicians, private industry, practicing veterinarians and their clients could be used to strengthen equine research by making possible larger clinical studies. In addition, it could assist product development by the animal biotechnology sector. However, such collaborative studies pose significant logistical and scientific difficulties.

Through the formation of the original Coordinating Committee on Equine Clinical Studies, under the guidelines of the USDA Multistate Research Activities program, we have begun to facilitate and encourage collaborative equine clinical studies in the North East. We have addressed pooling of resources through compilation of an asset inventory (attached). In addition we have developed research and outreach priorities to address equine wellness and disease (see attached logic model). In the near term we have identified gastrointestinal health and the equine microbiome as areas of interest. In addition, through a survey of horse owners in the North East, we have documented stakeholder interest in further pursuit of this line of work (see attached reprint (1)). In 2016 we submitted a conference grant through the 2016 USDA/AFRI program (Causey R, Biddle A, Williams C, Burk A. Making Clinical Sense of the Equine Microbiome. US Dept of Agriculture 2016. $49,050). Although this application was not successful, a grant by a member of NECC1200 (Amy Biddle PI, University of Delaware) for expansion of her equine microbiome project has been submitted to the Morris Animal Foundation and is currently pending.

We would like to continue the work of the equine clinical studies coordinating committee through pursuing multi-state activities related to the equine health, including the equine microbiome, hopefully leading to improved quality of life for horses in the North East.

Objectives

1. Foster development of new methods for diagnosis and therapy of equine diseases, and for improving equine gastrointestinal health.
   Comments: Creating new tools to improve equine health is difficult for isolated industry sectors - practitioners understand the need, basic researchers the technology, and industry the commercialization. Greater collaboration of these sectors could improve success in subsequent clinical trials. We therefore wish to encourage discussion between these groups early in the study design process.
2. Improve sample size in early phase equine clinical trials.
   Comments: For academic researchers, early trials in vivo would provide raw material for peer-reviewed publication. Pooling resources (such as horses) between institutions can improve statistical power, strengthening grants and manuscripts. We therefore wish to improve collaboration during these early phase trials, and make generally available the statistical methods necessary to analyze data in trials replicated in multiple sites.
3. Increase number and power of randomized, double blinded equine clinical trials.

Comments: Peer-reviewed journals generally accept the randomized, double blinded clinical trial as evidence of a drug's efficacy (2). Epidemiological rigor is also expected in validation of diagnostic tests, and identification of disease risk-factors. To encourage such studies, we wish to improve collaboration between researchers, practicing veterinarians, farms and private industry. The goal would be to allow field trials to be replicated in multiple sites and across state lines.

4. Development of a multistate research project.
   Comments: The committee's activities will encourage discussion between members who share a common goal of improving equine health. We intend that the committee will generate at least one multistate research project, with objectives specific to equine diseases prevalent in the North East. A goal currently is to develop a multistate project related to equine gastrointestinal health and the microbiome.
5. Educate equine industry stakeholders regarding new methods of diagnosis and therapy arising from objectives 1 through 4.
   Comments: To have impact, new discoveries and techniques need to be disseminated. We therefore wish to make available to all stakeholders, including veterinarians, horse owners, allied industry, state government etc, any new information generated by the committee's work.

Procedures and Activities

1. Continue committee, starting with current composition -The Coordinating Committee on Equine Clinical Studies currently consists of faculty interested in sharing research resources. Membership includes faculty in public institutions in the North East, but also collaborators in private institutions and institutions outside the North East. The committee may include a representive from the equine feed or biotechnology industries.

2. Meet annually - Gathering of the committee on an annual basis has been invaluable in helping the committee to forge and maintain relationships and plan activities. The meeting site will continue to rotate through sites in the North East US, usually hosted by members of the committee at their home institutions.

3. Develop Research Capacity - The inventory of shared resources will be updated to reflect our new membership. Increased research capacity will be sought through equipment grants, pooling animal numbers, and shared use of other resources.

4. Reach out to animal feed, supplements, and biotechnology industry partners -The animal feed, supplements, and biotechnology industry may be valuable collaborators in the development of new products, providing technical assistance, and in sponsoring outreach programs. It is hoped that commercialization of new products will result from the committee's work. This may include improved pre or pro-biotics, feeds, and supplements targeted to improve equine gastrointestinal health.

5. Reach out to practicing veterinarians -Practicing veterinarians will be end-users of new information generated by the committee, some playing roles in implementing clinical studies. It will therefore be valuable to forge relationships with veterinarians so that clinical trials can be conducted, and new products created.

6. Conduct regional outreach programs for all stakeholders -Coordinated outreach will be necessary to deliver new information to regional stakeholders (veterinarians, horse owners, animal feed and biotechnology industry, state government etc).

Expected Outcomes and Impacts

- Increased output of participating investigators and investigator-private industry partnerships. Comments: Additional resources, and new public-private research partnerships, could increase number of grants funded and manuscripts published.
- New animal health products brought to market Comments: Increased capacity to perform clinical trials will accelerate new product development and licensing. This may include new feeds, feed supplements, pharmaceuticals, and diagnostic assays.
- Improved animal welfare Comments: The greater power of clinical studies will improve diagnosis and therapy, and decrease incidence of equine disease.

Educational Plan

The coordinating committee will have a dedicated webpage, including profiles of participating members, inventory of resources available for pooling, plans for upcoming meetings etc. The annual meeting will include brief presentations by members of their work, with an annual report of the committee's activities. Nature and scope of outreach programs to stakeholders will be determined as part of the committee's initial deliberations. Because they are so dispersed, practicing veterinarians and lay groups can be difficult to access. Combining the annual meeting of the committee with a veterinary continuing education or equine industry conference may facilitate outreach on occasion. Additional methods to reach lay stakeholders groups will include non-technical bulletins distributed in print and online, targeted emails and the dedicated webpage. The use of video-conferencing and distance education technology may also be employed to solve specific needs of underserved stakeholders.

Organization/Governance

Governance will be standard.

Literature Cited

(1). Coffin D, Causey R, Staniar B, Williams C, McKeever K, Gradil C, Nadeau J, Sanchez A, Lichtenwalner A, Biddle A, Assessing Research and Education Needs to Improve Equine Gastrointestinal Health. Journal of the NACAA 2017; 10(1)

(2). Simoneit C, Heuwieser W, Arlt S. Evidence-based medicine in bovine, equine and canine reproduction:
quality of current literature. Theriogenology 2011; 76:1042-1050.

Land Grant Participating States/Institutions

ME,CT,NJ,IL,MN,AR

Non Land Grant Participating States/Institutions

Tufts University School of Veterinary Medicine, North Grafton, MA

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Causey, Robert C		Maine - University of Maine	1,2,3,4,5	311 311 311 310	3810 3810 3810 3810	1100 1020 1170 1010	0.00	0.00	0.00	0	0
Lichtenwalner, Anne B		Maine - University of Maine	1,4,5	311 0 0	3999 0 0	1160 1020 1090	0.00	0.00	0.00	0	311 313
McCoy, Annette	Yes	Illinois - University of Illinois	1,5	315	3810	1020	0.10	0.00	0.00	0	0
McCue, Molly	Yes	Minnesota - University of Minnesota	1,2,3,4	304 303 305 311	3810 3810 3810 3810	1080 1080 1080 1080	0.10	0.00	0.00	0	0
McKeever, Kenneth H		New Jersey - Rutgers University	1,2,3,4,5	315	3810	1020	0.00	0.00	0.00	0	0
Russell, Mark		Arkansas - University of Arkansas	1,2,3,4,5	307 306 315	3810 0 0	0 0 0	0.00	0.00	0.00	0	0

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
310-3810-1010	0	0	0
311-3810-1020	0	0	0
311-3810-1100	0	0	0
311-3810-1170	0	0	0
0-0-1020	0	0	0
0-0-1090	0	0	0
311-3999-1160	0	0	0
0-0-0	0	0	0
302-0-0	0.17	0	0
Grand Total:	**1.20**	**0.00**	**0.00**

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
305-0-0	0.17	0	0
307-0-0	0.17	0	0
311-0-0	0.17	0	0
313-0-0	0.17	0	0
315-0-0	0.17	0	0
315-3810-1020	0	0	0
315-3810-1020	0.1	0	0
303-3810-1080	0.03	0	0
304-3810-1080	0.03	0	0
305-3810-1080	0.03	0	0
311-3810-1080	0.03	0	0
311-3810-1010	0	0	0
313-0-0	0	0	0
315-0-0	0	0	0
306-0-0	0	0	0
307-3810-0	0	0	0
315-0-0	0	0	0
Grand Total:	**1.20**	**0.00**	**0.00**

Program/KA	Total FTE
0	0
311	0
313	0
307	0.02
302	0.25
305	0.25
307	0.25
311	0.25
313	0.25
315	0.25
0	0
0	0
0	0
0	0
0	0

Program FTE Total: 1.0 Total FTE

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1700: Equine Clinical Studies

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Good**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Excellent**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Good**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation

Approve/continue with revision (provide specific recommendations in Comments below).

Comments:

In regard to the following statement: 1) "In addition, it could assist product development by the animal biotechnology sector. question: How, specifically? 2) "However, such collaborative studies pose significant logistical and scientific difficulties." question: what are they (logistical and scientific difficulties)? 3) "We would like to continue the work of the equine clinical studies coordinating committee.. question: examples of these equine clinical studies? 4)"...including the equine microbiome, hopefully leading to improved quality of life for horses in the North East." question: What are the activities related to equine microbiome? Why do the authors consider microbiome is important? Specifically, how “equine microbiome” studies could “strengthen” equine research?

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1700: Equine Clinical Studies

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Excellent**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Good**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Excellent**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation
Approve/continue with normal revision.
Comments:
Collaboration and team work between sites will improve and facilitate research momentum. Microbiome work is currently exploding in other species and in the equine only the surface has been scratched.

Appendix J1: CC Evaluation (Submitted)

Status: Complete

Project ID / Title:
NECC_TEMP1700: Equine Clinical Studies

Questions

1. Goals and objectives clearly stated and appropriate to committee activity(s)	**Excellent**
2. There is a good potential to attain the objectives and plan identified in the activity.	**Excellent**
3. Activity addresses priority research and is not duplicative with existing activities.	**Good**
4. Activity has moved beyond individual activity(s) and ideas to a collective, interdependent activity.	**Excellent**
For renewal projects only:	
5a. Attendance of the preceding project has been adequate and reflects broad participation by designated project participants.	**Excellent**
5b. The project has developed and demonstrated technology transfer to clientele.	**Excellent**

Recommendation
Approve/continue with normal revision.
Comments:
This project brings together many resources from various institutions making equine research easier to accomplish. With small equine herd sizes and research budgets at single institutions, grouping resources is a terrific way to facilitate positive outcomes..

NE_TEMP1748: Mastitis Resistance to Enhance Dairy Food Safety

Status: Under Review

Duration 10/01/2017 to 09/30/2022
Admin Advisors: [Cameron Faustman]
NIFA Reps:

Statement of Issues and Justification

The United States dairy industry continues to experience significant monetary drain through the losses associated with common diseases. Bovine mastitis is the most costly infectious disease currently affecting dairy cattle. While significant advances have been made in controlling some types of mastitis, the complex etiology of the disease and ongoing changes in dairy practices dictate that new and more effective methods for control and treatment be developed over time. Single site studies are often limited in terms of expertise and cattle numbers. A multi-state project provides advantages in terms of increased numbers of herds and cattle as well as multiple levels of expertise.

Mastitis is defined as an inflammation of the mammary gland that is almost always associated with bacterial infection. Mastitis affects every dairy farm and approximately 38% of dairy cows in the United States experience clinical signs. The National Mastitis Council estimates that this devastating disease complex costs the dairy industry more than 2 billion dollars per year or approximately $180.00 per cow. These losses are primarily due to lost milk production, increased veterinary costs, increased cow mortality, and discarded milk.

Currently, intramammary antibiotic therapy is the most widely used and most effective management strategy to eliminate intramammary infections (IMI) and alleviate pain and suffering. Bovine mastitis is a unique disease wherein multiple infectious agents can trigger an inflammatory response. When considering treatment of an individual cow for mastitis, the causative infectious agent is usually unknown. Therefore, producers commonly treat with different combinations of antibiotics and routes of treatments. This common management strategy can lead to overuse of antibiotics, thus increasing the risk of residues in milk and the selection for antibiotic resistant pathogens. Growing consumer concerns regarding antibiotic use, the risk of antibiotic residues in milk and meat and the potential for antimicrobial resistance have led to the examination of alternative strategies for controlling mastitis while reducing the use of antibiotics on-farm, which is one of the primary goals of this multi-state group.

The identification of alternative therapeutics are advocated in an April, 2015 White House mandate titled “National Action Plan for Combating Antibiotic-Resistant Bacteria”, which only underscores our approaches. According to priorities within the 2014 farm bill, examining new management strategies to treat bovine mastitis will expand our knowledge regarding the use of non-antibiotic alternative therapies to treat disease thereby reduce production costs and enhance nutritional quality of products for human consumption while improving animal health. In addition, international agencies, including the Food and Agriculture Organization (FAO) of the United Nations, the World Health Organization (WHO) and the World Organization for Animal Health (OIE), have also emphasized the need to find alternative approaches to treatment of animal disease and to identify the role of antibiotics used in animal agriculture in the emergence of antimicrobial resistance of human pathogens.

The purpose of NE-1048 is to coordinate multidisciplinary research efforts on mastitis that are being conducted at various laboratories throughout the United States and internationally, e.g. Canada and Europe. The magnitude and scope of attempting to solve these problems extend far beyond the ability of any one institution. The ability to cooperate on a regional, national, and international basis allows the integration of resources and knowledge to address this problem. Recognition of the need for a coordinated effort to study resistance of the pathogen and the need for non-antibiotic alternative therapeutics for the dairy cow for the control of mastitis resulted in the design and initiation of multi-State Project NE-1048. The NE-1048 project has provided a forum for new and established researchers to develop collaborative relationships, and to share resources and expertise. NE-1048 meetings are well attended and 30-40 presentations are typically made by participants each year. International visitors and collaborators are often included in these presentations.

In the United States (US), cash receipts from marketing of milk during 2016 totaled $33.7 billion (NASS, 2017). In the US, the dairy industry contributes >$140 billion per year to the national economy and provides > 900,000 jobs making it a vital part of our nation’s economy and food system (Adcock et al., 2015; ERS, 2015). However, the dairy industry continues to experience significant monetary drain through the losses associated with common diseases. Bovine mastitis is the most costly infectious disease currently affecting dairy cattle. Recent estimates suggest that economic losses due to clinical and subclinical mastitis are in the range of $200 per cow per year (Liang et al., 2013). These losses are primarily due to lost milk production, increased veterinary costs, increased cow mortality, and discarded milk. While significant advances have been made in controlling some types of mastitis, the complex etiology of the disease, ongoing changes in dairy practices, and the pressure to reduce antibiotic usage dictate that new and more effective methods for control and treatment be developed over time. Single site studies are often limited in terms of expertise and cattle numbers. A multistate project provides advantages in terms of increased numbers of herds and cattle as well as multiple levels of expertise.

The purpose of NE-1048 is to coordinate multidisciplinary research efforts on mastitis that are being conducted at various laboratories throughout the United States. The magnitude and scope of attempting to solve these problems extend far beyond the ability of any one institution. The ability to cooperate on a regional and national basis allows the integration of resources and knowledge to address this problem. Recognition of the need for a coordinated effort to study resistance of the dairy cow to mastitis resulted in the design and initiation of original multi-State Project NE-1048. The NE-1048 project has provided a forum for new and established researchers to develop collaborative relationships, and to share resources and expertise. The NE-1048 project is comprised of three objectives 1) characterization of host mechanisms associated with mastitis susceptibility and resistance, 2) characterization and manipulation of virulence factors of mastitis pathogens for enhancing host defenses, and 3) assessment and application of new technologies that advance mastitis control, milk quality, and dairy food safety. Accomplishments in the last 5 years are listed below by objective.

Objective 1: Characterization of host mechanisms associated with mastitis susceptibility and resistance.

Achievements include the dietary supplementation of OmniGen ® (GA), 2,4-thiazolidinedione (OR), retinol-binding protein (RBP; ID) and vitamin E (MD) to improve the host immune response during mastitis. Other major achievements include the negative relationship between severity of negative energy balance and fat mobilization on important inflammatory mediators (MI), the ability of white blood cells to kill invading microorganisms (WA), the negative impact of antimicrobial resistance on the host immune response (NY), the response of peripheral tissues during mastitis (MD, OR), characterizing the nutrient utilization by leukocytes during mastitis (MD), identification of dermal fibroblasts as a model cell to investigate genetic and epigenetic differences between cows in their innate responses to mastitis causing pathogens (VT), and that CXCR1 may be a promising new candidate gene for mastitis susceptibility (TN). Whole genome SNP association studies also have led to a series of new candidate genes that will be evaluated (TN).

Objective 2: Characterization and manipulation of virulence factors of mastitis pathogens for enhancing host defenses.

Major achievements for this objective are 1) the identification of iron-sulfur cluster metabolism as a virulence factor associated with *S. aureus* (NJ); 2) *S. uberis* adhesion molecule (SUAM) is a relevant virulence factor (TN) and 3) certain genes are involved with enhancing antimicrobial resistance of mastitis causing pathogens such as Klebsiella spp. (Quebec), *Escherichia coli* (*E. coli*; NY) and *Staphylococcus aureus* (*S. aureus*; NY).

Objective 3: Assessment and application of new technologies that advance mastitis control, milk quality, and dairy food safety.

Achievements include controlling mastitis via the use of ultrasound scanning to monitor mastitis (CT), the use of an Automated Milk Leukocyte Differential (MLD) Test for detecting IMI (MN), teat dip efficiency trials to reduce the incidence of mastitis (WA), the development of multiple decision support tools aimed at improving milk quality, reducing mastitis and economics (KY), examining alternative therapeutics for the prevention or treatment of mastitis to reduce antibiotic usage (MO, MD, Quebec), continuing outreach efforts to promote better stewardship of antibiotic use on dairy farms (MI, MO, MN, WI) and improving animal welfare via the development of behavioral monitors (KY, VA, MA).

The mastitis research workers group has met in conjunction with the NE-1048 annual meeting for many years, and in recent years, the mastitis research workers topics have been included in NE-1048 minutes, showing current active areas of research by NE-1048 members. International visitors and collaborators are often included in these presentations. In addition to the mastitis research workers conference, the NE-1048 members provide new management strategies to reduce antibiotic usage and technology transfer to the scientific community and industry stakeholders. In the last 4 years, members of the project have collectively published multiple book chapters, in excess of 192 peer-reviewed journal articles, over 300 abstracts and proceedings, and presented numerous oral and poster presentations related to mastitis, milk quality, and food safety. Venues for oral and poster presentations have included the National Mastitis Council regional and annual meetings (attendees include researchers, veterinarians, dairy producers, and representatives from industry), Conference for Research Workers in Animal Diseases, American Association of Bovine Practitioners annual meetings, International Dairy Federation meetings, American Dairy Science Association meetings, World Buiatrics Congress meetings, American Society of Microbiology meetings, Conference on Production Diseases in Farm Animals, Plant and Animal Genome Conference, Agriculture and Agri-Food Canada - Food Safety meetings, American College of Veterinary Internal Medicine annual forum meetings, and several regional extension and veterinary continuing education meetings.

The continuation of the NE-1048 multistate project is of utmost importance to foster research in mastitis leading to the provision of science based information to dairy producers and the dairy industry. The impact of the European Union's strict enforcement of import regulations on milk quality highlights the need to continue efforts to reduce the incidence of mastitis and antibiotic use. These new regulations require milk export companies to certify that any farm contributing milk must show a bulk milk cell count below 400,000 cells/mL. This regulation has been supported by the National Mastitis Council as a goal for all US dairies. Mechanisms leading to improvement in milk quality, dairy animal welfare, and appropriate use of antimicrobial therapeutics form the basis of research conducted in the NE-1048 multistate project. It is clear that continued mastitis research and education are required to maintain the global competitiveness of the US dairy industry (USDA APHIS, 2016). Furthermore, the animal agriculture industry in general is under closer scrutiny than ever before by various interest groups. The work of NE-1048 is clearly focused on reducing mastitis, reducing antibiotic use and improving economic outcome and animal welfare. Mastitis is the most significant animal health issue in the dairy industry. In summary, continuation of the NE-1048 project is a productive group of collaborators that has provided new and meaningful information to all levels of the dairy industry from the bench scientist to the dairy producer with regard to bovine mastitis control, treatment and prevention. In the next 5 years we will continue to pursue collaborative projects under our 3 stated objectives which will lead to new information of value to the management of dairy cattle mastitis. Mastitis is an evolving disease syndrome, as is the science that studies mastitis; therefore, continued research efforts are needed.

Related, Current and Previous Work

The Multi-State Mastitis Research Project (MMRP) has a strong history of productivity in applied mastitis research. The project was begun in 1977 as NE-112, then renewed in 1982, 1987, 1992, 1997, in 2002 as NE-1009, in 2007 as NE-1028 and NE-1048 in 2012. A substantial percentage of international mastitis research is conducted by MMRP members and affiliates. Members of MMRP collaborate extensively within the project and with other national and international research groups that have interests in bovine mastitis. The 2012-2017 iteration of the MMRP had 3 main objectives pertaining to the host, the pathogen, and the use of new technology. In the current proposal we intend to continue work and begin new studies using these objectives but also incorporate the importance of reducing the use of antibiotics and improving animal welfare in the dairy industry. The following are brief reviews, listed by objective, of current and previous work conducted during the last 5 years by the MMRP. In this summary, we focus on the most recent accomplishments. Multiple stations have contributed to the various objectives and are listed following each sub-objective.

Objective 1:Characterization of host mechanisms associated with mastitis susceptibility and resistance.

(i) Environment, Nutrition, and Management Related Host Factors Associated with intramammary infections (IMI; DE, GA, NJ, OH, MD, WI, MI, WA, NY, OR, ID).

The risk of mastitis increases during the transition period from late-pregnancy to early lactation. During this period, cows are under the hormonal influence of pregnancy, and are most likely in negative energy balance during the early part of lactation. Research has, therefore, focused on developing dietary strategies aimed at improving the immune response during this time, as well as better understanding the relationship between negative energy balance, other nutritional factors, versus immunity.In Georgia (GA), OmniGen ® promoted L-selectin expression on blood leukocytes, increased in vitro phagocytic ability of blood neutrophils and monocytes and stabilized reactive oxygen species (ROS) production by blood neutrophils (Ryman et al. 2013). Scientists at Rutgers University (NJ) defined a function for a proteis (Nfu) involved in Fe-S cluster trafficking (Mashruwala et al., 2016). Data generated at Oregon State University (OR) indicated that 2,4-thiazolidinedione improved the liver response to mastitis, prevented the decrease of milk fat synthesis after mastitis induction, and improved the innate immune system (Bionaz et al., 2015). Scientists at the University of Wisconsin (WI) observed an association between teat apex diameter with occurrence of mastitis (Guarin et al., 2016). Michigan (MI) continues to study the impact of negative energy balance and fat mobilization on important inflammatory mediators (Sordillo, 2016).The primary objectives for MMRP members at Washington State University (WA) are to determine ability of isolated neutrophils to phagocytize and kill different strains of opsonized *Mycobacterium bovis* (*M. bovis*; Nicholas et al., 2016). Scientists at Cornell University (NY) continue to examine the antibiotic susceptibility of streptococci-like bacteria and the immune response after *E. coli* challenge in late gestation and compared this to the response in mid lactation (Locatelli et al., 2015). Researchers at the University of Idaho (ID) are investigating the effect of retinol-binding protein (RBP) status on IMI in periparturient Holstein cows (Rezamand et al., 2016).). In collaboration with scientists at Oregon State University (OR), RNAseq

technology showed a high level of communication from the mammary gland to the liver during host responses to *E.coli* mastitis challenge (Bionaz et al., 2016). Metabolic parameters after in vitro stimulation are altered and nutrient utilization improves neutrophil response (Garcia et al., 2016). Maryland continues to collaborate with scientists at the USDA, Beltsville, to identify the distribution of vitamin E isoforms in various tissues as well as blood and milk and their use as antioxidants (Qu et al., 2016).

(ii) Host-Pathogen Interactions at the Cellular Level (VT and VA).

Members of the MMRP have investigated the molecular epidemiology of, and interactions between, mastitis-causing organisms and host response at gene and protein levels. For example, MMRP members at the University of Vermont (VT) identified dermal fibroblasts as a model cell to investigate genetic and epigenetic differences between cows in their innate responses to mastitis causing pathogens (Benjamin et al., 2016; Green et al., 2014; Kandasamy et al., 2012). MMRP members and the University of Vermont are now examining epigenetic contributions to the differential responses. Furthermore, results gave minimal encouragement for the ranking technique on the basis of high (6 cows) or low (6 cows) expression of the TLR4 gene in ear notch samples. Further use of additional ranking parameters will be required to develop a more accurate test to predict a cow's response to *E. coli* mastitis. Candidate genes responsible for the between-animal differences are being investigated. Scientists at Virginia Tech (VA) are characterizing the T cell responses to dendritic cells presenting *S. aureus* antigens and their findings show differential IFNg production in response to stimulation of immune cells with irradiated as compared with live *S. aureus* (Garst et al., 2014; Lehtimaki et al., 2014). The scientists believe these changes support the ability to manipulate the mammary gland and that the immune environment may favor Th17 cell polarization. In addition to cytokine profiles, MMRP scientists are evaluating memory cell proliferation and identifying *S. aureus* specific antigen responses and data suggests an ability to manipulate SCC profiles of the mammary gland.

(iii) Candidate Genes of Mastitis Susceptibility (TN and UT).

Projects within the MMRP have focused on studying genes related to the immune response during mastitis. Their work may allow consideration of selective breeding for mastitis resistance, which may prove valuable to the dairy industry as a whole. For instance, MMRP members at the University of Tennessee (TN) observed that 1) CXCR1, an immune related gene, is expressed on mammary epithelial cells, fibroblasts, and leukocytes in the mammary tissue; 2) specific CXCR1 genetic haplotypes can distinguish *S. uberis* growth and subsequent strength of inflammatory responses following intramammary challenge with *S. uberis* suggesting that CXCR1 can be helpful in genetic selection decisions and provide a model system to better understand host responses that contribute to disease resistance; and 3) *S. uberis* with a mutated/non-functional SUAM gene induced a lower level of inflammation in the mammary gland following intramammary challenge indicating this gene is significantly tied to growth of *S. uberis* in the gland (Almeida et al., 2013; Kerro Dego et al., 2013; Pighetti et al., 2013). Also at TN, preliminary research using whole genome SNP association studies also have led to a series of new candidate genes that will be evaluated. At Utah State University (UT), scientists identified a number of genetic variations (SNPs) that were associated with resistance or susceptibility to bovine mastitis. Utah's analysis is ongoing for comparison of bovine whole genome analysis for SNP detection between cows repeatedly mastitic vs. cows continually free of mastitis. Preliminary bioinformatics is detecting many genetic SNP combinations more common among mastitis-resistant cows and others more common among mastitis-susceptible cows.

Objective 2: Characterization and manipulation of virulence factors of mastitis pathogens for enhancing host defenses.

(i) Characterization of Pathogen Virulence Factors (GA, NJ, WI, PA, TN, MO, VA).

Characterization of virulence factors is an essential step to developing strategies to prevent or treat mastitis. MMRP members at the University of Georgia (GA) characterized and manipulated virulence factors of mastitis pathogens for enhancing host defense. Results have led to the publication with other MMRP members from NY (Berry et al., 2016) and the University of Tennessee (Nickerson et al., 2013). MMRP members at Rutgers University (NJ) characterized the mechanisms by which *S. aureus* builds and maintains iron-sulfur clusters (Choby et al., 2016). Scientists have found that *S. aureus* stains defective in iron-sulfur cluster metabolism have increased multicellular behavior resulting in biofilm formation (Mashruwala et al., 2016). This is a deterministic process governed by the iron-sulfur cluster containing ArlSR two-component regulatory system. These researchers have also aided in defining a function for the giant staphylococcal adhesion (Ebh), which has a role in multicellular behavior and found that Ebh expression is governed by the ArlSR- two-component regulatory system (Walker et al., 2013). Scientists will continue to examine the mechanisms of *S. aureus* biofilm formation. The researchers are interested in the effects of an anoxic growth on biofilm formation and determining if the scientists can disperse fermentative biofilms by introducing a terminal electron acceptor.

MMRP members at the University of Wisconsin (WI) are determining how fungal cells thrive under conditions of zinc deficiency such as those encountered in a mammalian host. Investigators at Pennsylvania State University (PA) have identified a small cell variant that may play a role in the persistence of S. *aureus* infections. At the University of Tennessee (TN), 2 studies were conducted to prove *S. uberis* adhesion molecule (SUAM) is a relevant virulence factor in vivo where cows did not develop as severe an infection or inflammation when compared to the wild-type strain or *S. uberis* receiving antibodies not specific for SUAM (Almeda et al.,2012). Additionally, several new genes that potentially contribute to *S. uberis* were identified using a transcriptomic-based approach that identified *S. uberis* genes activated following intramammary challenge (Almeida et al., 2012) that identifies potential alternatives for factors associated with *S.uberis* mastitis.

The association between mammary inflammation, duration of infection, and coagulase negative staphylococcal (CNS) IMI in cattle and dairy goats continues to be a major focus of MMRP members at the University of Missouri (MO). In-depth genotypic characterization of predominant CNS species using whole genome sequencing is underway to elucidate putative virulence factors involved in mastitis pathogenesis. Using irradiated and live *S. aureus* cultures MMRP members at Virginia Tech (VA) are identifying a role for virulence factors in immune suppression, activation, and manipulation. Interestingly, primary challenge with irradiated *S. aureus* did not induce migration of immune cells to the gland as compared with live *S. aureus* (Garst et al., 2014).

(ii) Antimicrobial Resistance (Quebec, NY, WI)

A review evaluated whether testing mastitis pathogens for antimicrobial susceptibility was of use in predicting outcomes of antibiotic treatment (Barlow, 2011; MMRP member). The author's conclusion, based on data from 17 peer-reviewed publications, was that no clear evidence exists to indicate that such testing had predictive value for cure or non-cure outcomes in the treatment of mastitis. However, the importance of antibiotic treatment in dairy animal welfare and production, and its potential relation to the development of antibiotic resistance in bovine and human strains, indicates that further monitoring and research are warranted. At the University of Montréal (Quebec), MMRP members are currently investigating the impact of pathogen characteristics such as virulence genes, relative biofilm production, antimicrobial resistance phenotypic profiles on clinical mastitis recurrence in characterizing Klebsiella spp. isolates from bovine mammary gland infections (Franoz et al., 2016). At Cornell University (NY), full genome sequencing of a number of mastitis *E. coli* isolates was completed. Characterization and manipulation of virulence factors of mastitis pathogens for enhancing host defense is currently being investigated. Additional research at Cornell University is focused around antimicrobial resistance and virulence factors of environmental streptococci. Data generated at Cornell University suggests that certain strains of *S. aureus* are better adapted to live in hostile environments (Bardiau et al., 2016' Locatelli et al., 2016). The University of Wisconsin Milk Quality (WI) lab members indicated a strong shift to mastitis caused by a variety of opportunistic environmental pathogens. The association between exposure to antimicrobials and occurrence of resistance will be reported. The lab also completed a study that characterized the differences in-vitro susceptibility testing of Ceftiofur and Cephapirin antibiotics as compared to results using the active metabolites of the same compounds. Results may partly explain the variability between in vitro susceptibility test results and in vivo outcomes of intramammary treatments.

(iii) Use of Molecular Epidemiology & Diagnostic Tools (Saskatchewan, VT, VA, LA, GA)

Members of the MMRP have had a great impact on advancing vaccine development, implementing mastitis control programs, and the field of DNA-based characterization of mastitis pathogens, also known as molecular epidemiology. Researchers at the University of Vermont (VT) developed a multilocus sequence typing scheme for *S. chromogenes* and researchers have identified *S. aureus* strain types with increased antimicrobial resistance phenotypes (Mugabi et al., 2016). Scientists at the University of Saskatchewan (Saskatchewan) compared *cpn60* and *rpoB* for identifying the species of CNS isolates. Scientists at Virginia Tech (VA) are currently evaluating potential vaccine targets through an intramammary challenge model (Garst et al., 2014; Kanevsky-Mullarky et al., 2013). Louisiana (LA) continues to collect mastitis pathogens and determine their antimicrobial susceptibility to various antibiotics (Owens and Ray, 2016). Studies are underway to compare susceptibility patterns of veterinary isolated to human isolates of the same pathogens. In lactating mammals, LSU has increased goat milk submissions that has led to the isolation and characterization of mastitis pathogens from goats, the majority of which are CNS (Owens and Ray, 2016). Mastitis pathogens from cattle and goats are identified and their antimicrobial susceptibilities determined to screen mastitis pathogens for resistance to antimicrobials. At the University of Georgia (GA), the use of a bovine staphylococcal vaccine in dairy goats (Nickerson, 2016) and dairy heifers (Hall et al., 2015) is promising.

Objective 3. Assessment and application of new technologies that advance mastitis control, milk quality and dairy food safety (CT, VA, OH, KT, Quebec, Saskatchewan, Prince Edward Island, WI, MI, WA, MN, NY, PA, ME, MO, MD, VA , LA, UT).

Technology applications within the last 5 years have included extensive evaluation of relatively simple tools, such as teat treatments (dips and dry cow treatments; WA, Enger et al., 2016, Nicholas et al., 2016; MO, Hoerning et al., 2016), mastitis detection (LA, CT, Notestine et al., 2015; VA, Swartz et al., 2016); application of strategies such as on-farm culture systems (UT, MN, Godden et al., 2016; PA, Hovingh, 2016); non-antibiotic therapeutics for the treatment of mastitis (MO, MD, Scholte et al., 2017), of bedding systems (OH, Hogan et al., 2012; ME, Adhikari et al., 2013), technologies for training producers and professionals (MI, MO, MN, ME; Erskine and Middleton, 2014), milking systems and the risk of mastitis (MD, Moyes et al., 2014), diagnostic/milk quality test development (MO, MI; Erskine, 2016; NY, Gioia et al., 2016) and implementation strategies, as well as new technologies related to vaccine development.

Animal welfare has become more important and behavioral monitors have been developed that can have diagnostic utility as well as enhancing marketability of dairy products due to welfare certification needs for selected markets. MMRP members at Virginia Tech (VA) continue to work in the area of disease detection with the use of daily milk component and animal activity monitoring and feeding behavior in calves (Swartz et al., 2016). Work at the University of Kentucky (KY) has led to the development of multiple decision support tools aimed at improving milk quality and animal welfare and reducing mastitis and economics (Eckelkamp et al., 2016;Klefot et al., 2016).

International membership for MMRP continues to be a high priority. Members at the University of Montréal (Quebec) recently described the cost of mastitis in Canada (Belage et al., 2016). Scientists are currently investigating 1) selective quarter dry treatment for prevention and treatment of IMI during the dry period; 2) identifying sampling strategies for controlling misclassification bias in longitudinal udder health cohort studies; 3) investigating impediments to adoption of mastitis control practices on dairies; 4) examining the impact of recycled manure bedding on udder health; and 5) characterizing milk microbiota and identifying alternative treatments for prevention and treatment of IMI at dry-off. Scientists at the University of Saskatchewan (Saskatchewan) and the University of Prince Edward Island are currently examining a novel treatment for *S. aureus* mastitis (Roy and Keefe, 2012).

Following are examples of collaborative efforts resulting from participation in this group:

USDA grant (Milk Quality Alliance) with collaboration among MI, PN, and FL

USDA grant (Southeast Quality Milk Initiative) with collaboration among TN, VA, KY, FL, MS, GA

Continous coordination and cross pollination among members of both these groups

Collabaration on employee management between Calgary and MI

Godden (MN) has led a multi-state bedding analysis study including members of this group.

MU Collaborations with CBMQRN:

MU - Calgary CNS - initial isolate ID on some of isolates was done with USDA formula funds - two papers published

MU - Montreal CNS - this was funded with USDA formula funds - paper published

MU - PEI CNS MALDI-TOF - initial isolate speciation was funded with USDA formula funds - paper under review

MU-WSU - S. agnetis and S. aureus characterization funded by Phi Zeta - two published papers

In summary, the work conducted within the framework of this MMRP has resulted in over 150 refereed publications and over 300 presentations at various scientific and stake-holder forums. We are continuing to build on our past findings to reduce the incidence of mastitis through additional research and extension activities. Mastitis is clearly a multi-faceted disease that will require continued efforts to not only ensure the production of safe, high quality food, but to do so in a sustainable fashion and with continued improvements in dairy animal welfare and reductions the use of antimicrobial drugs.

Objectives

1. Characterize host mechanisms and pathogenic virulence factors associated with mastitis susceptibility and resistance to improve economic outcomes and animal welfare (ID, LA, MI, OR, PA, NJ, TN, UT, VT, WA, Canada).
2. Assess and apply new technologies that advance mastitis control, milk quality and/or dairy food safety (CT, KT, LA, MI, MN, MO, NY, PA, UT, VA, WA).
3. Identify and apply new strategies associated with the control of mastitis that can reduce the use of antibiotics in dairy herds (CT, ID, ME, MN, MO, NJ, TN, UT, VA, VT, WA, Canada).

Methods

Five-year plans, including collaborations among experimental stations, are listed below.

Objective 1: Characterize host mechanisms and pathogenic virulence factors associated with mastitis susceptibility and resistance to improve economic outcomes and animal welfare (ID, LA, MI, OR, PA, NJ, TN, UT, VT, WA, Canada).

At the University of Idaho (ID), researchers plan to continue their work on nutrition related host factors associated with intra-mammary infections. They will focus on the interaction of lipids and lipid-soluble vitamins, metabolism and mammary innate immunity and health. Today have also started working on the effect of dietary lipids and elevated internal lipomobilization on mediators of inflammation during the periparturient period. The overall goal is to improve the understanding of the mechanisms involved in lipid metabolism and mammary gland health in high producing dairy cows during the periparturient period that will lead to enhanced nutritional practices and enable the development of practical feeding intervention strategies to reduce inflammatory-based diseases and metabolic issues to reduce IMI and antibiotic use on dairy farms, improve animal health and productivity, and dairy farm profitability.

Scientists at Louisiana State University (LA) will identify mastitis pathogens from cows and goats for antimicrobial susceptibility testing. Resistance patterns for mastitis pathogens will be compared to resistance patterns for the same bacterial species isolated from humans to determine possible impacts of agricultural practices on resistance patterns.

The NE-1048 members at Michigan State University (MI) will continue to determine specific mechanisms by which high non-esterified fatty acid concentrations induce vascular proinflammatory changes, or the mechanisms by which resolvins, protectins, and lipoxins may modify endothelial inflammatory pathways. Additionally, they will elucidate the means to reduce the severity and duration of diseases, including mastitis, that are typically observed during periods of intense lipid mobilization, such as in the transition period of dairy cows. They also intend to further determine the mechanisms of reactive oxygen species generation, typical of lipid peroxidation and related to the transition period of dairy cattle, when metabolic demand and ensuing oxygen-derived respiration rapidly increases. From this work, the research group and Michigan State University hopes to gain better understanding of transition cow management and nutrition to reduce immune dysfunction caused by reactive-oxygen species.

The research group at Oregon State University (OR) plans to improve the resistance to mastitis and milk quality via diet and nutrient gene interaction. In particular, they will study the possibility of using Selenium-enriched hay to improve the immune system of cows and calves around parturition. They will also continue the work on the nutrigenomic interventions to improve mastitis and milk quality via activation of the transcription factors peroxisome proliferator-activated receptors (PPAR). They will develop a high-throughput system to study drug-discovery fashion dietary compounds that can activate PPAR. They will also study the role of non-esterified fatty acids on activating of PPAR using in vivo-in vitro hybrid system. They will also study the possibility of improving milk lactose and fat synthesis via activation of PPAR.

Scientists at Pennsylvania State University (PA) will use MALDI-TOF mass spectrometry for the identification of host-pathogen related biomarkers for the enhanced detection and diagnosis of mastitis. Researchers at Rutgers University (NJ) are actively pursuing the mechanism(s) of respiration dependent biofilm formation in *S. aureus*. *S. aureus* surviving in milk has decreased iron availability, and therefore decreased cellular respiration resulting in biofilm formation. They are actively pursuing if they can disperse bacterial biofilms in oxygen or iron starved environments. Such a discovery could lead to novel treatments for mastitis or prevention measures.

The University of Tennessee plans to evaluate the potential of host candidate genes identified through whole genome association studies as novel preventive or therapeutic agents against mastitis, as well as develop a more fundamental understanding of virulence factors associated with both *S. uberis* and *S. aureus* pathogens.

Genome-wide association study (GWAS) is ongoing in Utah to compare bovine nucleotide differences (SNPs) between cows repeatedly mastitic vs. cows continually free of mastitis. Analysis is in collaboration with researchers at the University of Utah; 777,000 different SNPs can be detected. A number of genetic variations were protective against mastitis, with 78% to 100% of cows with some genetic variations being mastitis resistant. In contrast, 94% to 100% of cows with alternative variations in the same gene were mastitis susceptible. Future work includes identification of additional SNPs as well as mapping identified SNPs to the bovine genome.

Scientists at the University of Vermont (VT) will determine the importance of cellular expression of TLR4 (receptor for LPS) in contributing to the dairy cow's response to intramammary challenge with *E. coli* and evaluate genetic and epigenetic factors that may regulate the expression of TLR4.

The successful establishment and persistence of intramammary *M. bovis* infection is governed by its virulence factors and the host's ability to successfully eliminate the infectious agent. The virulence factors of *M. bovis* with respect to mastitis are largely unknown and pathogenesis of the disease is poorly understood. To identify virulence determinants and genes affecting *M. bovis* virulence, researchers (WA) propose to use a transposon mutagenesis screen. In collaboration with fellow researchers in Israel, scientists at Washington State University (WA) propose to construct a library of thousands of random mutants of *M. bovis* type strain PG45. Next, the mutant library will be screened using*in-vitro* cell systems developed by the Israeli partners. Attenuated mutants will be validated using the murine mastitis model and the most promising mutants will be further validated by challenge studies in dairy cows. Scientists also plan to perform a molecular epidemiological screening of a collection of *M. bovis* strains isolated from mastitis for the presence of the identified virulence genes. To determine the host immune response to *M. bovis* infection, NE-1048 members will study bovine neutrophil function. They will determine this phagocyte's function in vitro when incubated with various strains of *M. bovis* from cattle with different disease histories. They will examine the effects of different strains on the ability of the neutrophil to phagocytize and kill *M. bovis*. They will also contrast these differences with and without glucocorticoid in the incubation mixture. The latter effort will be used to determine how a "stress event" might affect phagocyte function in the face of *M. bovis* strains.

Canada: International members will 1) describe antimicrobial resistance on dairies and associations with antimicrobial usage (Dufour); 2) investigate the impact of Staphylococci IMI on quarter milk yield and composition (Dufour, Keefe, Middleton);3) investigate economics of mastitis on Canadian dairies (Dufour, Barkema, Keefe); 4) investigates how modulation of the negative energy balance during the early lactation impacts mastitis risk (Dufour); 5) investigate how bedding modulates udder health and bulk tank milk's microbiota (Dufour); and 6) understand the impediment to adoption of best udder health practices by dairy producers (Dufour).

Objective 2: Assess and apply new technologies that advance mastitis control, milk quality and/or dairy food safety (CT, KY, LA, MI, MN, MO, NY, PA, UT, VA, WA).

Researchers at the University of Connecticut (CT) will continue work regarding the validation of ultrasound-guided detection of bovine mastitis that will provide a tool for the detection of mastitis in non-lactating bovines, i.e., heifers and cows during the dry period. This will provide information on existing IMI and evidence of mammary tissue damage that can be used for advancing mastitis control.

The University of Kentucky (KY) research group will focus on evaluation of economic factors associated with mastitis decisions. This work will include development of decision support tools for mastitis treatment decisions, determination of economically optimal SCC, and mastitis prevention strategies. These tools will be designed to help dairy producers make more economically sound mastitis management decisions. Additionally, mastitis detection technologies using precision dairy monitoring technologies will be examined.

Researchers at Louisiana State University (LA) will develop novel food grade products from plants that are being evaluated in vitro for antibacterial activity and potential use as teat dips and disinfectants.

A major thrust of the research conducted at Michigan State University (MI) research station has been to develop an on-farm evaluation system for use by producers and veterinarians to assess challenges in milk quality (Quality Milk Alliance [**QMA**]; qualitymilkalliance.com). Although the QMA system will evaluate traditional areas of farm management related to mastitis control (milking techniques, milking equipment function, cow environment, treatment and monitoring of infected cows), this evaluation system will be unique in that it will also include the management culture of the farm; which will help identify communication barriers with employees regarding mastitis control. Information collected from focus group discussions among producers, veterinarians and employees, have identified key concerns of dairy stakeholders with respect to herd mastitis control programs: 1) the desire for producers to improve employee training and education, 2) the potential role that veterinarians can play in providing this need, and 3) the desire of employees to be further educated and receive more consistent training. The scientists are in a position to help address these stakeholder concerns by applying the QMA evaluation as part of intervention study in 130 dairy herds in Florida, Michigan, and Pennsylvania. Additionally, they will further develop novel uses of 1) remote clicker technology to assess employee training and education, and 2) digital vacuum recorders to assess milking protocol performance. These technologies, along with the QMA evaluation, will serve as a basis for employee training and education. They will amplify the findings by training veterinarians, Extension educators, and other allied dairy professionals by offering an education program that will lead to certification on how to evaluate on-farm milk quality by use of the QMA system.

At the University of Minnesota (MN), scientists will continue a research program aiming to better understand the relationship between bacteria counts in bedding and udder health, as well as to identify bedding characteristics and/or bedding management practices that result in reduced bacteria counts in bedding and improved udder health.

Scientists at the University of Missouri (MO) will continue to assess and utilize molecular tools and emerging diagnostic technologies to assess mastitis pathogen epidemiology in dairy cattle and dairy small ruminants. They will explore potential pathogen related factors associated with persistent infections and elevated SCC and determine if a simple method can be identified to differentiate more different species and strains coagulase negative staphyloccci. With this, different strain typing methods will be explored, including the use of MALDI-TOF mass spectrometry for strain typing. Collaborations with members of the Canadian Bovine Mastitis and Milk Quality Research Network will continue. In addition, members of NE-1048 have an ongoing collaboration to evaluate the diagnostic utility of MALDI-TOF for identifying mastitis pathogens.

At Cornell University (NY) for the next 2 years, researchers plan to develop a tool which can predict the genetic and economic performance of US dairy farms which are planning to adopt genomic selection for higher milk quality for the next 10-15 years. They will devise effective experimental designs (that will be run using the model) which can compare various possible replacement selection strategies, which can simultaneously optimize milk quality and bulk tank revenues. Their long-term goal for the last 3 years of this multi-state project is to be actively involved in development of an approximate dynamic programming model which can aid in early warnings about diseases (including mastitis) in dairy production systems.

At Pennsylvania State University (PA), researchers will investigate, using MALDI-TOF, species' profiles of proteolytic and lipolytic bacteria in bulk tank milk. The association of these profiles with farm management practices and milk quality will also be explored. Scientists will also explore the relationship between milking-time claw and mouthpiece vacuum characteristics, pre-milking udder preparation routines, milk flow patterns, management practices, and the risk of mastitis.

In Utah, a blind comparison study will be conducted between a private veterinary laboratory (conventional milk culture results to species level except for *S. aureus* and *E. coli*) and Utah State University (matrix-assisted laser desorption/ionization time of flight [MALDI-TOF]), and Missouri (16S rRNA genomic identification). An earlier study found 85% to 97% agreement between MALDI-TOF and culture for most milk bacterial species. Agreement so far between all 3 methods is 93.9%. Future expansion of the comparisons, including additional mastitis pathogens and collaborating institutions is anticipated.

Scientists at Virginia Tech University (VA) will study a variety of technologies that are available for use on commercial dairy farms. However, researchers are still working to determine how best to use these data. Over the next 5 years, they will continue in our efforts to develop novel disease detection models using data from these technologies.

The research group at Washington State University (WA) will improve the diagnosis of *M. bovis* and they will study culture parameters for *M. bovis* mastitis pathogens in an effort to determine what conditions will more likely improve growth and apparent viability. Diagnosis of mycoplasma mastitis has been hampered by the pathogens slow growth and fastidious growth requirements. Moreover, culture conditions for *M. bovis* associated with mastitis have not been empirically derived. Moreover, they will develop milk testing procedures for PCR that can diagnose mycoplasma mastitis. The later efforts will lead to a marked reduction in turn-around time from sample submission to mycoplasma mastitis determination.

Objective 3: Identify and apply new strategies associated with the control of mastitis that can reduce the use of antibiotics in dairy herds (CT, ID, ME, MN, MO, NJ, TN, UT, VA, VT, WA, Canada).

Scientists at the University of Connecticut (CT) will use ultrasound-guided intramammary scanning ated as a tool to provide additional information about IMI and tissue damage that can potentially be used to target dry-off treatment as part of a total program to reduce the amount of antibiotic use in dairy cattle.

The NE-1048 research group at the University of Maine (ME) plans to assess the impact of paper mill lignin byproducts (PMLBs) as conditioners for dairy bedding, in an effort to help develop products to reduce the incidence of mastitis without additional use of antibiotics. Maine will evaluate selected PMLBs against major mastitis pathogens (bacterial and fungal) *in vitro*, assess their efficacy in the context of commonly used organic bedding materials *in vitro*, and extend these observations into practical advice for regional dairy farmers.

Researchers at the University of Minnesota (MN) will continue to develop and evaluate different strategies for applying successful and cost-effective selective dry cow therapy programs, as an alternative to blanket dry cow therapy. Applied properly in appropriate herds, selective dry cow therapy offers an opportunity to significantly reduce antibiotic use at dry off while maintaining and promoting udder health. One arm of this research program is to evaluate the accuracy and practical considerations of using different on-farm rapid diagnostic systems (e.g. direct tests: milk culture; indirect tests: milk leukocyte differential counts, somatic cell counts, enzymes, other) for identifying infected cows or quarters that should be treated with an antibiotic in a selective dry cow therapy program.

The University of Missouri (MO) is aiming to explore the effects of intramammary antimicrobial usage on the fecal microbiome and resistome. This will include exploring if an increase in pathogenic bacteria are found in the feces after the administration of intramammary antibiotics, which could be a concern for dairy food safety. Future work will also identify if antimicrobial resistance patterns of fecal pathogens are affected by intramammary antibiotic administration. The University of Missouri is also evaluating antimicrobial peptides as potential therapeutics for diseases of cattle.

Mastitis caused by *S. aureus* require these bacterium to form complex communities called biofilms. Biofilm formation is necessary for *S. aureus* pathogenesis. Scientists at Rutgers University (NJ) have recently found that the addition of a small molecule that stimulates cellular respiration can disperse *S. aureus* biofilms that had formed in low oxygen environments such as the udder of mastitic cows. They are now trying to determine if such a small molecule can disperse *S. aureus* biofilms in models of infection. Such a finding could lead to new strategies to control or present mastitic infections.

At the University of Tennessee (TN), scientists plan to evaluate the role of internal teat sealants with or without antibiotics in dairy heifers during times of projected wet, muddy conditions in the Southeast to minimize the risk of IMI.

Casein hydrolysate (CH) intramammary infusion for cessation of lactation in one chronically mastitic mammary quarter in dairy cows is being studied in Utah and Idaho. Total milk lost per cow (14%) after the mastitic quarter was involuted, recovery of treated quarters' milk production after the cows calved again (24% of total-cow milk), and reduction in total cows' milk SCC after infusion (decreased by approximately 1,000,000/mL) all suggested that this can be an alternative method of drying off one mastitic quarter with a good prospect for return of that quarter's production following the next calving. Future work includes study of CH as an adjunct, or possible replacement for dry cow antibiotic treatment with or without teat sealant at time of dryoff. Mechanistic studies of mammary involution and immunity following CH will involve collaboration with other laboratories.

Based on the developed disease detection models, researchers at Virginia Tech University (VA) will examine early intervention strategies for clinical mastitis in an effort to reduce antimicrobial usage.

Scientists at the University of Vermont (VT) will quantify the antibacterial activity of potential alternative therapies including plant-derived essential oil products. In addition, scientists will characterize the microbial community structure of bovine teat skin with a focus on the potential antagonistic interactions between *Staphylococcus* species that are either opportunistic mastitis pathogens or normal commensal organisms with the goal of identifying potential beneficial commensal organisms.

Intervention strategies that prevent a disease will lead to a reduction in antibiotic use to treat clinical manifestations. Mycoplasma mastitis is a disease syndrome that is difficult to diagnose and therefore when clinical is often treated with antibiotics before diagnostic results are returned to the dairy manager. Thus efforts to better understand the epidemiology of the disease are warranted so that the critical control points can be identified and developed into intervention strategies to control mycoplasma mastitis. Research efforts at Washington State University will be made to continue to study the epidemiology and test newly developed intervention strategies to control mycoplasma mastitis.

Canada: International members will 1) investigate quarter-level selective dry cow therapy to reduce use of antimicrobials on dairies while maintaining udder

health (Dufour and Keefe); and 2) describe the current use of antimicrobials on dairies, investigate producers and veterinarians' motivations for using them, and develop and evaluate a continuous antimicrobial usage surveillance system for Canadian dairies (Dufour);

Measurement of Progress and Results

Outputs

- Peer reviewed publications Comments: Membership in NE-1048 has allowed researchers to 1) build a network of collaborators, 2) receive meaningful feedback on project design and execution, 3) provide formal means of idea exchange and collaboration; 4) expand ideas beyond the State, 5) opened opportunities for collaborative funding, 6) allowed access to resources such as mastitis bacterial isolates from across a broad geographic distribution, 7) provided a forum for trainees to meet seasoned investigators and fellow trainees to discuss and present their work and receive constructive feedback.
- Presentations at national and local meetings
- Non-peer reviewed publications
- Extension publications and meetings
- Bacterial isolate collections with epidemiological data
- Joint projects/collaborations

Outcomes or Projected Impacts

- Models developed for mastitis transmission on dairies.
- Risks and benefits of antibiotic use in lactating dairy animals evaluated.
- Experimental intramammary treatments, both conventional and organic, studied.
- Examined alternative therapeutics for the prevention or treatment of mastitis to reduce antibiotic usage.
- On-farm culture and other methods of reducing antibiotic use on dairies evaluated.
- Effectiveness of teat dips, teat sealants, bedding types and treatments and dry cow treatments in deterring mastitis evaluated.
- Identified virulence factors of mastitis pathogens.
- New diagnostic tests for select organisms, including high-risk human pathogens and non-bacterial causes of mastitis, developed.
- Developed multiple decision support tools aimed at improving milk quality, reducing mastitis and economics.
- Nutritional effects, including enhancing the host immune system, on mastitis evaluated.
- Identified candidate genes relating to mastitis susceptibility.
- Strategies developed to improve immune responses during the dry and transition period, using molecular analyses of host responses.
- Use positional/behavioral patterns to predict IMI in dairy cattle.
- Describe the molecular epidemiology of mastitis pathogens.
- Describe host cytokine and other genetic predictors for mastitis susceptibility, milk production, reproductive performance, and survival.
- Describe selected mastitis pathogen's gene distribution and genetic diversity in milk.
- Develop potential mastitis vaccine candidates.

Milestones

(**2018**):Submission for publication of findings in studies of the immune and metabolic dynamics and their relationship to host and/or pathogenic response.

(**2019**):Submission for publication of findings in studies regarding improving animal welfare.

(**2020**):Submission for publication of findings in studies regarding new technologies to advance mastitis control, milk quality and/or dairy food safety.

(**2021**):Submission for publication of findings in studies regarding antibiotic use and alternative therapeutics for mastitis control.

(**2022**):Completion and submission for publication of the remaining studies on focused research objectives, as well as summaries of surveillance studies.

Outreach Plan

Multiple centers have described outreach projects in their plans for the upcoming period. A number of stations are involved in Extension-based proposals to improve milk quality. This includes at least two currently funded programs – the Milk Quality Alliance (MI, PA) and the Southeast Quality Milk Initiative (TN, KY, VA, MS, GA) – that include members of NE-1048. These programs are developing and continue to develop meeting materials and online resources in both English and Spanish (http://qualitymilkalliance.com; http://sequalitymilk.com/). These projects, and thus the MMRP, will be characterized by their emphasis on producer communications, and on including experts in communication, sociology, economics, dairy management, mastitis, and milk quality programs. The MMRP has, and continues to, involve numerous Cooperative Extension members. This factor, and the willingness of the dairy industry to seek new tools for improvement, will enhance the current and future effectiveness of the MMRP. In the words of William Owens of Louisiana, "A major impact of the multistate projects is the credence or impact that a prestigious organization gives to data it generates. The reputation and long history of this project and the many years of scientific expertise that it represents greatly increased the weight of its recommendations. Many of the scientists participating in this project have been continuously involved with this project since the 1980s. This long history allows a continuity of purpose that provides valuable leadership and helps maintain the focus of the group. This in turn makes the outputs of the projects more focused and more valuable."

Dufour (Montreal) received a grant to develop an online course in mastitis management and control with content to be complied by many members of this group including:

Kasey Moyes

Isis Kanevsky

Gina Pighetti

Chris Luby

Sarne DeVliegher

John Middleton

Christina Petersson-Wolfe

Larry Fox

Satu Pyörälä

Heidi Hiitiö

JP Roy

John Middleton

Herman Barkema

Trevor Devries

Mario Lopez

John Penry

Erin Royster

Paivi Rajala-Shultz

John Wenz

Dave Kelton

Jeffrey Bewley

Sheila Andrew

Marina von Keyserlingk

Organization/Governance

Administrative Advisor:

Dr. Cameron Faustman, cameron.faustman@uconn.edu

Professor, Department of Animal Science

Associate Dean of Academic Programs, CANR

Director, Radcliffe Hicks School of Agriculture

Chairman, NERA

1. B. Young Building, Room 202

University of Connecticut

Storrs, CT 06269-4040

Phone: (860) 486-2919

Dr. Richard Rhodes III, rcrhodes@uri.eduExecutive director, NERA

University of Rhode Island
Aquaculture Center
14 East Farm Road

Kingston, RI 02881
Ph 401-874-2468

USDA/CSREES Representative: Gary Sherman, **gsherman@nifa.usda.gov**

National Program Leader, Veterinary Science-USDA, NIFA

Ph: 202-401-4952

Fax: 202-401-6156

URL (USDA - Sherman):

http://www.nifa.usda.gov/about/AllUnits/staff_view.cfm?record_id=1680&CFID=1300542&CFTOKEN=35668490

URL (USDA - NIFA): http://www.nifa.usda.gov

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Britten JE, **Wilson DJ**, Rood KA: The intramammary use of casein hydrolysate for cessation of lactation in a single quarter. Proc 55th Ann Mtg Natl Mast Council:120-121, 2016.

Wilson DJ, Rood KA, Whitehouse C, Bunnell J, Goodell GM, Byrem TM: Johne's disease and Bovine Viral Diarrhea bulk milk surveillance in the Western U.S. - regional prevalence and positive farm characteristics. Proc XXIX World Assoc Buiatrics: 369, 2016.

Kelly EJ, **Wilson DJ**: *Pseudomonas aeruginosa* mastitis in two goats associated with contaminated essential-oil based teat dip. Proc 59th Ann Conf Am Assoc Vet Lab Diag: 181, 2016.

Wilson DJ, Rood KA, LaRose JP, Wang Z: Holstein single nucleotide polymorphisms analyzed by genome wide association study for associations with

mastitis resistance and susceptibility. Proc 59th Ann Conf Am Assoc Vet Lab Diag: 70, 2016.

University of Wisconsin:

Fuenzalida, M. J., C. Baumberger, and **P. L. Ruegg**. 2016. Preliminary results of a clinical trial evaluating effects of treatment of culture negative cases of clinical mastitis on somatic cell count and bacteriological outcomes. Pages112—113 in National Mastitis Council Annual Meeting Proceedings, Glendale, AZ.

International:

University of Montreal

Francoz, D., Wellemans, V., Dupré, J.P., Roy, J.P., Labelle, F., Karreman, H., Lacasse, P.,**Dufour, S.**, 2016. A systematic review of non-antimicrobial treatments of clinical mastitis in dairy cows. In, 2nd Canadian organic science conference, Montréal-Longueuil, QC, Canada.

Francoz, D., Wellemans, V., Dupré, J.P., Roy, J.P., Labelle, F., Karreman, H., Lacasse, P.,**Dufour, S.**, 2016. A systematic review of non-antimicrobial treatments of clinical mastitis in dairy cows. In, World buiatric congress, Dublin, Ireland.

Jamali, H., Barkema, H.W.^, Jacques, M., Lavallée-Bourget, E.M., Malouin, F., Saini, V., Stryhn, H.,**Dufour, S.**, 2016. A systematic review and meta-analysis of clinical mastitis recurrence in dairy cows. In, World buiatric congress, Dublin, Ireland.

Jamali, H., Barkema, H.W.^ Jacques, M., Malouin, F., Saini, V., Stryhn, H.,**Dufour, S.**, 2016. Clinical mastitis recurrence in dairy cows. In, NMC 55th annual meeting, Glendale, Arizona, USA.

Belage, E., Kelton, D.F., Bauman, C., **Dufour, S.**, 2016. National dairy study - A focus on Udder Health and Milking management on Canadian dairy farms. In, The 2016 meeting of the Canadian Association of Veterinary Epidemiology and Preventive Medicine, Guelph, ON, Canada.

Poster Presentations

University of Georgia:

Enger, B.D., R.R. White, **S.C. Nickerson**, and L.K. Fox^. 2016. Factors influencing new intramammary infection rate in teat dip efficacy trials by meta-analysis. Poster and oral presentation. National Mastitis Council Technology Transfer Session and Research Development Session. NMC 55th Annual Meeting, January 31-February 2, 2016, Glendale, Arizona.

University of Idaho:

2016. Chen, K. C. Ramsey, C. Y. Tsai, M. A. McGuire, and**P. Rezamand**. 2016. Interaction among energy status, dietary protein, and vitamin A in periparturient dairy cows: Effects on milk fatty acid profile and gross milk yield efficiency. The 2016 Joint Annual Meetings, Salt Lake, Utah.

Michigan State University:

Moore, R. and R. J. Erskine. Let the cows score the milking protocols. Poster presented at the 55th Annual Mtng National Mastitis Council, Glendale, AZ, February,2016.

University of Minnesota:

Patel, K., **S. Godden**, E. Royster, J. Timmerman, B. Crooker, and N. McDonald. Pilot study: Evaluation of the effect of selective dry cow therapy on udder health. University of Minnesota College of Veterinary Medicine Points of Pride Research Day. Oct. 5, 2016.

University of Missouri:

Limberg E, Adkins PRF, **Middleton JR**. 2016. Effect of freezing and storage time on culture yields of body site swabbing samples from dairy heifers. Proceedings of the 39th Annual CVM Research Day (Phi Zeta). 6 May 2016. Abstract #21 – Veterinary Professional Student Poster Presentations.

Arroyo G, Adkins PRF, Fox LK^, **Middleton JR**. 2016. Comparison of MALDI-TOF and PFGE for strain-typing Staphylococcus aureus isolated from cow's milk. Veterinary Research Scholars Symposium, Ohio State University, 28-31 July 2016.

Adkins PRF, **Middleton JR**. 2016. Molecular characterization of coagulase negative staphylococci from heifer intramammary infections and potential body site reservoirs. Proceedings of the 55th Annual Meeting of the National Mastitis Council, Glendale, AZ. Jan 31 – Feb 2.

Bernier Gosselin V, Adkins PRF, **Middleton JR**. 2016. Prevalence of coagulase negative staphylococcal species intramammary infection in dairy goats. Proceedings of the 55th Annual Meeting of the National Mastitis Council, Glendale, AZ. Jan 31 – Feb 2.

Lopez-Benavides M, Romero-Saurez S, Henderson M, Adkins EC, Denbigh J, **Middleton JR**. 2016. Iodide residues in bulk tank milk when using iodine and non-iodine pre-milking teat disinfectants. Proceedings of the 55th Annual Meeting of the National Mastitis Council, Glendale, AZ. Jan 31 – Feb 2.

Lopez-Benavides M, Vandaveer W, Leibowitz S, Adkins EC, Denbigh J, **Middleton JR**. 2016. Glycolic acid is present in bulk tank milk when using non-glycolic acid and glycolic acid based teat disinfectants. Proceedings of the 55th Annual Meeting of the National Mastitis Council, Glendale, AZ. Jan 31 – Feb 2.

Rutgers University (New Jersey):

Poster. Rosario-Cruz Z*., Gandhi S., **Boyd JM**. Copper homeostasis in *Staphylococcus aureus.* American Society of Microbiology National Meeting. New Orleans, LA 2015.

Poster. Rosario-Cruz Z*., Gandhi S., **Boyd JM**. Copper homeostasis in *Staphylococcus aureus.* Meeting of the New Jersey Antimicrobial Resistance Working Group. Piscataway, NJ 2015.

Poster. Mashruwala A.A., van de Guchte, A., **Boyd JM**. Cellular respiration as a trigger for multicellular behavior in *Staphylococcus aureus*. Meeting of the New Jersey Antimicrobial Resistance Working Group. Piscataway, NJ 2015.

Poster. Mashruwala A.A., van de Guchte*, A., Roberts C., Eveleigh D.E., **Boyd JM**, Microbes, Miracles, Medicine—A history of antibiotics at Rutgers. Meeting of the New Jersey Antimicrobial Resistance Working Group. Piscataway, NJ 2015.

Poster. Bernhardt, C., and **Boyd JM**. investigating of how Zinc and Tin inhibit Streptococcus mutans. Aresty Undergraduate Research Symposium. New Brunswick, NJ 2016.

Poster. Mashruwala A., Earle,C., van de Guchte A., and **Boyd JM**. Regulation of Clp proteases by SrrAB in *Staphylococcus aureus.* New Jersey American Society of Microbiology Meeting in Miniature (Theobald Smith Society). New Brunswick, NJ 2016.

Poster. Roberts C., Jasim H., Mashruwala A.A., Rosario-Cruz Z*. Sause W., Torres V., **Boyd JM**. The Suf iron-sulfur cluster biosynthetic system is essential for *Staphylococcus aureus* viability and decreased Suf function results in global metabolic defects and decreased survival in human neutrophils. New Jersey American Society of Microbiology Meeting in Miniature (Theobald Smith Society). New Brunswick, NJ 2016.

Poster. Al-Tameemi, H.M.*, Mashruwala A.A., Tanner A.W., Carabetta, V.J., Dubnau, D., Boyd J.M. The YaaT, YlbF, and YmcA proteins are necessary for sporulation in Bacillus subtilis, but what are their functions in the non-sporulating bacterium *Staphylococcus aureus*? New Jersey American Society of Microbiology Meeting in Miniature (Theobald Smith Society). New Brunswick, NJ 2016.

Poster. Mashruwala A., Earle,C., van de Guchte A., and **Boyd JM**. Regulation of Clp proteases by SrrAB in *Staphylococcus aureus*. Joint molecular biosciences graduate student association meeting. Rutgers University. 2016

Poster. Roberts C., Jasim H., Mashruwala A.A., Rosario-Cruz Z*. Sause W., Torres V., **Boyd JM**. The Suf iron-sulfur cluster biosynthetic system is essential for *Staphylococcus aureus* viability and decreased Suf function results in global metabolic defects and decreased survival in human neutrophils. Joint molecular biosciences graduate student association meeting. Rutgers University. 2016

Poster. Al-Tameemi, H.M., Mashruwala A.A., Tanner A.W., Carabetta, V.J., Dubnau, D., **Boyd JM**. The YaaT, YlbF, and YmcA proteins are necessary for sporulation in Bacillus subtilis, but what are their functions in the non-sporulating bacterium *Staphylococcus aureus*? Joint molecular biosciences graduate student association meeting. Rutgers University. 2016

Poster. Rosario-Cruz Z* Liu G., Montelione G.,**Boyd JM**. The ACME Encoded copBcbl operon protects *Staphylococcus aureus* from copper intoxication: Cbl is an extracellular membrane-associated copper-binding protein. Joint molecular biosciences graduate student association meeting. Rutgers University. 2016.

Poster. Mashruwala A., Earle,C.*, van de Guchte A., and **Boyd JM**. Regulation of Clp proteases by SrrAB in *Staphylococcus aureus*. Rutgers Microbiology symposium. Rutgers University 2016

Poster. Rosario-Cruz Z., Liu G., Montelione G.,**Boyd JM**. The ACME Encoded copBcbl operon protects *Staphylococcus aureus* from copper intoxication: Cbl is an extracellular membrane-associated copper-binding protein. Rutgers Microbiology symposium. Rutgers University 2016

Poster. Al-Tameemi, H.M., Mashruwala A.A., Tanner A.W., Carabetta, V.J., Dubnau, D.,**Boyd JM**. The YaaT, YlbF, and YmcA proteins are necessary for sporulation in Bacillus subtilis, but what are their functions in the non-sporulating bacterium *Staphylococcus aureus*? Rutgers Microbiology symposium. Rutgers University 2016

Poster. Roberts C., Jasim H., Mashruwala A.A., Rosario-Cruz Z*. Sause W., Torres V.,**Boyd JM**. The Suf iron-sulfur cluster biosynthetic system is essential for *Staphylococcus aureus* viability and decreased Suf function results in global metabolic defects and decreased survival in human neutrophils. Rutgers Microbiology symposium. Rutgers University 2016

Poster. Mashruwala A.A., Bhatt S., **Boyd JM**. The Duf59 containing protein SufT is required for the maturation of iron-sulfur (FeS) proteins during condictions of high FeS cofactor demand in *Staphylococcus aureus*. Rutgers Microbiology symposium. Rutgers University 2016.

Cornell University (New York):

Scillieri Smith J., **Moroni P.,** Santisteban C., Rauch B., Warner B., and Nydam D. Lactococcus and other organisms we are calling “Other Streptococci”: an investigation in Northern New York. National Mastitis Council Regional Meeting pp.10-16. July 28-29, 2015, Syracuse, New York.

Barberio A., Natale A., Ceglie L., Guerrini E., Zuliani F., Lucchese L., Capello K., and**Moroni P.** Patterns of Coxiella burnetii shedding in cow and goat milk. Proceeding of the 54nd National Mastitis Council Annual Meeting pp.187-188. February 1-3, 2015, Menphis, Tennesse.

Utah State University:

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Kelly EJ, **Wilson DJ**: *Pseudomonas aeruginosa* mastitis in two goats associated with contaminated essential-oil based teat dip. Am Assoc Vet Lab Diag, Greensboro, NC, 2016.

University of Wisconsin:

Fuenzalida, M. J., C. Baumberger, and **P. L. Ruegg**. 2016. Preliminary results of clinical outcomes of treated and non-treated culture negative cases of clinical mastitis. Poster presentation at Wisconsin Alumni Research Foundation, Discovery Challenge, Univ. Wisconsin, Madison

International:

University of Montreal

Aghamohammadi, M., Kelton, D.F., Barkema, H.W.^, Hogeveen, H., Keefe, G.P., Singh, K.,**Dufour, S**., 2016. Mastitis associated economic loss in Canadian dairy farms. In, World buiatric congress, Dublin, Ireland.

Skoulikas, S., **Dufour, S.,** Haine, D., Perreault, J.Y., Roy, J.P., 2016. Early lactation extended therapy against*Staphylococcus aureus* intramammary infections in heifers: a randomized controlled trial. In, World buiatric congress, Dublin, Ireland.

Krug, C., DeVries, T.J., Morin, P.A., Roy, J.P., Dubuc, J.,**Dufour, S**., 2016. Validation of the algometer for measuring udder discomfort in postpartum lactating dairy cows. In, World buiatric congress, Dublin, Ireland.

Belage, E., Kelton, D.F., Bauman, C., **Dufour, S**., 2016. National Dairy Study – A Focus On Udder Health And Milking Management on Canadian Farms In, NMC 55th Annual Meeting, Glendale, AZ, USA.

***bold** = technical member for the station

^Scientist from an NE-1048 Experimental Research Station

2014:

Peer-Reviewed Literature

Connecticut:

Wichmann F, Udikovic-Kolic N, Andrew S, Handelsman J. 2014. Diverse antibiotic resistance genes in dairy cow manure. mBio 5(2):e01017-13. doi:10.1128/mBio.01017-13

Michigan:

Kabara, E. L.M. Sordillo, S. Holcombe, and G.A. Contreras. 2014. Adiponectin links adipose tissue function and monocyte inflammatory responses during bovine metabolic stress. Comp. Immunol. Microbiol. Infect. Dis. 37:49-58.

Mattmiller, S.A., B.A. Carlson, J.C. Gandy, and L.M. Sordillo. 2014. Reduced macrophage selenoportein expression alters oxidized lipid metabolite biosynthesis from arachidonic and linoleic acid. J. Nutr. Biochem. 25: 647-654.

Raphael, W., L. Halbert, G.A. Contreras, and L.M. Sordillo. 2014. Association between polyunsaturated fatty acid-derived oxylipid biosynthesis and leukocyte inflammatory marker expression in periparturient dairy cows. J. Dairy Sci. 97: 3615-3625.

Missouri:

Calcutt MJ, Foecking MF, Hsieh HY, Perry J, Stewart GC, Middleton JR. 2013. Genome sequence analysis of Staphylococcus equorum bovine mastitis isolate UMC-CNS-924. Genome Announc. Oct 17;1(5). pii: e00840-13. doi: 10.1128/genomeA.00840-13.

Calcutt MJ, Foecking MF, Hsieh HY, Perry J, Stewart GC, Middleton JR. 2013. Draft genome sequence of Staphylococcus simulans UMC-CNS-990, isolated from a case of chronic bovine mastitis. Genome Announc. Dec 12;1(6). pii: e01037-13. doi: 10.1128/genomeA.01037-13.

Fry PR, Middleton JR, Dufour S, Perry J, Scholl D, Dohoo I. 2014. Association of coagulase negative staphylococcal species, mammary quarter milk somatic cell count, and persistence of intramammary infection in dairy cattle. J Dairy Sci. 97(8):4876-4885. [Epub ahead of print 12 Jun 2014].

Fry PR, Calcutt MJ, Foecking MF, Hsieh HY, Suntrup D, Perry J, Stewart GC, Middleton JR. 2014. Draft genome sequence of Staphylococcus chromogenes MU-970 isolated from a case of chronic bovine mastitis. Genome Announc. August 14;2(4). pii: e00835-14. doi: 10.1128/genomeA.00835-14.

Calcutt MJ, Foecking MF, Fry PR, Hsieh HY, Perry J, Stewart GC, Scholl DT, Messier S, Middleton JR. 2014. Draft genome sequence of bovine mastitis isolate Staphylococcus agnetis CBMRN 20813338. Genome Announc. Sept 4:2(5). pii: e00883-14. doi: 10.1128/genomeA.00883-14.

Utah:

Wilson DJ, Rood KA, Bunnell J, Whitehouse C, Byrem TM, Goodell GM: Johne's disease, mycoplasma and BVD in Utah - bulk tank milk testing and comparison to previous regional prevalence and individual herd results over time. J Veterinar Sci Technol 5:3:1-7, 2014.

Vermont:

Green, B.B., and D.E. Kerr. 2014. Epigenetic contribution to individual variation in response to lipopolysaccharide in bovine dermal fibroblasts. Veterinary Immunology and Immunopathology. 157:49-58.

Virginia:

Kanevsky-Mullarky, I., A. Nedrow, S. Garst, W. Wark, M. Dickenson, C. Petersson-Wolfe and R. Zadoks. 2014. Comparison of virulence factors in Klebsiella pneumonia strains associated with multiple or singles cases of mastitis. J. Dairy Sci. Apr;97(4):2213-8.

Neal S., W. Wark, S. Garst, R. James, M. McGilliard, C. Petersson-Wolfe, and I. Kanevsky-Mullarky. Impact of feeding whole as compared to cell-free colostrum on calf immune status. I. The neonatal period. J. Dairy Science. Accepted.

Books

Michigan:

Ruegg PL, RJ Erskine and DE Morin. 2014. Mammary Gland Health. In Large Animal Internal Medicine, 5th edition, BP Smith, editor, pp. 1015-1043.

Abstracts

Kentucky:

Lowe, J.L., K.A. Akers, A.E. Sterrett, J.D. Clark, and J.M. Bewley. 2014. Case study: Effect of alley floor scraping frequency on environmental mastitis-causing pathogen counts. Abstract 29. American Dairy Science Association Annual Meeting. Kansas City, MO.

Nolan, D.T. and J.M. Bewley. 2014. A decision support tool to estimate the economic potential of SCC hot sheet data. Abstract 289. American Dairy Science Association Annual Meeting. Kansas City, MO.

Eckelkamp, E.A., J. L. Taraba, R. J. Harmon, K. A. Akers, and J.M. Bewley. 2014. Somatic cell counts, mastitis infection prevalence, and mastitis pathogen distribution in compost bedded pack and sand freestall farms. Abstract 557. American Dairy Science Association Annual Meeting. Kansas City, MO.

Nolan, D.T., M.J. Bakke, and J.M. Bewley. 2014. Comparison of milk components before and after passing through a novel inline milk filter. Abstract 1504. American Dairy Science Association Annual Meeting. Kansas City, MO.

Sterrett, A.E., B.A. Wadsworth, K. Akers, J.D. Clark, C.L. Wood, K.J. McQuerry, R.J. Harmon, L.M. Arnold, W.J. Silvia, and J.M. Bewley. 2014. Milk yield, reticulorumen temperature, rumination time, and neck activity changes around mastitis. Abstract 62. NMC Regional Meeting

Missouri:

Webster RN, Finger AM, Fry PR, Middleton JR. 2014. Identification of coagulase-negative*Staphylococcus species* in dairy heifer calves and their environments. MU Life Sciences Week. April 14-19, 2014.

Finger AM, Webster RN, Fry PR, Middleton JR. 2014. Identification of coagulase-negative*Staphylococcus* species in dairy heifer calves and their environments. Phi Zeta Research Day. May 9, 2014. Columbia, MO. Abstract #2.

Fry PR, Middleton JR, Fox LK. 2014. Identification of*Staphyococcus aureus* genotype B among staphylococci isolated from cases of subclinical bovine mastitis in the USA. Phi Zeta Research Day. May 9, 2014. Columbia, MO. Abstract #12.

Fry PR, Middleton JR, Fox LK. 2014. Genotyping staphylococci from cases of subclinical mastitis previously identified as*Staphylococcus hyicus*. *J Vet Int Med* 28(3):1127.

Walljasper N, Fry PR, Middleton JR. 2014. Understanding Coagulase-negative Staphylococcal Mastitis in Dairy Heifers. Veterinary Research Scholars Symposium, Cornell University, Ithaca, NY. July 31 – August 3.

Cline T, Fry PR, Ericsson A, Middleton JR. 2014. Comparison of Milk and Udder Skin Microbiota of Dairy Heifers. Veterinary Research Scholars Symposium, Cornell University, Ithaca, NY. July 31 – August 3.

Vermont:

Kerr, D.E. 2014. Understanding animal-to-animal variation in disease management. ADSA-ASAS Joint Annual Meeting (JAM). Kansas City, MO.

Green, B.B., S.D. McKay, and D. E. Kerr. 2014. Age dependent changes in heifer fibroblast DNA methylation and LPS-induced gene expression. ADSA-ASAS Joint Annual Meeting (JAM). Kansas City, MO.

Benjamin, A.L., W.J. Weber, S.D. McKay, B.A. Crooker, and D.E. Kerr. 2014. Investigating innate immune response differences between Angus and Holstein cattle with the dermal fibroblast model. ADSA-ASAS Joint Annual Meeting (JAM). Kansas City, MO.

Elsasser, T.H., S. Kahl, D.E. Kerr, E. Zudaire, and F. Cuttitta. 2014. Proinflammatory Responses of a hTERT-Transformed, Immortalized Line of Cultured

Bovine Mammary Epithelial cells (BME). ADSA-ASAS Joint Annual Meeting (JAM). Kansas City, MO.

Conference Proceedings

Michigan:

Erskine, R.J. and J.R. Middleton. 2014. Failure of Mastitis Therapy: Is it the Bugs, Drugs, or Us? Shortcourse presented at the 53rd Annual Mtng National Mastitis Council, Ft Worth, TX, January.

Erskine, R.J. 2014. Don't Forget Antibiotic Residues….and Other Related Topics. Great Lakes Regional Dairy Conference, Mt Pleasant, MI, February.

Erskine, R.J. 2014. Who is Making the Treatment Decisions on the Dairy Farm? Michigan Dairy Industry Conference, Frankenmuth, MI, May.

Erskine, R.J. and J.R. Middleton. 2014. Failure of Mastitis Therapy: Is it the Bugs, Drugs

Land Grant Participating States/Institutions

NY,PA,KS,MO,KY,ME,UT,LA,NJ,MD,VT,WA,IA,TN,CT,MI,VA,WI,OR,NC,MN,IL,MS

Non Land Grant Participating States/Institutions

University of Montreal, University of Saskatchewan

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Adkins, Pamela		Missouri - University of Missouri	2,3	311 311 311	3410 3410 3410	1040 1100 1170	0.20	0.20	0.00	0.05	311
Almeida, Raul		Tennessee - University of Tennessee	1,2,3	311	3450	1100	0.10	0.00	0.00	0	0
Barlow, John W		Vermont - University of Vermont		0	0	0	0.00	0.00	0.00	0	0
Bewley, Jeffrey	Yes	Kentucky - University of Kentucky	2	307	3410	3010	0.05	0.05	0.05	0.5	307
Bionaz, Massimo	Yes	Oregon - Oregon State University	1	302 304	3410 3450	1010 1020	0.15	0.00	0.00	0	0
Boyd, Jeff M		New Jersey - Rutgers University	1,3	311 722	4010 0	1100 0	0.30	0.00	0.60	0	0
Constable, Peter	Yes	Illinois - University of Illinois	1,2,3	311 311	3410 3410	1100 1170	0.10	0.00	0.00	0	0
Dufour, Simon	Yes	University of Montreal	1,2,3	307	3410	1170	0.30	0.00	0.00	0.05	307
Erskine, Ron	Yes	Michigan - Michigan State University	1,2	311	3410	1100	0.50	0.50	0.00	0.75	311
Fox, Larry	Yes	Washington - Washington State University	1,2,3	308 307	3410 4010	1100 1170	0.10	1.00	0.00	0	0
Godden, Sandra M.	Yes	Minnesota - University of Minnesota	2	311	3410	1100	0.10	0.00	0.00	0	0
Grohn, Yrjo t		New York -Ithaca : Cornell University		311	3410	1170	0.10	0.10	0.00	0	0
Hernandez, Laura		Wisconsin - University of Wisconsin	2	305	3410	1020	0.10	0.50	0.00	0	0
Hovingh, Ernest	Yes	Pennsylvania - Pennsylvania State	2,3	308 307	3450 3410	1100 1102	0.00	0.00	0.40	0.2	311 711
Kerr, David E.		Vermont - University of Vermont	1	305	3410	1090	0.25	0.00	0.00	0	0
Kerro Dego, Oudessa		Tennessee - University of Tennessee	3	311	3450	1090	1.00	0.00	0.00	0	0
Lichtenwalner, Anne B		Maine - University of Maine	3	311 0	3410 0	1020 1103	0.10	0.00	0.10	0	0
Luby, Christopher D		University of Saskatchewan	3	0	0	0	0.00	0.00	0.00	0	0
Middleton, John	Yes	Missouri - University of Missouri	2,3	311 311 311 311	4010 4010 3410 4010	1040 1170 1100 1170	0.50	0.20	0.00	0.05	311

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Moyes, Kasey M	Yes	Maryland - University of Maryland	1,3	304 305 307 302 311	3450 3499 1160 3410 1170	1020 1100 1090 1010 712	0.10	0.00	0.00	0	0
Owens, W. E.	Yes	Louisiana - Louisiana State University	1,2	311	3410	1100	0.30	0.00	0.00	0	0
Petersson-Wolfe, Christina S	Yes	Virginia - Virginia Polytechnic Institute and State University (VA Tech)		311	3410	1100	0.10	0.50	0.50	0.2	311
Pighetti, Gina	Yes	Tennessee - University of Tennessee	1,2,3	308 311	3410 3410	1090 1090	0.25	0.00	0.00	0	0
Roy, Jean-Philippe		University of Montreal	1,2,3	305	3410	1170	0.30	0.00	0.00	0	0
Ruegg, Pamela		Wisconsin - University of Wisconsin	2	311	3410	3100	0.10	0.50	0.00	0.1	311
Schukken, Ynte		New York -Ithaca : Cornell University	1,2,3	311	0	0	0.10	0.00	0.00	0.1	0
Schultz, Bruce	Yes	Kansas - Kansas State University		307 307 311	3410 3450 3410	1100 1100 1070	0.10	0.00	0.00	0	0
Sordillo, Lorraine		Michigan - Michigan State University	1,2,3	311	3410	1090	0.10	0.00	0.00	0	0
Timms, Leo	Yes	Iowa - Iowa State University	2,3	311	3410	1020	0.10	0.00	0.00	0.1	311
Wilson, David J.	Yes	Utah - Utah State University	1,2,3	308 307	3410 3450	1060 1170	0.20	0.00	0.00	0.45	308 307
Worku, Mulumebet	Yes	North Carolina A&T State University	1,2,3	311	3450	1040	0.50	0.00	0.00	0	0

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
311-3410-1170	0.1	0.1	0
307-3410-1102	0	0	0.4
308-3450-1100	0	0	0.4
307-3410-1100	0.03	0	0
307-3450-1100	0.03	0	0
311-3410-1070	0.03	0	0
311-3410-1100	0.13	0.2	0
311-4010-1040	0.13	0.2	0
311-4010-1170	0.25	0.2	0
307-3410-3010	0.05	0.05	0.05
0-0-1103	0.05	0	0.1
311-3410-1020	0.05	0	0.1
307-3450-1170	0.1	0	0
308-3410-1060	0.1	0	0
311-3410-1100	0.3	0	0
0-0-0	0	0	0
311-4010-1100	0.15	0	0.6
722-0-0	0.15	0	0.6
302-3410-1010	0.02	0	0
304-3450-1020	0.02	0	0
305-3499-1100	0.02	0	0
307-1160-1090	0.02	0	0
Grand Total:	**6.35**	**3.55**	**1.65**

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
311-1170-712	0.02	0	0
0-0-0	0	0	0
311-0-0	0.1	0	0
307-4010-1170	0.05	1	0
308-3410-1100	0.05	1	0
311-3410-1020	0.1	0	0
311-3410-1040	0.07	0.2	0
311-3410-1100	0.07	0.2	0
311-3410-1170	0.07	0.2	0
305-3410-1090	0.25	0	0
307-3410-1170	0.3	0	0
308-3410-1090	0.13	0	0
311-3410-1090	0.13	0	0
311-3410-1060	0.15	0	0
311-3410-1100	0.5	0.5	0
305-3410-1170	0.3	0	0
311-3410-1090	0.1	0	0
0-0-0	0	0	0
311-3410-1100	0.1	0.5	0.5
311-3410-3100	0.1	0.5	0
305-3410-1020	0.1	0.5	0
311-3450-1090	1	0	0
311-3450-1100	0.1	0	0
302-3410-1010	0.08	0	0
304-3450-1020	0.08	0	0
311-3450-1040	0.5	0	0
311-3410-1100	0.1	0	0
302-3410-1010	0.08	0	0
304-3450-1020	0.08	0	0
311-3410-1100	0.05	0	0
311-3410-1170	0.05	0	0
Grand Total:	**6.35**	**3.55**	**1.65**

Program/KA	Total FTE
0	0
311	0.07
711	0.07
0	0
311	0.02
307	0.17
0	0
308	0.15
307	0.15
0	0
0	0
0	0
0	0
0	0
0	0.03
0	0
311	0.03
311	0.02
0	0
307	0.02

Program/KA	Total FTE
305	0.07
311	0.07
311	0.25
0	0
0	0
0	0.27
311	0.07
311	0.03
0	0
0	0
0	0
0	0
0	0
0	0
0	0
0	0
Grand FTE Total:	**3.55**

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1748: Mastitis Resistance to Enhance Dairy Food Safety

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project with revision
2. Achievable goals/objectives:
Excellent
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Excellent
5. Overall technical merit:
Excellent
Comments
I support this proposal and these researchers have made great strides in mastitis research.
I have primarily edits dealing with typographical errors.
Paragraph 7 NE-10448?
Under obj 3 and throughout the proposal the abbreviation for Kentucky is KY not KT
Is MA in the grp? Do you mean ME or LA? please correct
In the paragraph before " Related, current and Previous work- The sentence: In summary .... needs to be reworked- it does not make sense.

Under obj 1 i
Should it be phagocytize not phagocytized?
should it be nutrient utilization not "nutrients"

Last sentence second paragraph under obj.2 i
... that determines months factors associated.... ? What does this mean?
Obj 2 iii
"In lactating mammals" sentence needs to be reworded
Methods section
obj 1 Today have also... reword this sentence
Add (LA) when LSU is mentioned

In discussing the OSU work it appears that the sentence beginning with " They will develop... is missing some commas

The paragraph starting with " The successful establishment... " talks about "we propose..." Who are we?

Paragraph beginning with: At the University of Minnesota (MN) should have the "the" omitted after (MN)

The paragraph about the Utah blind study is confusing needs to be reworded.

The paragraph discussing the UCONN research is confusing and needs to be reworded

Please make these corrections to improve the proposal, otherwise this is group has made great contributions to the effort to control and minimize the impact of mastitis on our dairy industry.
Your Recommendation:
Approve/continue project with revision

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1748: Mastitis Resistance to Enhance Dairy Food Safety

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project
2. Achievable goals/objectives:
Excellent
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Excellent
5. Overall technical merit:
Excellent
Comments
First, this project is a historically shining example of what multistate projects can accomplish. The list of members reads like a "Who's Who" of mastitis research in North America.

Other reviewers have pointed out some technical edits and style changes, such as consistency with state abbreviations, present versus past tense, and so on. The final version before acceptance and posting would benefit from a careful technical edit.

There are three comments that I would like to offer more as food for thought and about how this project operates going forward.
1. The truly is much benefit to this multistate group coming together to share research results. What is much less evident, however, is the evidence for true collaboration on projects to span multiple states. The report of previous work and the proposed work clearly read more like a collection of efforts of independent projects. What is the true collaboration in the proposed work, in other words, is a multistate project really necessary. Evidence of grants obtained by collaborations among multiple institutions, planned work leveraging resources at multiple institutions, and highlighting examples of those would bolster the case for a multi-state project. In my opinion, this work would continue by these researchers whether or not there were a multistate project.
2. It did not appear that the membership and contributions entirely matched all of the work and collaborating institutions mentioned. For example, WI had been an instrumental contributor, but does not appear to be involved going forward.
3. In this proposal, even though there was mention of Extension and outreach efforts, like many other proposals, it appeared to be more as an afterthought because a n outreach plan is required. There is a reasonably large number of participants with Extension appointments, so why the hesitancy to include a coordinated outreach plan? Extension, as I understand is a big part of the SQMI and the MI and PA projects, so why not include a coordinated multistate outreach plan to tie the individual data collected into a readily accessible resource?
Your Recommendation:
Approve/continue project

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1748: Mastitis Resistance to Enhance Dairy Food Safety

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project
2. Achievable goals/objectives:
Excellent
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Excellent
5. Overall technical merit:
Excellent
Comments
The objectives and potential impacts of this project are outstanding. Mastitis incidence and its associated antibiotic use is a very important issue for dairy farms. This project has contributed to major improvements through past research, and the future course of action is very well-described and well-planned. The researchers do an excellent job of including the many aspects that need to be addressed in order to the objectives, from the need for basic science discoveries to the development of practical on-farm decision-making tools and farmer training. My only minor suggestion is that the State abbreviations used throughout vary from being defined in text to using USPS 2-letter State abbreviations. Please review and correct so that the correct abbreviation is used for each State participating in the project (i.e. KY not KT for Kentucky). Some states may also be misidentified (Is MA included in the project?).
Your Recommendation:
Approve/continue project

NE_TEMP1701: Mycobacterial Diseases of Animals

Status: Under Review

Duration 10/01/2017 to 09/30/2022
Admin Advisors: [Gary A. Thompson]
NIFA Reps:

Statement of Issues and Justification

The proposed multi-state initiative will focus on two of the most important mycobacterial diseases of animals; **paratuberculosis (Johne's disease; JD)** and the **bovine tuberculosis complex (TB)**. These two mycobacterial diseases represent some of the most prevalent and economically significant infections of livestock, and each has a long and rich history. A brief background, including significance and need for work, on each of these diseases, is provided below. Johne's Disease (JD) is a chronic granulomatous inflammatory intestinal disease that results from infection with *Mycobacterium avium* subspecies *paratuberculosis*. JD is recognized as a serious economic and animal health problem in domesticated ruminants including dairy and beef cattle, sheep, and goats throughout the world. It results in more than $200 million in annual losses to the United States (US) dairy industry each year with additional losses incurred by the other species. The growing recognition of *M. paratuberculosis* infection in wildlife species is also of considerable concern. Similarly, recent evidence of the presence of *M. paratuberculosis* in retail milk sources is of concern from a milk quality and potential food safety standpoint. The growing recognition of MAP infection in wildlife species is also of considerable concern, as well as contaminations in environments such as grassland, soil, and even water-supply systems. Despite considerable efforts, JD remains a major concern for producers with very high prevalence rates (68% of all US dairy herds and 95% of those with over 500 cows have at least one JD positive animal) based on culturing of fecal samples. MAP and JD are now considered endemic in the US and in most dairy producing nations, and without major breakthroughs, efforts at controlling pathogen are likely to remain salutary and the disease will continue to spread unabated.

There have been considerable ongoing efforts made to identify knowledge gaps, define research priorities, and develop recommendations for implementing JD control measures in the field. For instance, a 2003 report from the National Research Council of the US National Academies of Sciences on JD comprehensively reviewed the literature, identified major gaps in knowledge, and provided clear recommendations for future research priorities and strategies for the prevention and control of JD. In brief, the report concluded that JD is a significant animal health problem whose study and control deserves high priority from the USDA. It was recognized that the problems associated with JD stem from: (i) difficulties in diagnosis because of an unusually long incubation period and a lack of specific and sensitive diagnostic tests for detecting early infections; (ii) a lack of vaccines or other effective measures for infection control; and, (iii) general lack of awareness of the disease and its true economic and animal health consequences by producers and veterinarians. The report made 25 specific recommendations regarding implementation of strategies for the control of JD, educating and training of producers and veterinarians, and filling of key gaps in knowledge relating to JD. In 2005 and 2006, specialty working groups were formulated by the USDA-APHIS-VS and the Johne's Disease Integrated Program (JDIP; http://mycobacterialdiseases.org/**)** to review knowledge gaps and opportunities for research, extension, and training in JD.

Some of the community needs that were identified as gaps included: (i) the development of new and improved diagnostics and candidate vaccines; (ii) improving research efficiencies by developing shared resources and guidelines for basic and translational research in JD; and, (iii) developing strong education and extension programs. ***While considerable progress has been made in all areas, the proposed multi-state initiative will facilitate meeting remaining major unmet needs.***

The TB complex of diseases of livestock results from infection of animals with mycobacterial pathogens, primarily *M. bovis* and *Mycobacterium avium* subspecies *avium* (MAA). These organisms can cause disease in multiple livestock and wild animal species and can be readily transmitted to humans. *M. bovis*, whose disease and infections will be the primary focus of the activities proposed in this multi-state initiative, is closely related to the organism that causes human tuberculosis, *Mycobacterium tuberculosis* (MTB).

TB is a disease of antiquity that has resulted in a considerable economic loss to animal agriculture and, as a zoonotic disease, contributed greatly to human suffering prior to the widespread requirement for milk pasteurization. In fact, at the turn of the 20th century, *M. bovis* was considered to be the cause of greater economic losses to livestock production than all other infectious diseases combined. The implementation of rigorous control and disease eradication programs, including test and slaughter or test and segregate programs, have reduced or eliminated tuberculosis in cattle in the US and most developed countries. However, reservoirs in wildlife have precluded complete eradication. TB continues to be a significant recurring concern in many countries, including Ireland, the United Kingdom (UK) and New Zealand. In addition, both bovine tuberculosis and *M. bovis* infections in humans remain common in less developed countries, resulting in considerable economic losses due to disease and trade restrictions.

While TB incidence in the US remains low, there is considerable concern that we may be experiencing a resurgence of this disease in livestock species, primarily cattle. In 1994, a white-tailed deer (WT deer) from northeastern Michigan was found to be infected with *M. bovis*. This led to the wide-scale testing of cattle and deer with subsequent identification of *M. bovis* in both populations within this area. The spread of *M. bovis* in Michigan was slowed by a strict policy of total herd depopulation upon identification of positive cattle, as well as large-scale hunter education programs and a massive testing initiative in WT deer. Still, in Michigan, over 650 cases of *M. bovis* infection in WT deer and 49 positive cattle herds have been identified to date. Alarmingly, *M. bovis* has now spread to other states. *M. bovis* was recently detected in 27 WT deer and 12 cattle herds in Minnesota and has been confirmed in cattle from Colorado, Nebraska, Indiana, Kentucky, North Dakota, South Dakota, New Mexico, and California. Detection of *M. bovis* infection has lead to quarantine and depopulation of nearly all affected herds. Clearly, this disease is continuing its resurgence throughout the US, particularly where cattle and WT deer commingle.

A second major source of *M. bovis* infected cattle in the US is imported animals from other countries where the disease is endemic, particularly Mexico. Indeed, molecular epidemiology studies have demonstrated that *M. bovis* cases in all states other than Michigan are likely of Mexican origin. Although USDA regulations stipulate that imported cattle must be tested within 60 days of import, the low sensitivity of most approved *M. bovis* diagnostic tests suggests that some

infected animals will be missed. Because cattle are only held at the border for 48 to 72 hours, there is little time to conduct additional testing at the point of entry. In addition, the lack of mandatory animal identification in the US limits the ability to track cattle after introduction into the country. Clearly, it is crucial to have rapid diagnostics with improved sensitivity that could be deployed at points of entry. It is equally important to improve information on cattle movements to control importation of *M. bovis* infected cattle.

1. *bovis* is of significant concern to government agencies and cattle industries due to associated economic, social and potential public health problems. The inclusion of *M. bovis* research, teaching and extension in this multi-state project will address serious concerns from cattle industry representatives, government agencies, and public health officials that the US is experiencing a resurgence of *M. bovis* that will have devastating economic effects, cause a disruption or severe restrictions in movements of cattle including exports, and have profound effects on producers, who own positive herds and must suffer depopulation or quarantine.

Finally, the generation of new knowledge relative to the diagnosis, management, and control of mycobacterial diseases of animals is critical if we are to prevent the spread, lower the prevalence and minimize the impact of the diseases in our livestock populations. USDA NAHMS studies and other work, including the National Dairy Producer Johne's survey, have shown that while producers are increasingly aware of the diseases, they often lack knowledge relative to their management and control. Therefore, there is a critical need for developing coordinated approaches for education and outreach programs related to mycobacterial diseases of animals.

Taken together, the proposed multi-state initiative described below ***will facilitate the development of shared research as well as the leveraging of intellectual and physical resources to address some of the most important mycobacterial diseases of animals.***

Related, Current and Previous Work

The proposed multi-state initiative will focus on two of the most important mycobacterial diseases of animals; paratuberculosis (Johne's disease; JD) and the bovine tuberculosis complex (TB). These two mycobacterial diseases represent some of the most prevalent and economically significant infections of livestock, and each has a long and rich history. A brief background, including significance and need for work, on each of these diseases is provided below. Johne's Disease (JD) is a chronic granulomatous inflammatory intestinal disease that results from infection with *Mycobacterium avium* subspecies *paratuberculosis*. JD is recognized as a serious economic and animal health problem in domesticated ruminants including dairy and beef cattle, sheep, and goats throughout the world. It results in more than $200 million in annual losses to the United States (US) dairy industry each year with additional losses incurred by the other species. The growing recognition of *M. paratuberculosis* infection in wildlife species is also of considerable concern. Similarly, recent evidence of the presence of *M. paratuberculosis* in retail milk sources is of concern from a milk quality and potential food safety standpoint. The growing recognition of MAP infection in wildlife species is also of considerable concern, as well as contaminations in environments such as grassland, soil, and even water-supply systems. Despite considerable

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There have been considerable ongoing efforts made to identify knowledge gaps, define research priorities, and develop recommendations for implementing JD control measures in the field. For instance, a 2003 report from the National Research Council of the US National Academies of Sciences on JD comprehensively reviewed the literature, identified major gaps in knowledge, and provided clear recommendations for future research priorities and strategies for the prevention and control of JD. In brief, the report concluded that JD is a significant animal-health problem whose study and control deserves high priority from the USDA. It was recognized that the problems associated with JD stem from: (i) difficulties in diagnosis because of an unusually long incubation period and a lack of specific and sensitive diagnostic tests for detecting early infections; (ii) a lack of vaccines or other effective measures for infection control; and, (iii) general lack of awareness of the disease and its true economic and animal-health consequences by producers and veterinarians. The report made 25 specific recommendations regarding implementation of strategies for the control of JD, educating and training of producers and veterinarians, and filling of key gaps in knowledge relating to JD. In 2005 and 2006, specialty-working groups were formulated by the USDA-APHIS-VS and the Johne's Disease Integrated Program (JDIP; http://mycobacterialdiseases.org/**)** to review knowledge-gaps and opportunities for research, extension and training in JD.

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Taken together, the proposed multi-state initiative described below ***will facilitate the development of shared research as well as the leveraging of intellectual and physical resources to address some of the most important mycobacterial diseases of animals.***

Related Current and Previous Work

In terms of prior and current related work, during the fall of 2004, the USDA-CSREES-NRI's Coordinated Agricultural Projects (CAP) helped bring *together leading scientists in the field of JD to form a comprehensive, multi-institutional, interdisciplinary Johne's Disease Integrated Program for research, education, and extension, or JDIP.* We started with a team of approximately 70 scientists from two-dozen leading academic and government institutions in the US, who represented the diverse disciplines of microbiology, immunology, pathology, molecular and cellular biology, genomics, proteomics, epidemiology, clinical veterinary medicine, public health, extension, and public policy. Since inception, membership in MDA has grown to more than 220, and the program has become international in scope.

Based on the success of the program, JDIP was renewed in 2008, and the Multistate Initiative program in the Mycobacterial Diseases of Animals-Multistate initiatives enabled JD research, education, and extension to rapidly move forward in a manner that would not be possible through traditional funding mechanisms from the USDA. In particular, the founding and continued support of MDA has enabled the community, for the first time since JD was described more than a century ago, to develop an integrated and coordinated program with a focus on developing a strong translational pipeline of new diagnostic tests, vaccine candidates, strategies to manage, prevent and control the disease, and the formulation of an outstanding education and training program. As detailed in the sections below, in the brief period since the founding of the program, JDIP investigators have conducted path-breaking research and development that has resulted in:

- A better understanding of *paratuberculosis* on-farm transmission dynamics that is helping identify critical control points in the transmission chain.
- The development of alternative sampling and testing strategies for detection of infected animals and herds that are being adopted by the national voluntary control program for JD.
- The optimization and standardization of laboratory protocols for *paratuberculosis* culture and PCR for reducing timelines for rapid and sensitive detection of infected animals.
- Characterization of genetic differences between isolates of *paratuberculosis* for molecular epidemiologic analyses and tracking of strains in infected animals and the environment.
- Development of standards for animal challenge models with *paratuberculosis* for the evaluation of vaccine efficacy.
- Identification of key genes, proteins and lipids unique to *paratuberculosis* for development of the next generation of diagnostic tests and vaccines.

- Development and widespread use of an on-line JD veterinary certification program.
- Development of educational modules for producers as well as field and laboratory technicians providing milk ELISA tests for producers.
- Development of community resources including *paratuberculosis* isolates, serum samples and other clinical material for the development and validation of diagnostic tests, genomic microarrays, recombinant proteins, and mutant strain banks of *M. paratuberculosis* for identification of potential vaccine candidates.
- Development an individual-based dairy herd model by incorporating basic herd dynamics in a closed herd environment where no new animals have been bought from outside.
- Development of a useful platform for gene discovery and analysis by isolating three novel mutants for each transposon.
- Establishment of high quality longitudinal data collection which turned out to be an essential tool in our understanding of pathobiology and epidemiology of MAP infections in dairy herds
- Development of a peptide-based vaccine for cattle using the PLGA NP delivery systems
- Evaluation of the Bovine Leukemia Virus and Mycobacterium avium subsp. paratuberculosis relationship with Shiga Toxin-Producing Escherichia coli Shedding in Cattle
- Evaluation of the humoral immunity and atypical cell-mediated immunity in response to vaccination in cows naturally infected with bovine leukemia virus
- Screen the bovine serum samples with MTB and MAP protein microarray for antigen discovery
- Research on the evaluation of prevention of infection by stimulating innate response using*Mycobacterium bovis* as the model of infection.
- Establishment of model systems that can be used to obtain crucial information that would unveil key aspects of MAP pathogenesis, and would enable the researchers to compare the different phases of the disease between in vitro and in vivo systems.
- Determining the role of luxR homolog gene in invasion of MAP into epithelial cells using*Mycobacterium smegmatis* as a model of infection.
- Investigation of the phenotypic diversity in the immune response against*Mycobacterium avium paratuberculosis* in MAP-infected dairy cows.
- Identification of several candidate MAP proteins of potential utility for the early detection of MAP infection.
- Detection of pathogens and control pathogen transmission, both within-herd transmission and between-herd transmission.
- Development of a quantitative methodology for incorporating whole genome sequence (WGS) data into bacterial transmission models for infectious diseases incorporating *ecology, economics, molecular biology, and epidemiology.*
- Better understanding of the principles and dynamics governing transmission of mycobacterial infection.
- Development, assessment, and implementation of vaccines for JD and bTB.
- Providing veterinarians, producers of potentially impacted species, state and federal policy makers, and other stakeholders with accurate, high quality, up to date, and easy to access information and education to assist efforts that will effectively address mycobacterial diseases.

In addition to our research accomplishments, we have developed a strong communications and extension plan that includes workshops, newsletters, regular conference calls, and an annual

conference of JD researchers. Hence, MDA has brought together scientists and stakeholders with a shared vision and well-defined plan to support and facilitate research, extension and education activities and enhance animal health through biosecurity by addressing well-documented and emerging needs in JD.

Workshop on Accelerating bovine Tuberculosis (bTB) Control in Developing Countries

With funding from Bill & Melinda Gates Foundation, The University of Georgia, Cornell University, and The

Pennsylvania State University, a Workshop on Accelerating bovine Tuberculosis (bTB) Control in Developing Countries was conducted on December 8-10, 2015 in Rabat, Morocco. The workshop was a representation of the collective efforts of a committed and diverse global group of bTB experts who convened to develop a shared vision and forward-looking research agenda for developing and implementing effective bTB control strategies in developing countries.

The workshop was co-chaired by Vivek Kapur (Penn State, US), Martin Vodermeier (Animal and Plant Health Agency, UK), Yrjo Grohn (Cornell, US), and Fred Quinn (UGA, US). The workshop brought together a diverse group of 40 leading bTB investigators from 16 countries, which worked with policy makers and funding agency representatives to develop a shared vision and strategic framework for the implementation of bTB control programs in developing countries in which the disease is endemic in livestock, humans, and wildlife.

Participant presentations and discussions provided key insights on seven topical areas including: (1) vaccines and diagnostics, (2) the zoonotic impact of bTB, (3) bTB control efforts that have worked to date, (4) the World Organization for Animal Health (OIE) perspective, (5) the African perspective, (6) implications of bTB in wildlife, and (7) the India and China perspectives. Participants generated an initial 175 insights and 154 questions through discussions, and an “idea sorting” round-robin exercise worked to enhance the robustness of the knowledge base and identify the top five most critical insights and questions for each topic area. The group developed an integrated strategy map and detailed five-year action plan to help meet these three key inter-dependent and inter-related needs: (i) Establishment of the business case through rigorous bTB risk and economic impact assessments and the development of advocacy tools for bTB control programs, (ii) Establishment of technical capabilities to ensure the widespread availability of and access to fit-for purpose diagnostic tests and vaccines, (iii) Establishment of key market and public investment operational drivers and the creation of value-chain for bTB control by small-holder farmers.

Hence, the renewed multi-state proposal seeks to continue to build the considerable progress we have made during the past two phases of JDIP so that we can continue to leverage the financial and scientific resources even after the completion of the second Phase of the program. We are convinced that the accomplishments of this CAP project thus far have created a momentum that will continue to grow through the proposed multi-state initiative that expands the focus from JD to include TB and mycobacterial diseases in animals.

Objectives

1. Objective 1 will focus on understanding the epidemiology and transmission of JD and TB in animals through the application of predictive modeling and assessment of recommended control practices.
   Comments: To accomplish our overall objective of developing a better understanding of the epidemiology and transmission of JD and TB.
2. Objective 2 will seek to develop and implement new generations of diagnostic tests for JD and TB.
   Comments: Improved methods for the rapid, specific, sensitive, and cost-efficient diagnosis of JD or TB-infected remain a major priority.
3. Objective 3 will focus on improving our understanding of biology and pathogenesis of Mycobacterial diseases, as well as the host response to infection
   Comments: It is well recognized that the ability to identify the route of invasion and the host-pathogen interactions at a molecular level is important for the future development of strategies to prevent infections or to limit the spread of the infection Similarly, the elucidation of gene products specific to in vivo growth holds great promise in identifying new antigens for diagnostics or vaccine development, as well as products essential to pathogenesis. Hence, as part of the proposed multi-state initiative, we envision studies of the basic biology of the causative organisms of JD and TB and their interaction with the host. Specifically, we anticipate studies that will employ state-of-the-art microbiological, molecular biology, genomic, proteomic, metabolomic, immunology, and or bioinformatic approaches.
4. Objective 4 will focus on development of programs to create and evaluate and develop new generations of vaccines for JD and TB.
   Comments: Under the auspices of this multi-state initiative, we propose specific research projects to help achieve each of the 4 objectives and include a strong education and extension plan. We envision many of the projects to be crosscutting in nature (i.e. cut across objectives and/or address both diseases) that will together help address the major animal, human, and societal issues surrounding detection and control of mycobacterial diseases in animals. It is important to note that our research objectives are closely linked and coordinated with our education, extension and outreach plan.

Methods

Objective 1 will focus on **understanding the epidemiology and transmission of Mycobacterial diseases in animals.** To accomplish our overall objective of developing a better understanding of the epidemiology and transmission of JD and TB, we propose studies that include:

- Continued development of mathematical models of JD and TB transmission dynamics, including within-host, between individuals, within and between domesticated dairy and beef herds and wildlife, as well as on an ecological scale. For example, several investigators have initiated the process of development of mathematical models for JD and TB (2-4) and we will continue the process with studies such as estimating the performance of JD vaccines, defining the impact of wildlife infection on JD and TB dynamics, analyzing the spread of JD and TB through cattle trading networks, and finding economically optimal JD and TB control strategies. Examples of the types of investigations that will be carried out are presented in(5-7).

- Characterization of herd and environmental distribution of specific genotypes of*paratuberculosis* and *M. bovis* using state-of-the-art methods for strain differentiation using simple sequence repeats and or single nucleotide-based typing approaches and applying this knowledge to characterize the genetic diversity and molecular epidemiology of *M. paratuberculosis* and *M. bovis* infections;

- Delineation of mycobacterial disease transmission dynamics, including*paratuberculosis* transmission within calf-rearing systems, risk of *M. paratuberculosis* transmission from infected dams to daughters, and risk of*M. paratuberculosis* infection associated with ‘super-shedders’ and calf-to-calf transmission;

- Clarification and delineation of critical management practices for control, prevention, and eradication of mycobacterial diseases; and,

- Identification and optimization of surveillance methods and strategies.

Taken together, these studies will significantly advance our understanding of the epidemiology and transmission dynamics of mycobacterial diseases of animals.

Objective 2 will seek to **develop and implement new generations of diagnostic tests for JD and TB**. Improved methods for the rapid, specific, sensitive, and cost-efficient diagnosis of JD or TB infected remain a major priority. Hence, as part of this multi-state initiative, we anticipate carrying out investigations that include:

- Development of methods for the early detection of *paratuberculosis* and *M. bovis* infected animals, including newer generations of molecular, serological and microbiological assays with greater sensitivity, specificity, speed, and or ease-of-use, by using state-of-the art molecular biological, immunological, and materials science and engineering methods and approaches; and,
- Development of resources for validation and standardization of diagnostic assays, including well-accessioned biological sample collections (strains, tissue, clinical samples, etc.), and processes to make these accessible to the scientific community.

Together, these studies and efforts will facilitate the development, validation, and implementation of the next-generation of improved diagnostic tests for mycobacterial diseases of animals.

Objective 3 will focus **on improving our understanding of biology and pathogenesis of Mycobacterial diseases of animals**, as well as the host response to infection. Our understanding of the basic biology and mechanisms of pathogenesis of *M. paratuberculosis* and *M. bovis* is far from complete. It is well recognized that the ability to identify the route of invasion and the host-pathogen interactions at a molecular level is important for the future development of strategies to prevent infections or to limit the spread of the infection. Similarly, the elucidation of gene products specific to *in vivo* growth holds great promise in identifying new antigens for diagnostics or vaccine development, as well as products essential to pathogenesis.

Hence, as part of the proposed multi-state initiative, we envision studies of the basic biology of the causative organisms of JD and TB and their interaction with the host. Specifically, we anticipate studies that will employ state-of-the art microbiological, molecular biology, genomic, proteomic, metabolomic, immunology, and or bioinformatic approaches to carry out studies that include:

- Investigations into the basic mechanisms of pathogen invasion of host cells and tissue using state-of the art methods in mycobacteriology, cell biology, and genomics;
- Identification of mycobacterial genes and proteins whose inactivation or alternated expression results in reduced virulence. This will be accomplished by screening large libraries of mutants, as well as by characterizing these mutant strains using state-of-the art genomics and proteomics based methods and will also lead to the identification of genes associated with the ability of the pathogen to survive in the host as markers for virulence and pathogenicity; and,
- Characterization of the microbial factors that contribute to the innate and adaptive immune response using sophisticated in vitro cellular immunologic assays and animal models of infection.
- Exploitation of knowledge from immune response studies to create new methods of diagnosis.

Taken together, we anticipate that these investigations will reveal important insights on the basic

biology of the causative organisms of JD and TB and their interaction with their hosts.

Objective 4 will focus on the **evaluation and development of new generations of vaccines for JD and TB.** It is well recognized that defining the host genetic, cellular and molecular events associated with susceptibility to JD and TB is essential for the development of candidate vaccines and host genetic selection for resistance. For TB in particular, the experience in the UK and elsewhere have shown that traditional test/slaughter and abattoir inspection campaigns fail to control the spread of bovine TB (bTB), most likely due to the presence of a wildlife reservoir. Vaccine research must become a priority. Similarly, in the US where a wildlife reservoir exists, control efforts have not eradicated bTB and are unlikely to do so. Hence, the development of a vaccine against bTB is required to control disease. Under the auspices of this multi-state initiative, we envision projects that will seek to develop candidate vaccines, identify genes and markers associated with susceptibility of animals to mycobacterial infection, and define the cellular and molecular events associated with development of immune responses to *M. paratuberculosis* and *M. bovis* in cattle. Specifically, we anticipate the development of projects that will:

- Analyze the early immune response to infection as well as the host response to animals at different stages of disease using well-characterized in vitro models and animal experimentation;
- Develop and validate animal models for vaccine development;
- Identify genetic markers for susceptibility to infection in cattle using genome wide association studies with well-defined resource populations. A combination of candidate gene identification with whole genome SNP typing promises to rapidly identify a set of markers that could be used to select for resistance to disease caused by mycobacteria;
- Compare the efficacy of candidate vaccines in animal models of infection. We hypothesize that live attenuated vaccines are likely to elicit a protective response superior to the response elicited by currently available killed vaccines. However, it will be essential to develop vaccine candidates that are able to differentiate vaccinated from naturally infected animals. To test this hypothesis, we anticipate studies that include: (a) use of flow cytometry, long-oligo microarrays, and real time RT-PCR to compare immune responses elicited by candidate mutant vaccines; (b) Determine if mutant vaccines elicit development of effector memory CD4 and/or CD8 T cells that kill infected autologous macrophages or arrest replication of intracellular bacteria; and, (c) Determine if animal immunized with mutant vaccines are protected against challenge;
- Evaluate the ability of recombinant or vector expressed proteins and mycobacterial lipids to elicit effector T cells with the capacity to kill infected macrophages or arrest replication of intracellular bacteria. The working hypothesis is that modification of mycobacterial antigens by attachment of Trojan peptides will selectively enhance development of long-lived memory CD4 and/or CD8 effector T cells and may be suitable candidate antigens for use as subunit vaccines; and,
- Determine the role of regulatory T cells in the immunopathogenesis of mycobacterial infections in animals. The working hypothesis is that dysregulation of the immune response to *paratuberculosis* and *M. bovis* is, at least in part, attributable to development of regulatory T cells (Tregs). Evidence suggests that Tregs may be responsible for down-regulating effector memory CD4 cells in an antigen-specific manner. This hypothesis will be tested by characterizing cell surface markers of Tregs using flow-cytometeric and expression analysis techniques.

Taken together, we anticipate that these investigations will reveal important insights into the immune response of animals to mycobacterial infections, as well as lead to the identification and evaluation of candidate vaccines.

Measurement of Progress and Results

Outputs

- The outputs, including research data, methods Comments: a. A better understanding of the epidemiology and transmission of JD and TB in animals, and the development of predictive models of infection; b. New generations of diagnostic tests for JD and TB that are sensitive, specific, rapid, and cost-efficient; c. Improved understanding of the biology and pathogenesis of mycobacterial diseases of animals, as well as the host response to infection; d. Development and evaluation of new generations of vaccines for JD and TB; e. Development of shared resources and protocols; and, f. Development of education materials and delivery plan to provide veterinarians, producers of potentially impacted species, state and federal policy makers and other stakeholders with accurate, high quality, up to date, and easy to access information related to mycobacterial diseases of animals.

Outcomes or Projected Impacts

Milestones

(**0**):We anticipate the following programmatic milestones. a. Each of the four objectives and the outreach and education plan will start during year 1 and continue through the duration of the project. b. An annual meeting of investigators. c. During year 3, working in concert with our stakeholders, we anticipate carrying out a needs assessment for both the research and outreach components of the program. d. Year 4 will involve a comprehensive evaluation of progress of the multi-state initiative, and focus on developing renewal application.

Outreach Plan

We recognize and appreciate that outreach and education efforts are vital components in achieving the objectives of this multi-state initiative, as described above. The underlying mission of our outreach plan is to provide veterinarians, producers of potentially impacted species, state and federal policy makers, and other stakeholders with accurate, high quality, up to date, and easy to access information and education to assist efforts that will effectively address mycobacterial diseases. To accomplish this, we need to better understand the factors that encourage or deter veterinarians and their producer clients from adopting JD and TB control or eradication practices, as well as the educational needs of these populations, to develop educational materials based on current, evidence-based information and deliver these materials in a flexible, convenient, cost-effective, and readily available manner.

As part of our education and outreach plan for this multi-state initiative, we envision using currently available and relevant information as well as generating new information. In addition, we will seek to use and enhance existing information distribution systems but also develop new tools for this purpose. The following are objectives for the education and outreach component of this multi-state initiative:

- Create an internet portal to provide access to information related to mycobacterial diseases, specifically JD and bTB Internet access provides the most rapid, cost effective means to sharing information with a widely distributed audience. The site will provide convenient access to information generated through the initiative and seek to be as comprehensive as possible by sharing previously developed information through links to existing sites such as jdip.org, www.johnes.org, and www.johnesdisease.org. Links to international sites will allow US scientists, producers, and policy makers access to information on the success of domestic herd and wildlife control programs, such as the badger vaccination program in Ireland. These sites already exist and are supported from various extramural and intramural sources, and we anticipate that we will continue to seek funding for the development, management, and curation of these web-sites.

- Encourage, monitor and increase awareness of the publication of work of initiative collaborators in peer-reviewed journals and through other scientific outlets. Publication of research results in peer reviewed journals is important to the initiative and to those who collaborate in the effort, since it validates the credibility of the work and makes it more widely available. The Education/Outreach team will strongly encourage publication of initiative research in appropriate journals. We will seek to make others in the industry aware of work as it is published and also monitor the publications for work that may be shared with producers and others through the initiative. Current Johne's efforts have developed a strong international network of

scientists and interested professionals, through the International Association for Paratuberculosis (IAP), who are effectively sharing information as they work to address this world-wide disease. Efforts in other nations are also looking to address a wider range of mycobacterial diseases, so this initiative will fit well into expanding international efforts. We will seek to maintain and enhance current working relationships and explore new ones that will allow the most effective use of existing resources.

- Enhance and strengthen working relationships and communication links with producer and professional organizations.While many good working relationships currently exist, expanding these networks will increase awareness of the initiative, build confidence in the results and help to make them more readily available to our target audiences. It is anticipated that activities in this area will include:

    1. Partnering with the Animal Health committee for the Joint Annual Meeting (JAM) of the American Dairy Science Association and the American Society of Animal Science to include specific oral and poster presentation sections for mycobacterial diseases at the JAM. Include, as appropriate, mycobacterial sessions/symposia in the scientific sessions of the American Association of Bovine Practitioners (AABP), the Association of Veterinary Consultants (AVC) and the American Veterinary Medical Association (AVMA). This will provide an opportunity to reach large and very important target audiences in a cost effective manner. It will also assure inclusion of abstracts of the work presented in highly respected journals that are readily available nationally and internationally.

    2. Holding “Interest Group” meetings at the JAM, the annual meeting of the American Association of Bovine Practitioners (AABP), the Association of Veterinary Consultants (AVC) and similar meetings to reach extension and industry professionals with interests in this area by providing them with information from the initiative, seeking input on current and planned activities, and inviting their participation in the initiative.

    3. Coordinate preconference seminars, or clinical forums, on a periodic basis at the annual conference of the AABP to reach professionals who are on the farm with timely information and solicit their input on additional needs that the initiative is equipped to address.

    4. Facilitate discussion with government and industry to consider expansion of the National Johne’s Work Group (NJWG), currently a subcommittee of the US Animal Health Association (USAHA)’s Johne’s Disease Committee, to become a Mycobacterial Disease Work Group, working with the Tuberculosis and other appropriate USAHA committees. It is anticipated that this group would meet annually at the USAHA’s annual meeting and “as needed” at the annual meeting of the National Institute for Animal Agriculture (NIAA) to share information and identify additional research and education needs.

    5. Partner with relevant organizations in organizing scientific and educational information sessions for producers focused on relevant topics. Potential collaborators include:

        1. NCBA Cattlemen’s College

        2. National Dairy Herd Information Association (NDHIA)

- World Dairy Expo

1. The Joint Annual Meeting of the National Milk Producers Federation (NMPF), the National Dairy Board (NDB) and the United Dairy Industry Association (UDIA)

2. Dairy and beef breed associations

3. The American Farm Bureau Federation (AFBF)

1. Partner with USDA to assist in training programs on related diseases
2. Organize, with industry, extension, and government agency collaboration, a national symposium on mycobacterial diseases of animals every five years
3. Develop and conduct webinar's on "high interest" topics in conjunction with extension and or other industry partners

- Provide convenient access to comprehensive, high quality, and consistent education materials for veterinarians, producers and others. We will seek out and use existing tools, such as those currently available at http://ce.vetmed.wisc.edu/Johnes_Disease,that are developed and reviewed by experts in the field. Additional information that is needed will be identified and resources/collaborators needed to produce and deliver the material will be identified. Materials will be delivered electronically, but will include supporting material that can be printed locally.
- Leverage existing information/education delivery mechanisms to more comprehensively reach target audiences with information about mycobacterial diseases. We will work actively with trade media and partner with groups like the Johne's Education Initiative (JEI), DAIReXNET, the eXtension Wildlife Damage Management Community of Practice, and the Internet Center for Wildlife Damage Management (ICWDM) in this effort.
- Reach non-traditional audiences, including policy makers and interested members of the public, with accurate and timely information relative to mycobacterial diseases in livestock and serve as a point of contact for further information needs. Social media tools such as "Linked In" and "Facebook" will be used to reach these audiences. We will seek to partner with and draw on expertise from industry groups to make the most effective use of these tools in a timely manner as this effort moves forward.
- ICP – Coauthored presentation on JD programs in the U.S.

  2016 JAM
- Annual Meeting – MDA interest session, material available in press room and registration
- World Dairy Expo – met with 10 dairy trade publications, material available
- USAHA – Display and presentations to JD Committee, State, extension and Federal vets

  Sample

Taken together, the above approach will help us achieve our objectives of providing veterinarians, producers, and other stakeholders with high quality, up-to-date information and education to foster a cost-effective approach of managing JD and TB risk and preventing and controlling mycobacterial

diseases in animals.

Organization/Governance

We build on our experience with the JDIP and TB-CAP initiatives and have formulated a robust plan for the administration of the multi-state initiative.

In brief, we have proposed the formation of an **Executive Committee** that will be responsible for all strategic, scientific, and management policy decisions for this multi-state initiative, and serve to advise the Administrative Advisor of the program. The Chair of the Executive Committee is responsible for the implementation and facilitation of programmatic goals and will serve as the primary liaison with the USDA, Experiment Station Directors, and external stakeholders. We also propose the formulation of an **External Advisory Board**, which will consist of public and private stakeholders (regulatory agencies, members of industry, and prominent scientists from related disciplines and Experiment Station Directors), to provide advice on programmatic matters, and ensure that the initiative stays true to its mission. The Chair of the External Advisory Board will be a member of the Executive Committee. The composition, membership and voting structure of the Executive Committee is described below:

Executive Committee. The initial Executive Committee will be comprised of a total of nine members, representing individuals with leadership in Mycobacterial disease research, extension, and education, a documented commitment to helping the community realize a shared vision, and a history of working together as a team. The proposed members of the Executive Committee are:

- **John Bannantine** (National Animal Disease Center, USDA-ARS).
- **Luiz Bermudez** (Oregon State University, OR).
- **Paul Coussens** (Michigan State University, MI).
- **Ian Gardner** (University of Prince Edward Island, Canada).
- **Yrjö Gröhn** (Cornell University, NY).
- **Vivek Kapur** (Penn State, PA). Initial Chair of the multi-state initiative.
- **Don Lein.** (Cornell University, NY). Initial Chair of the External Advisory Board.
- **Kenneth Olson** (KEO Consulting, IL).
- **Scott Wells** (University of Minnesota, MN).

Governance of the Executive Committee:

1. **Chair:** The chair of the committee is responsible for organizing the meeting agenda, conducting the meeting, and assuring that task assignments are completed. The chair will be elected for at least a two-year term to provide continuity and be eligible for reelection.

2. **Chair-elect:** The chair-elect will succeed the chair, and is expected to support the chair by carrying out duties assigned by the chair. The chair-elect serves as the chair in the absence of the elected chair. Normally the chair-elect is elected for at least two years and be eligible for reelection.

3. **Secretary:** The secretary is responsible for the distribution of documents prior to the meeting and is responsible for keeping the minutes, preparing the accomplishments report (i.e., the SAES-422). The secretary will succeed the chair-elect and be eligible for reelection.

4. **Responsibilities of the Executive Committee.** The Executive Committee is responsible for the overall management and administration of the program and will make all responsible efforts to achieve unanimous consent or make decisions through simple majority vote. The executive committee may appoint sub-committees (that may comprise of any member of the multi-state initiative) whenever needed in order to make flexible and informed decisions and provide guidance to the program chair and executive committee and will nominate and vote on the composition of the external advisory board.

Program Members: In addition to carrying out the agreed research collaboration, research coordination, information exchange, or advisory activities, project members are responsible for reporting progress, contributing to the ongoing progress of the activity, and communicating their accomplishments to the committee's members and their respective employing institutions.

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Land Grant Participating States/Institutions

IL

Non Land Grant Participating States/Institutions

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Lee Smith, Rebecca	Yes	Illinois - University of Illinois	1,3	311	3910	1100	0.05	0.00	0.00	0	0

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
311-3910-1100	0.05	0	0
Grand Total:	**0.05**	**0.00**	**0.00**

Program/KA	Total FTE
0	0
Grand FTE Total:	**0**

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1701: Mycobacterial Diseases of Animals

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project
2. Achievable goals/objectives:
Good
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Good
5. Overall technical merit:
Excellent
Comments
The proposed NC group is an extension of the highly successful JDIP CAP. The objectives are sound and personnel well-qualified to take on the needed scientific and leadership roles that will make this project a success. With more than $200 million in losses, the US dairy industry would have a desire to develop a plan for control and eventual eradication. One challenge is to turn passive information gathering into active engagement that will lead to measureable impacts and eventually transformation of the industry. It is difficult to gauge how far this project will take the industry and research community along this path.

In examining the material on the JDIP website, there is a description of a pending MDA-CAP proposal. Is there a connection? And if so, what is it?

Can effective control and eradication occur with existing tools and technologies? There are obvious barriers to eradication. The proposal describes incremental improvements in several areas, which are covered in the objectives. But there are no endpoints that describe a deliverable that could be applied in an eradication effort. For example, a diagnostic test to be an effective eradication tool will need to achieve a needed sensitivity, specificity, turnaround time and cost. What are the endpoint deliverables for epidemiology, risk modeling, vaccines, and pathogenesis?

How will the project extend beyond engaging the traditional partners and animal health audience? Even though there was recognition of a significant public health risk, it is interesting to note that there seemed to be no discussion of how the project can leveraged into current “one health” initiatives.

There was no discussion of how the project supports young investigators and students

The objectives are set along traditional lines. Disease can be described in terms of the interaction between host and pathogen genomes. Could genetics be added as standalone objective, instead of listed as part of vaccines? A separate genetics objective will recognize the importance of how host genes participate in pathogenesis, diagnostics, epidemiology, etc? For example, the identification of genomic markers linked to resistance or susceptibility, or linked with super shedding, could represent a longer term benefit through the application of marker-assisted selection. Genetic modification for improved resistance is also a possibility. Is genetics a distinct tool for disease control?
Your Recommendation:
Approve/continue project

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1701: Mycobacterial Diseases of Animals

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project
2. Achievable goals/objectives:
Good
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Excellent
5. Overall technical merit:
Excellent
Comments
The objectives of this proposal are sound. The personnel involved are very well experienced and I have no doubt that they will successfully complete the project. I also hope that the proactive approach envisaged in this project will translate in practical applications for control of this costly disease for the dairy industry.
Your Recommendation:
Approve/continue project

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1701: Mycobacterial Diseases of Animals

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project
2. Achievable goals/objectives:
Good
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Excellent
5. Overall technical merit:
Excellent
Comments
This is an excellent proposal with a team of participants who are pioneer in their respective research area. Most of the investigators are participants of the highly successful JDIP consortium; so their involvement in this multistate-state initiative would provide a head-start for such proposal. “Bovine TB eradication plan – a comprehensive strategy to achieve TB free status in England by 2038” was announced few years back in England. A partnership with experts involved in such plan would improve the probability of success of proposed project.

I have some suggestions for the investigative teams:

Objective one should also emphasize on the remote sensing methods for the prediction and control strategies of JD and MTB.

For objective two there should be emphasis on the differential tests to detect M. paratuberculosis and M. bovis; also the diagnostics test should be high-throughput.

Objective three should have inclusion of epigenetic components in the research plans.

JD and MTB are two major diseases of animals that have a very drastic impact on the health of animal as well as human. To some extent, the spread of these diseases could be controlled by educating the dairy farmers, producers and stakeholders who are directly involved with the business associated with the dairy cattle. This reviewer would emphasize to have knowledge dissemination and education methods to these individuals/parties in a layman language. This would promote the awareness of the disease, as well as, their willingness to participate in diagnostic and control program.
Your Recommendation:
Approve/continue project

NE_TEMP1749: Enhancing Rural Economic Opportunities, Community Resilience, and Entrepreneurship

Status: Under Review

Duration 10/01/2017 to 09/30/2022
Admin Advisors: [Tim T. Phipps]
NIFA Reps:

Statement of Issues and Justification

Statement of Issues and Justification

The NE1049 group (**Community Health and Resilience**) formally requests consideration for a revision/replacement as its five-year term ends. The group is in its fourth incarnation (NE1029, NE1011, and NE162), and was originally organized prior to the establishment of the new NIFA focus areas. This project will extend the group's efforts by extending and expanding previous areas of research, while also exploring new issues facing rural areas.

Overview. Rural communities face a wide range of economic growth and development issues ranging from changing economic structure to public service provision. A recent Congressional Briefing on the changing demographics of rural America, "Changing Demographics Reshape Rural America" (Population Reference Bureau, 2017) noted that around 2010, for the first time rural counties began experiencing an overall population loss, reflecting out-migration of young adults, decreasing births, and older adults aging in place. Populations with large shares of old, poor, or minorities have different needs for medical care, legal assistance, and social services, yet rural areas characterized by chronic out-migration are unlikely to attract highly educated professionals to provide those services as these areas lack urban amenities, good schools, and high-quality health care. A related area is retirement/wealth distribution issues, as we are facing the retirement of the first generation to fully embrace individual retirement accounts, which could lead to an intergenerational shift in wealth which didn't occur with pension-based systems. Rural areas are also more diverse now than they were 20 years ago, as jobs in construction, manufacturing, agriculture, and food processing brought an influx of immigrants.

Additionally, U.S. military veterans are disproportionately represented in rural areas. Since 36 percent of veterans who use the Veteran's Administration (VA) for health care live in rural areas, distances to VA facilities pose challenges. These veterans could be an important resource for rural communities, bringing educational skills and leadership experiences. Finally, considering health**,** urban mortality rates have been dropping faster than rural rates since 1985. "Deaths of despair" due to suicide, alcohol abuse, and drug overdoses are most prevalent in rural parts of the nation. "Accumulated disadvantage" related to low education levels, unemployment, poor mental and physical health, and isolation puts rural residents at higher risk of premature death (Population

Reference Bureau, 2017).

USDA's Research, Education, and Economics (REE) Action Plan (February, 2012) presents a vision to address these rural problems using "Impact-driven agricultural science" to expand economic opportunity through innovation, promote sustainability and conservation, enhance environmental quality, and improve quality of life for farmers, farm workers, and society. Of the seven goals identified in the REE plan, four are relevant to the new NE1079 proposal:

1. **Rural-Urban Interdependence and Prosperity**. While many rural communities have taken advantage of new economic opportunities, others have experienced persistent outmigration, poverty, and/or stagnant labor markets. How rural areas position themselves through diversification and enhanced entrepreneurship to better compete in a global environment where skills, knowledge, and innovation are key drivers of economic growth will be key to enhanced resiliency. Rural communities need to take advantage of market opportunities (e.g. local/regional/organic food systems) and technologies (e.g. broadband, green technologies, and renewable energies). There is also a need to establish determinants of rural prosperity and develop indicators to measure regional assets and performance.

2. **Sustainable Use of Natural Resources**. Technologies and management prescriptions need to be developed to produce needed products while conserving natural resources, and provide reliable water sources forenergy, ecosystem services, and water-rights claims of Native Americans.

3. **Education and Science Literacy**. Decreases in the rural workforce will exacerbatelabor costs in rural areas; economic conditions in rural areas already make it difficult to attract and retain workers, particularly young people who leave rural areas for better social and career options.

4. **Responding to Climate and Energy Needs**. Agricultural and forestry producers, land managers, and other decision makers need tools to help with greenhouse gas mitigation and adaptation.

It is notable that there is substantial overlap between these goals and the recent Presidential Executive Order on Promoting Agriculture and Rural Prosperity in America (The White House, 2017) which establishes an Interagency Task Force on Agriculture and Rural Prosperity. Some of the functions of this task force include identifying legislative, regulatory, and policy changes to promote rural America agriculture, economic development, job growth, infrastructure improvements, technological innovation, energy security, and quality of life, specifically promoting long-term, sustainable rural development, expanding educational opportunities for students in rural communities (especially in agricultural fields), ensuring access to a reliable workforce, and issues regarding property rights, public lands, and advancing traditional and renewable energy production.

Recent and ongoing projects in these areas by members of NE1049 include local foods and sustainable small scale agriculture, water and environmental issues pertaining to rural communities, rural amenities and economic growth and development, rural tourism, agricultural tourism and recreation, rural access to information technology, links between broadband provision and employment, impacts of state tax and expenditure limitations on state and local governments, economic impacts of renewable energy industries on the local economy, and new measures to implement the community capitals framework. In its 2017 annual meeting, the group identified **three primary research areas** which link to the priorities set out by REE and the Interagency Task Force on Agricultural and Rural Prosperity around which it wishes to engage in the coming years: **Rural Entrepreneurship and Community Well-being**; **Community Resilience**; and **Energy and Land Use** policies in rural areas. In developing a vision for the next iteration of the research project, we note that many rural areas continue the economic shift from extractive industries to

retirement or tourism based economies, while some regions are moving toward energy development (e.g. fracking). Changes in labor availability in rural areas, due partly to population decline, may cause substantial shifts in economic opportunity. If labor becomes more expensive, more automation may result. Land use issues also may play a major role in development and change in rural areas, with proposed changes in federal policies, federal land and water management, and land ownership which could affect income and employment. Development of renewable energy sources like wind and solar also have the potential to cause changes in land use and economic structure in rural areas. More "traditional" energy sources also affect local conditions, with the siting of pipelines and powerlines creating both opportunities and controversy. These issues and the research they will motivate fit well under the goals outlined by REE's Action Plan, as described in the objectives listed in a later section.

Related, Current and Previous Work

Related, Current, and Previous Work

The team of researchers associated with the proposed project and its predecessors NE1049, NE1029, NE1011, and NE162 has a history studying the wide variety of issues surrounding entrepreneurship and resiliency. We will discuss past and current work by NE1049 members and others related to the key rural community issues we have identified. The lingering effects of the Great Recession, coupled with a financial crisis, left many rural communities lagging their urban counterparts. From 2006 to 2015 metropolitan employment grew by 9.1% for U.S. overall but only 1.1% for nonmetropolitan regions. Over this period metro wage & salary employment grew by 4.9% but declined by -1.7% in nonmetro counties. Much of the work done by project members focused on this disparity in growth, development, and recovery from the recession. We have also, as part of these efforts, worked on the theoretical bases for regional economic development, which are not as well defined as the foundation for other areas of economics.

Through studying the overall community economic development process the importance of wealth creation, broadly defined, has gained wide acceptance as an important element in understanding economic growth and development (Pender, Marré and Reeder 2011). The wealth of the community is composed of both the tangible and intangible assets at the disposal of the community. The Floras (Flora and Flora 1993, 2008) talk of these assets in terms of seven community capitals including built, financial, political, social, human, cultural and natural capitals (Flora and Gillespie 2009). Built capital includes machinery, equipment and buildings along with public infrastructure such as roads and water treatment systems. Financial capital is access to credit, loans and debt that is necessary to finance private and public investments. Political capital refers to the ability of the community to influence laws and regulations that determine what is or is not legal as well as access to resources from higher levels of government. Social capital includes density of acquaintance, collective identity, trust, and reciprocity. Human capital includes education, skills, experiences of individuals, and ability of people to use those resources. Cultural capital speaks to the way people think of the world and how they fit into and contribute to that world

and, as well as their traditions and language. Each of these capitals represents an important piece of the community economic development puzzle.

Extensive research by Levine and Renelt (1992), Pack (1994), Sala-i-Martin (1997), Schultz (1999), Durlauf and Quah (1999), Durlauf (2000), Brock and Durlauf (2001), Brock, Durlauf and West (2007), Deller and Lledo (2007) and Deller, Lledo and Marcouiller (2008) argues that theory identifies multiple ways to measure development factors. Within the rural wealth creation or community capitals framework, theory suggests that each form of wealth or capital is important. The challenge is to identify which capitals are the most important within different contextual settings. The second element here centers on measurement. Consider one of the community capitals, social capital, which is considered by many (e.g., Shaffer, Deller and Marcouiller 2004, 2006; Rupasingha, Goetz, and Freshwater 2006; Kangayi, Olfert and Partridge 2009) to be fundamental to resilient and viable communities. Social capital describes the quality of connections between individuals and how well they are leveraged to achieve success within the region creating a whole that is greater than the sum of the parts.

Fannin, Barreca and Detre (2012) used the community capitals framework to explore how natural disasters associated with hurricanes have affected the fiscal health of local governments in Gulf Coast states and Chen and Weber (2012) explore how community capitals have helped rural communities in the Pacific Northwest adapt to changes in Federal forestry policies. Their results suggest that community assets or capital matter in how communities can respond and adjust to both natural and human-made disasters. But this line of work points to four research issues that need to be addressed: (1) while we can conceptualize the notions of community assets or capital, can we quantify them for rigorous analysis? (2) how do these quantified notions of community assets or capitals affect the community economic growth and development process with an eye toward community resilience from disasters, whether they be natural or human-made? (3) which type(s) of community capitals influence community economic growth and development processes most? and (4) how can policies be crafted to positively influence the key forms of community capital?

Current research also points to the importance of entrepreneurial ecosystems that reflect the social interactions, attitudes, and norms of the larger community in which the entrepreneur operates. As noted by McKeever, Anderson and Jack (2014) individual entrepreneurs and the processes to start and grow a business are embedded in the social context of their community; studying the individual entrepreneur outside of local context is misdirected. The Floras (1993) speak of “entrepreneurial social infrastructure” where community attitudes and norms help drive the well-being of the community. Gedajlovic et al. (2013) note that entrepreneurs and entrepreneurship are embedded within these social and cultural norms of their community.

With respect to human capital, access to high quality child care supports both the current workforce and future human capital development, yet not all families have opportunities for their children to participate in and benefit from high quality child development programs. Studies have demonstrated the influence of child care prices and availability on parental employment, particularly for mothers (e.g. Connelly, 1992; Davis and Connelly, 2005; Mammen et al. 2009). Herbst and Barnow (2008) estimate how variation in child care supply across geographic areas within a state influences female participation in the workforce; it is well known that there is wide spatial variation in the availability and price of child care (Davis and Li, 2009; Gordon and Chase-Landsdale, 2001; Kimmel, 2006). Projections of worker shortages in rural areas have increased interest in research on links between rural labor force availability and lack of child care. Recent concerns about shortages of child care options in rural areas have been widespread (Malik et al. 2016). A Center for American Progress report estimates that 54% of the rural ZIP code areas examined in eight states meet their definition of a “child care desert” based on an insufficient number of child care centers for young children residing in the area. Ohio and Minnesota had the highest rates of rural child care deserts (Malik et al. 2016). Yet few studies have closely examined links between local labor markets and child care availability. Only recently has the focus of research shifted from family decision-making to the influence of federal, state and local policy on local child care markets and providers (e.g., Kimmel 2006). One recent study notes the connection between shortages of health care workers in rural communities and availability of child care (Henning-Smith and Kozhimannil, 2016). There are growing calls for early childhood development programs to be considered and supported as part of economic development policies (Rolnick and Grunewald 2003). One objective of this project is to determine how workforce policies (related to child care, education, and training) and economic development policies (increasing job opportunities) can improve labor market outcomes for rural families and communities.

Regarding physical capital (infrastructure) issues, North Carolina researchers analyzed the link between broadband provision and employment using county-level data over the period 2008-2012 from the 48 contiguous states. Their results indicate no significant relationship between 2010-2012 employment growth and broadband growth in the preceding biennial period, and were unable to detect meaningful predictive causality running from increasing broadband penetration to employment growth (or vice versa) (Dinterman and Renkow, 2017; Kandilov et al. 2017). Another recent study highlights the connection between broadband and other types of infrastructure to the possibility of job loss due to automation, especially in rural areas (Devaraj et al. 2017). In related work on rural entrepreneurship, Wisconsin research highlighted the role of women entrepreneurs and women farmers, the latter of which overlaps significantly with local foods (Deller, Conroy, and Watson, forthcoming). Research on the impact of state restrictions, often referred to as tax and expenditure limitations, on state and local governments found that these types of restrictions seldom have the anticipated outcome and indeed results in several negative unintended consequences such as underinvestment in infrastructure, reduced credit rates, higher interest costs on debt, higher levels of debt and overall weaker fiscal health (Deller, Stallmann, and Amiel, 2012). Researchers in North Dakota assessed the economic impact of renewable energy industries on the local economy (Coon et al. 2015).

In one specific body of research on the effect of small entrepreneurs on local economies, NE1049 researchers analyzed local/regional food systems as a component of the entrepreneurial economy from different perspectives. Researchers in Colorado and Oklahoma evaluated the role of small and mid-size farms and their impacts in local and regional food systems, as well as the rural economic impacts of local food systems. Researchers in Colorado also developed a toolkit to assess the Outreach, Training and Proof of Concept of USDA AMS Economic Impact Assessment through Cooperative Agreement with USDA-AMS. Additionally, Colorado researchers are collaborating with researchers from University of California at Davis and University of Northern Colorado to develop an integrated approach to agritourism development in the western US. Researchers in New Hampshire continue their efforts on a NIFA-funded project to assess the potential for local food production and the constraints faced by suppliers of produce grown in Maine, New Hampshire and Vermont. Their surveys use contingent choice modeling on food characteristics to identify "status quo bias" and spatial dimensions associated with local food systems, drawing heavily on previous survey and econometric work done at Colorado State University and the University of Wisconsin, among others. Researchers in Idaho investigated the local food system by examining the role of intermediaries in the food system. They are currently surveying restaurants and stores to determine the role of intermediaries in local food systems, which will inform nascent work in New Hampshire on the same topic. In related policy work, researchers in Wisconsin conclude that evidence that local foods enhance rural economic growth is limited (though this is not to say that there are no unique business opportunities for entrepreneurs). West Virginia researchers have also examined the more general topic of how and why some rural regions prosper while others stagnate or lag behind (e.g. Stephens and Partridge, 2011; Stephens, Partridge, and Faggian, 2013).

On the general topic of resilience, the effects of fiscal policy and government institutions was researched by NE1049 members in Wisconsin, Missouri, Nevada, Oregon, and Oklahoma (e.g. Dabson et al. 2013; Stallmann et al. 2013). Wisconsin researchers investigated impacts of tax and expenditure limits on government resiliency by cataloging the unintended consequences associated with these fiscal policies. Oregon researchers examined spatial evolution of municipal government structures and how this might affect community resilience to natural disasters. Oklahoma researchers examined the effects broadband can have on marginalized populations. Colorado researchers are developing new measures to implement the Community Capitals framework. North Dakota researchers examined the effects of casino development on county level economic and job growth. These efforts are especially important as they all contribute to our search for an elusive unifying paradigm of rural economic development. Research in Michigan also examined how Google searches can predict suicide rates as a potential indicator of mental health, while Ohio researchers examined the effects of opioid addiction on economic development potential across counties, tying in with the "deaths of despair" problem noted earlier in this proposal.

Spatial analysis techniques have been and will continue to be a specialty of many NE1049 contributors. Past work on spatial economic issues by NE1049 researchers includes areas as diverse as regional labor markets (Davis and Weber 2003; Goetz, Han, Findeis, and Brasier 2010; Renkow 2003, 2007), rural industrial restructuring (Olfert and Partridge 2010; Barkley and Henry 2005), rural impacts of investment in broadband technologies (Stenberg, et al 2009), rural governance (Skidmore and Scorsone 2009; Skidmore et al. 2009), rural poverty (Partridge and Rickman 2008; Deller 2010), and fiscal impact analysis (Johnson, Otto, and Deller 2006). Researchers in NE1049 have been at the forefront of economic and impact modeling (Johnson, Otto, and Deller 2006; Swenson and Otto 2000; Partridge, Rickman, and Li 2009; Irwin, Isserman, Kilkenny, and Partridge 2010; Monchuk, Brewin, and Partridge 2009; Goetz et al. 2010; Hansen and Kalambokidis 2010). These skills are applicable to most of the empirical research undertaken in addressing sectoral and locational issues affecting community resiliency.

Regarding the general issues of the previous work by NE1049 researchers, one of the major strengths of NE1049 and its predecessors has been the extent to which researchers have collaborated across state boundaries and shared theoretical, survey design, and quantitative expertise. A review of publications of project members over recent years show that a majority are co-authored by individuals from different states, often multiple states. An excellent example is the edited book by Pender (IFPRI), Weber (Oregon State University), Johnson (University of Missouri), and Fannin (Louisiana State University) ***Rural Wealth Creation***, which has drawn universal accolades, and Johnson, Otto (Iowa State University), and Deller's (University of Wisconsin) widely read 2006 book on community policy analysis modeling. Some of the areas of research where either direct or indirect (i.e. building directly on previous project work) collaboration has occurred includes taxation and fiscal impact analysis (e.g. Amiel, Deller, and Stallman, 2012; Sands and Skidmore, 2014; Kalambokidis, Laura. 2014; Maher et al. 2016; Stallman et al. 2012), child health and welfare (e.g. Skidmore, Anderson, and Eiswerth, 2014; Krafft, Davis, and Tout, 2017; Davis et al. 2014), natural disasters (e.g. Skidmore and Toya, 2014; Atreya, Ferreira, and Kriesel, 2013), sectoral and economic impact analysis (e.g. Coon et al. 2015; Gabe and Lisac, 2014; Winkler, Deller, and Marcouiller, 2015; Wojan, Brown, and Lambert, 2014; Janeski and Whitacre, 2014; Winfree, Watson, 2014; Hardesty et al. 2014; Harris, Deller, and Goetz, 2014; Hill et al. 2014; Pyburn et al 2016; Lim, 2016), location theory (e.g. Conroy, Deller, and Tsvetkova, 2016; Fortenbery, Deller, and Amiel, 2013; Fallah, Partridge, and Rickman, 2014), broadband development (e.g. Dinterman and Renkow, 2017; Whitacre, Gallardo, and Strover. 2014; Kandilov et al. 2017), social capital (e.g. Halstead and Deller, 2015; Deller and Deller, 2012), land use and environmental issues related to regional economies (e.g. Atreya, Kriesel, and Mullen, 2016; Irwin, Jeanty, and Partridge, 2014; Lim, 2014), and general rural economic development and resiliency issues (e.g. Deller and Conroy, 2017; Deller and Watson, 2016a; Deller, and Watson, 2016b; Kirk, Allen, and Shideler, 2014; Stephens, Partridge, and Faggian, 2013). It is of course worth noting that many of these previous research accomplishments feed directly into the goals of the current proposal and the priorities identified by USDA and the White House.

Surveys (e.g., of consumer behavior regarding local food purchase) have been conducted over multiple states with multiple PIs, and new efforts have built on previous efforts. Two of our quantitative centerpiece methods, input-output modeling and spatial econometrics, are featured in many research efforts with the help of NE1049 “specialists” in these techniques. Project members have collaborated to construct multi-state research projects funded by USDA/AFRI and other agencies. Finally, the mix of appointments of NE1049 members between those with heavy research responsibilities and those with mixed extension/outreach appointments leads to a research agenda which better reflects current rural concerns and enhances outreach.

An effective strategy for promoting information sharing and collaboration across individual state projects has been timing the annual NE1049 Business Meeting to coincide with annual regional science association meetings (most often the Southern Regional Science Association, though occasionally the Western Regional Science Association). NE1049 members generally stay on and actively participate in the meetings, often hold office in these associations, and have a history of sponsoring substantial numbers of graduate students at these meetings.

Objectives

1. Enhancing rural economic opportunities and entrepreneurship. This is an exceptionally broad, multi-faceted objective which encompasses both the need for advancing the theoretical structure of community economic development and the need for empirical, focused, policy relevant research. Some of the areas which NE1049 researchers have pursued and will expand in the new project are discussed in the comments section.
   Comments: a. The Theory of “Community capitals” (Flora and Flora 1993, 2008). These seven community capitals include built, financial, political, social, human, cultural and natural capitals (Flora and Gillespie 2009). NE1049 researchers have done substantial research on social capital over the past five years (e.g. Goetz and Rupasinga, 2006; Halstead and Deller, 2015). Research in the capitals overlaps with many sub-topics in both this and the second proposal objective, and helps in the pursuit of a broad paradigm for economic development. b. Issues of wealth/income distribution and rural economic development. Country-level studies have largely found that income inequality and economic growth are inversely related (e.g. Person and Tabellini, 1994; Alesina and Rodrik, 1994; Banerjee and Duflo, 2000). Income and wealth distribution is also an issue in rural areas. Bishaw and Posey (2016) noted that rural Americans have lower median household incomes than urban households, but rural areas have lower poverty rates than their urban counterparts. c. Non-agricultural development opportunities. A particular area of research for NE1049 has been the economics of local agriculture. However, many rural communities have tried to expand into tourism and recreation with mixed success; in any case, employment opportunities generated in some of these sectors tend to be relatively low-income. Diversification of local economies (e.g. export base and local agriculture; business attraction and retention) through both expanding the small business sector (Eschker, Gold and Lane, 2017) and fostering retention and expansion of existing businesses (Halstead and Deller, 1997) are key development objectives which clearly affect resiliency in the face of natural and human caused shocks to the system. How entrepreneurs behave socially, exchange information, and procure resources and establish reciprocity, are key areas of research (Markeson and Deller 2015). d. Infrastructure needs, development, and deficiencies. Infrastructure is a broad concept, including both Economic Overhead Capital (which includes roads, bridges, powerlines, etc.) and Social Overhead Capital (health, education, etc.) (Hansen, 1965). Built infrastructure has been researched by team members since the 1980s (e.g. Johnson et al. 1988). Such investments have the potential to affect virtually all the subtopics in both proposed objectives. Specific topics under scrutiny by NE1049 researchers include impacts of broad band internet availability/deficiency on economic development and availability and affordability of child care as a deterrent to availability of affordable labor, and its effects on rural quality of life. e. Chronic and progressive labor availability problems, related to the issues raised in the third REE goal listed above. If labor becomes more expensive, more automation may result (Devaraj et al. 2017). This can cause economic distortion, and affect labor participation rates, economic goal setting, and other key features at the community level f. The impact of entrepreneurship on rural areas. There is evidence from previous research that entrepreneurs can contribute to growth in rural areas (e.g. Sepehns et al. 2013; Rupasingha and Goetz, 2013) and understanding what types of policies can contribute to this growth will be critical to deal with the restructuring of rural areas.

2. 2. Evaluating Factors and Policies Affecting the Resiliency of Rural Communities. Many of the natural and human induced "shocks" which impact rural communities are external i.e. communities have little or no control over whether the shock occurs. Examples include major storms (Hurricane Harvey, Superstorm Sandy), restructuring of the tax code or health care system, or State and Federal changes in energy, land, and water use policy. However, there are proactive and reactive mechanisms communities can adopt to minimize negative effects and enhance positive effects of these shocks, and to mitigate effects which do happen. The degree to which a community can bounce back from these changes is a measure of resiliency. Proposed and ongoing research areas under this objective are discussed in the comments section.
Comments: 1. objective are: a. Impacts of federal infrastructure investment plans. Funding mechanisms for proposed infrastructure upgrades and expansion are not yet determined and may be quite different from historical funding efforts and effects on tax bases (Deller, Amiel, Stallmann, and Maher, 2013a; Janeski and Whitacre, 2014). b. Changes in health care availability due to changes in the Affordable Care Act and possible new health care legislation. Many rural counties currently have few or no health care providers, and often suffer from substance abuse issues (Henning-Smith and Kozhimannil, 2016; Skidmore et al. 2014). The disproportionate representation of veterans in rural areas presents both problems and opportunities; veterans may require health care and counseling services difficult to find in rural areas. c. Why are some areas lagging in recovering from the recession (Stephens, H., Partridge, and Faggian, 2013; Stephens and Partridge, 2011)? What did we learn from the recession? What policies aided resilience and recovery (Deller and Watson, 2016)? There is movement away from extractive industries to retirement/tourism based economies in rural areas, a trend partially offset with opposite effects in, for example, fracking areas; how will this effect community resilience in the face of future shocks? What contexts increase the likelihood a rural community will benefit from retirement-, tourism-, or recreation-based economies as they consider moving away from extractive industries (Hill et al. 2014; Lim, 2016)? d. The impact of changes in federal policies affect land and water use in rural areas (Chen and Weber, 2012). For example, transfer of ownership of federal lands from federal to state government has been proposed, which might affect income, employment, and taxation at the local/state level. Other issues include changes in public land policy and forest resource management. e. Understanding the Impacts of changes in the retirement system. For example, the current generation of retirees is the first to experience a shift from traditional pension plans to personal retirement accounts, with implications for intergenerational wealth transfer. f. Understanding the impact of policies regarding climate change and efforts to support alternative forms of energy on rural areas. What impacts does the renewable energy sector have on rural jobs, income, and household and community well-being? Are some locations better equipped with transport infrastructure, land and forest resources, and human and social capital to support the expansion of this emerging sector? What is the effect of clean energy development on rural counties? Increased focus on sources of renewable energy has raised questions of aesthetic damages, issues of regional vs. local energy, and storage capacity for solar generation. How can rural areas participate? g. Understanding the impact of policies geared at reinvigorating or encouraging fossil fuels on rural areas. How do rural residents value this development which brings jobs but also can damage natural resources and affect long-term amenity-led growth? h. Considering the interplay between traditional sources of energy and renewables. How do higher oil prices factor in? How do the interaction between weather and output in solar power link into/with "traditional" energy suppliers? For example, much of the coal fired power of eastern Montana which went to Seattle has been supplanted by other sources. What are the local/regional effects of renewable energy pipelines, powerlines, and other energy infrastructure requirements (Coon et al. 2015; Fortenbery, Deller, and Amiel, 2013)?

Methods

Methods

A primary motivation of this project is to continue and redirect the work performed under Regional Research Project NE1049, reestablishing the multi-state research effort in the context of the USDA REE Action Plan and its vision of using impact-driven agricultural science to expand economic opportunity, and the goals of the Interagency Task Force on Agriculture and Rural Prosperity established by Presidential Executive Order. NE1749 will continue to build on the many past and current outreach and multi-state activities. While the project has two, arguably broad, objectives, research questions and methods for each overlap and complement the other.

Two important forms of cross-state cooperation are evident in our proposed research. First, a large share of the research will be conducted collaboratively across states. Second, research methods and approaches which have been developed in one state have historically been subsequently employed by researchers in other states. Although many challenges are the same, states also differ. This interstate variation helps to statistically identify relationships between dependent and

explanatory variables. Thus, interstate collaboration provides more suitable cross-section time series databases. Multi-state collaboration also lends valuable support to innovation, which is by definition the application of an existing invention to a new purpose. We will build on our knowledge base, better use our resources through the synergies of collaboration, help create more efficient rural policy, and help improve the sustainability and vitality of rural communities. Additionally, rural areas in the United States are not homogeneous and the impact of policies may vary across regions. By conducting analysis in various types of rural regions using similar methods we can improve our understanding of the impact of policies on various types of rural areas which can be used to improve policymaking.

Researchers within the group have the expertise and are conducting research in each of the proposal's focus areas and are poised to extend this work. For example, members have and continue to work on issues such as sustainability and resilience of communities and local governments in periods of crises (Arkansas, Idaho, Iowa, Michigan, Minnesota, Missouri Ohio, Tennessee, West Virginia, Wisconsin); rural change and migration (Arkansas, Iowa, Ohio, Oregon, Pennsylvania, West Virginia, Wisconsin); and local/regional foods and agri-tourism (Colorado, Tennessee, Texas, Wisconsin, New Hampshire). The researchers in the group will employ a variety of social science methods to address the research objectives, bringing to bear the appropriate methods for different topics, and allowing for triangulation across methods and states for broader interpretation of findings. Surveys, interviews, and focus groups allow for in-depth examination of particular issues; for example, surveys of consumer behavior regarding local food purchase. Quantitative methods include regression analysis, input-output modeling and spatial econometrics. Expansion of use of GIS methods will allow the group to expand analysis of the spatial evolution of municipal government structures, of community capitals, and of workforce supports such as access to child care. The collaboration of researchers with research and Extension appointments will enhance cross-fertilization of ideas on methods and relevance to rural concerns. Examples of specific methods being used by project members are presented in the following two sub-sections.

Objective 1. Enhancing Rural Economic Opportunities and Entrepreneurship. Supporting the goals of USDA’s REE Action Plan, the methods employed to meet the research objectives of this project will increase understanding of the changing determinants of rural prosperity and develop indicators to measure specific community and regional assets and outcomes.

In our long-run community sustainability focus we take a community capitals or community assets framework approach. There are, however, primarily two methodological challenges with the approach. First, the comprehensiveness of the capitals or community assets can drive the research agenda in several different directions at the same time. Second, many of these capitals are fairly straightforward to describe from a theoretical perspective but extremely difficult to quantify. On-going research by Penn State, Kentucky, Tennessee, Wisconsin, and other project members use various types of data to build a range of social capital measures. From a methodological perspective, this follows the extensive work that has been undertaken exploring the relationship of natural capital and rural economic growth and development as well as the role of the

creative class, one interpretation of human capital, in rural economic growth.

Social capital theory, which focuses on networks, norms, and trust (Halstead and Deller, 2015) will provide the basis for much of the work on enhancing entrepreneurial stock in rural communities, with particular emphasis on the network component. Social capital broadly defines social influences and how, taken together, human interaction can shape economic choices. Networks, however, specifically focus on the social connections between actors. Because networks must first form before repeated interaction leads to behavioral norms and mutual trust, they are the most fundamental component of social capital. Networks also provide a mechanism through which social capital can lead to enhanced entrepreneurial outcomes, namely as information transmission mechanisms (Conroy and Weiler, 2017). Network channels are important because they provide access to information for entrepreneurs. The information about resources, market demand, feasible financing, and other factors that entrepreneurs can access and leverage through networks has been shown to help entrepreneurs identify new opportunities, assess risk, develop successful strategies, and ultimately, enhance productivity and profitability (Bauernschuster, Falck and Heblich 2010; Bhagavatula et. al., 2010; Westlund, Larsson, Olsson 2014). Access to broader networks can also increase a firm's visibility and reputation within the community (Podolny, 2001) as well as help them gain legitimacy (Elfring and Hulsink, 2003, 2007; McKeever, Anderson and Jack 2014).

On researching the links between child care availability and local labor markets, we need a greater understanding of child care markets, and how they function in rural areas. In Minnesota and other states, the research team will develop measures of child care accessibility based on the spatial distribution (travel time) between families and child care providers. We will examine how policy changes, including funding for child care assistance and early learning scholarships, as well as quality improvement grants to providers, affect the supply of child care over time and across rural areas. Examining areas with low levels of child care accessibility, we will identify strategies that work to increase supply of child care. The access measures developed project can be applied to other states, and examined in the context of state and local policy differences.

Regarding financing issues, which are certainly key when discussing the nation's massive infrastructure investment shortfall (ASCE, 2016), researchers at Missouri and Wisconsin with a colleague at the University of Nebraska-Omaha have published research results on the impact of tax and expenditure limitations (TEL) on economic growth, state budgets, credit ratings and infrastructure quality. There is a long history of states placing limits on the taxation powers of local governments. Proponents argue that government is too large and as a result is inefficient and impedes economic growth. These are testable hypothesis (e.g. Deller et al. 2013a; Deller et al. 2013b). Overall TELs seldom have the intended outcome their proponents promise, neither limiting expenditures nor revenues because governments shift to other revenue streams to maintain services. The limited evidence also suggests that TELs do not foster economic growth and development and may, indeed, hinder economic performance. The literature also indicates unintended consequences such as lower credit ratings and less robust infrastructure (e.g. Amiel et al. 2014; Maher et al. 2016).

In a natural progression of rural entrepreneurship via local agricultural development, researchers at the University of New Hampshire, Maine, and North Carolina A & T are examining the role of intermediate actors in the local food network (e.g. restaurants, grocery stores, food hubs). This somewhat neglected area will identify and close information gaps between local farmers and intermediate channels. The next major step is to construct and implement a survey of NH restaurants and grocery stores to examine the potential for marketing local produce in these venues. Researchers will construct and pretest this survey using information obtained from face to face surveys previously conducted. Researchers will also seek to include NH Seagrant in this effort, to incorporate fresh local seafood into the study. Previous survey results in New Hampshire and Massachusetts also indicate that consumer demand functions for different types of produce may differ substantially even within relatively small geographic areas (Pyburn et al. 2016; Shi et al. 2016), so a spatial econometrics component will be added to previous modeling efforts. The multistate research project will allow the findings from this type of research to be applied to other rural areas.

Researchers in West Virginia are starting a project to examine the impact of entrepreneurship, both in total and by industry, on employment and other measures of growth. They propose to measure entrepreneurship using census data to consider the number of non-employer firms (total and by industry), the number of small businesses (total and by industry, and using various size cutoffs), as well as births (total and by industry) as measures of entrepreneurship. These measures will be used to examine the impact of entrepreneurship on growth using various definitions of communities, including census tracts, townships, or other geographically-defined areas. In addition to looking at changes in employment or changes in the total numbers of firms in the same area, they will use difference in difference (DID) approaches, or changes in the growth of employment or changes in the growth of firms, to difference out many of the unobservable factors thus reducing endogeneity concerns. They will also include measures such as educational attainment of the population that might affect the relative supply of entrepreneurs. Spatial spillovers of economic activity will be addressed using spatial variables or spatial econometric methods. The new multistate research project will allow this type of research to expand to a multitude of rural areas and to address how entrepreneurship can be supported to enhance rural opportunities.

Objective 2. Factors and Policies Affecting the Resiliency of Rural Communities Our objective here is to identify and analyze policies and strategies contributing to the viability and resiliency of communities in responding to economic and policy changes as well as natural and human-made shocks. Our focus is on long-run socio-economic sustainability and ability of communities to respond to changes and to develop economically. The challenges that communities have faced, and will continue to face, have come from natural disasters such as floods, hurricanes, and tornados, as well as human-caused shocks such as major changes in tax and health policy, and regional and national recessions.

An often-overlooked area is the impact of recessions on local government budgets, since these governments provide many of the day-to-day goods and services that affect resilience of local businesses and families. Using a panel of 15 years of data from the budgets of 89 rural counties, researchers at Missouri propose to focus on the effects of recessions on local government budgets. Using trends in fiscal ratios, they are attempting to identify counties 1) in which fiscal stress is related to long run trends, prior to the recession, and trends beginning with the recession, 2) tax and/or expenditure budget structures that lead to faster and slower budget recovery. Missouri is also working with Iowa State, Kansas State and Michigan State Universities to identify state policies that have helped and hindered county government recovery from the recession, and to identify innovative responses to fiscal stress. This project is in progress and will continue as data collected from both on-line surveys and telephone interviews with the executive directors of state associations of counties are analyzed.

Researchers in West Virginia are commencing efforts to identify how energy development affects rural economies, and its prospects for enhancing community resilience. Using data on the location and timing of shale gas development, they propose to examine the impact of drilling on various definitions of communities, including census tracts, townships, or other geographically-defined areas. To control for the fact that communities with shale development may be quite different from those without, the project team will follow Heckman et al.'s (1997, 1998) recommendations to combine matching techniques with difference-in-difference (DID) methods. The change or difference in the economic outcomes of communities which experience drilling will be estimated, focusing on changes in overall employment growth rates, changes in employment growth in specific industries, and changes in the number of new establishments created or closed both total and by industry. Spatial spillovers of economic activity across communities and within certain distances of drilling activity will be addressed using spatial econometric methods and/or by interacting key variables with spatial weight matrices.

Climate change and the growing exposure to climate-related extreme events present another major challenge for rural communities not only on agriculture but also on health and poverty. Synthesizing county-level socio-economic data with climate-related extreme events data from NOAA and applying quasi-experimental design methods, researchers at Oregon propose to modify the community economic resilience measure in Han and Goetz (2015) to better quantify rural community resilience to climate-related extreme events. The researchers will also explore how rural community resilience to climate-related extreme events are associated with ecological/environmental, socio-economic, infrastructural and social-capital related factors. Impact of future climate change on rural community resilience will be simulated. This project is in progress and will help to shed light on how to incorporate climate change in the development planning of rural communities. It will also help to promote the climate-resilient development strategies of the United Nation Development Program because the climate-resilient development is not only about climate-friendly development but also about the communities' ability to adapt to climate changes and the related extreme events. The latter might be a more pressing concern considering the first-

ever period (2010-2015) of rural population decline in America.

As noted in Objective 2, health issues are of special concern to rural communities, and may affect their ability to plan for or react to external shocks. West Virginia researchers propose to study problems of drug abuse in rural areas using health and drug use data through West Virginia University's School of Public Health and the West Virginia University Health Care System. While drug use (or abuse) has received the most attention, other health issues may also lead to lower economic growth. Using housing data and business data as proxies for overall economic conditions in an area, and incorporating socio-demographic data and other community-level variables from the U.S. Census and from other state, local, and federal datasets, they will consider the relationship between health outcomes and changes in economic conditions such as changes in employment, number of firms, or housing prices. Causality issues will be addressed using DID methods, instrumental variable methods that explicitly test for reverse causality, and granger casualty tests. This state level effort is the type of project that has provided the basis for multistate-level collaboration to expand the study area via external funding.

Measurement of Progress and Results

Outputs

- Policy Relevant Information Dissemination Comments: Measurement of Progress and Results Outputs: 1. Journal articles, extension publications, popular press articles, edited books, and book chapters. These publications will communicate research results and synthesize findings across themes and states. 2. Integrated analyses of cross-cutting issues such as the interrelationships between community capitals or assets and residential choice, labor markets, businesses and economic growth. 3. Timely information for policymakers to use in developing policy to deal with changes occurring in rural communities with an eye toward infrastructure, health, and economic recovery from natural and human-made disasters.

Outcomes or Projected Impacts

- Relevance of Project Research • Increased knowledge of the forces impacting rural communities in terms of labor markets, industry, governance, and quality of life. • Improved understanding among community leaders and citizens of the dynamics of labor markets and businesses and their impact on rural communities, and the role of entrepreneurship. • More informed discourse on the role and organizational structure of government and the public sectors investment in community capitals for economic resiliency, growth and development. • Better understanding of the causes of local fiscal stress and the implications of tax and expenditure limitations on rural communities. • Stronger synergies between participating rural development scholars via collaborative research and outreach activities. • Economic and workforce development policies that account for recent economic structural and labor market changes and that may reduce rural poverty and improve economic outcomes for rural families. • Better use of public resources. • Better strategies to take advantage of non-agricultural development opportunities. • Better understanding of the role of infrastructure in economic development, and the funding issues that accompany it • Better understanding of the impact of policies that affect rural areas on the range of types of rural communities

Milestones

(**1**):Organize the technical committee, develop and share specific research methodologies across states, identify data sources, and conduct preliminary analyses. At the first year technical meeting we will discuss and compare research methodologies for each objective and develop a framework for understanding local food markets and community capitals.

(**2**):(Years 2-4) Conduct analyses for each objective, with particular focus on producing results that are comparable across the participating states. Build stronger synergies across rural development scholars. Conduct outreach activities including input from stakeholders on objectives and results.

(**5**):Synthesize results across states and across objectives, complete comparative analyses, and identify policy implications and next steps. Continue outreach activities.

Outreach Plan

Educational/Outreach Plan

The project will engage in outreach to the scientific community, the policy community, and local citizens and decision makers. Project investigators will present the research results and seek professional input into their research at professional meetings of the American Agricultural Economics Association and of regional science associations (Southern Regional Science Association, Western Regional Science Association, North American Meetings of the Regional Science Association International), and through associated professional journals.

Outreach to the policy community will be facilitated by close affiliation of various project members with the four Rural Development Centers (Northeast, North Central, Southern, and Western), Rural Policy Research Institute, the Rural Poverty Research Center, the Farm Foundation, and the Federal Reserve Bank of Kansas City's Center for the Study of Rural America. Project investigators have strong links to the Cooperative Extension System through the state and local offices of the university Extension Services. Technical committee members will also share information in local forums. Results will be summarized in publications like extension bulletins, policy briefs, and mass media to increase awareness and understanding of the forces impacting change in rural communities.

Organization/Governance

The project will be organized and governed in the standard way by a Technical Committee. Each participating state or agency will have an official representative appointed by the Experiment Station Director and an administrative advisor will be designated by the Experiment Station Directors. The Technical Committee will meet at least once per year, usually in the winter or early spring to coincide with professional association meetings (usually the Southern or Western Regional Science Associations). The committee will evaluate work plans to ensure adherence to the project outline and accomplishment of projected outcomes.

A chair and secretary will be elected annually by the Technical Committee. The secretary also serves as the chair-elect. The chair, in consultation with the administrative advisor, calls and presides over the meeting of the Technical Committee. The chair is responsible for preparing the annual report of the project. The secretary records and distributes the minutes and performs other duties as assigned by the Technical Committee.

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Land Grant Participating States/Institutions

MI,MN,OR,PA,CT,IL

Non Land Grant Participating States/Institutions

Texas A&M University

Participation

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Chen, Yong	Yes	Oregon - Oregon State University	1,2	605	120	3010	0.10	0.00	0.00	0	0
Davis, Elizabeth		Minnesota - University of Minnesota	1	608 610 802 805	6050 6099 6020 6099	3010 3010 3010 3010	0.10	0.00	0.00	0	0
Fiala, Nathan	Yes	Connecticut -Storrs	1	601	6110	3010	0.10	0.00	0.00	0	0
Goetz, Stephan	Yes	Pennsylvania - Pennsylvania State		608 603	6050 6050	3010 3010	0.12	0.00	0.00	0	0
Kalambokidis, Laura T	Yes	Minnesota - University of Minnesota	2	608 610 602	6110 6110 6110	3010 3010 3010	0.10	0.00	0.00	0.6	608
Kelsey, Timothy W		Pennsylvania - Pennsylvania State	1,2	608	6050	3010	0.50	0.00	0.00	0	0
Skidmore, Mark	Yes	Michigan - Michigan State University		608	6050	3010	0.10	0.00	0.00	0	0

Participant	Is Head	Station	Objective	Research						Extension	
				KA	SOI	FOS	SY	PY	TY	FTE	KA
Teran-Garcia, Margarita	Yes	Illinois Cooperative Extension	1,2	0	0	0	0.00	0.00	0.00	0.1	801 803
Weber, Bruce		Oregon - Oregon State University	1,2	608	6050	3010	0.10	0.00	0.00	0	0
Zeoli, April		Michigan - Michigan State University	2	608	6050	3010	0.10	0.00	0.00	0	0

Combined Participation

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
0-0-0	0	0	0
608-6050-3010	0.1	0	0
602-6110-3010	0.03	0	0
608-6110-3010	0.03	0	0
610-6110-3010	0.03	0	0
608-6050-3010	0.03	0	0
610-6099-3010	0.03	0	0
802-6020-3010	0.03	0	0
805-6099-3010	0.03	0	0
605-6110-3010	0.02	0	0
606-6199-3010	0.02	0	0
605-120-3010	0.1	0	0
608-6050-3010	0.1	0	0
608-6050-3010	0.1	0	0
608-6050-3010	0.5	0	0
608-6050-3010	0.2	0	0
603-6050-3010	0.06	0	0
Grand Total:	**1.35**	**0.00**	**0.00**

Combination of KA, SOI and FOS	Total SY	Total PY	Total TY
608-6050-3010	0.06	0	0
601-6110-3010	0.1	0	0
Grand Total:	**1.35**	**0.00**	**0.00**

Program/KA	Total FTE
801	0.03
803	0.03
0	0
608	0.2
0	0
605	0.33
0	0
0	0
0	0
0	0
0	0
0	0
0	0
Grand FTE Total:	**1.7**

RESPONSE TO REVIEWERS' COMMENTS ON PROPOSAL FOR NE 1079

Clearly, the first cut of this proposal needed more focus and a better narrative flow, as all three reviewers pointed out. In particular, there was some confusion about the goals USDA/REE laid out in their report and NE 1079's project's goals, which are a related, adapted subset of the REE goals. We have attempted to address this by restructuring the proposal so that justification-objectives-methods are presented sequentially to better tie the three together. We tried to eliminate redundancy and excess verbiage, trimming our justification section to clearly lead into the objectives, and providing specifics in the methods section about data, topics, and tools that directly address the objectives (we also added page numbers!). Responses to specific concerns of the reviewers follow.

Reviewer #1

1. "I simply cannot figure out what their actual objectives are this time around. There is the list of seven goals at the beginning which are loosely tied to "three primary research areas" (community resilience, rural entrepreneurship and community well-being, and energy and land use policies in rural areas).

   We have selected and highlighted the four relevant goals from the USDA REE list of 7 to reduce confusion. We follow this with a better transition into objectives, which ties back to justification/goals.

2. They immediately lay out reasoning for land use, but don't provide an action plan or examples of planned work there. In the methods they say there are two objectives. Following their methods, they provide information about (1) rural economic opportunities and entrepreneurship and (2) resiliency of rural communities. It seems that land use got dropped, which is fine although it's not clear why or why it alone was discussed previously.

   This is now hopefully clearer as it relates to energy development and its effects on rural communities, which ties in with land and water use issues as spelled out in objectives 2d and 2f. It is also discussed in the methods section on objective 2 with an example of research getting underway in West Virginia.

3. "But I cannot see how these two objectives tie to their seven goals, many of which are extremely important topics."

   We have tried to tie the 'goals'—which are drawn from USDA documents--and objectives together by only listing those of the seven goals that relate to our two objectives. We have underlined key terms in the goals which tie directly into the objectives section. There are more 'goals' listed than objectives because the USDA goals are subsumed into the two broad objectives.

4. It is possible that goals 1-3 fall within objective 1, but only the local foods movement is discussed related to these goals. Childcare and finance/infrastructure presumably related to goal 7, although it's not clear how they promote rural-urban interdependence. Perhaps goal 7 should simply read Infrastructure and Prosperity.

   As mentioned in the response to comment #1, we have deleted the full list of goals and now only mentioned the relevant ones. Goal # 1 in the revised proposal, Rural-Urban Interdependence and Prosperity, reflects what we believe to be the broadest goal of our proposed work.

5. "On community resiliency, they come back to local finance and also discuss disasters and spatial economic issues. So where do goals 4-6 (Nutrition and childhood obesity, food safety, and education and science literacy) come into play?"

   Nutrition, obesity, food safety etc. are not relevant to our proposal, so are not specifically mentioned (so as to avoid the confusion we initially caused!). Education and Science literacy is related to education and skill levels, which in turn is related to the chronic labor problems faced by rural communities. It also relates to the "seven capitals" (human capital in particular).

6. How closely related are the goals and the two objectives? Furthermore, the application opens with concerns about an aging population, health concerns and deaths of despair, and statistics about rural veterans. Health and aging concerns are CRITICAL to many rural areas!!! But there is nothing here that addresses health and aging (other than perhaps a transfer of wealth as an economic opportunity) or veterans. But I'd like to see a more cohesive idea of where the project is headed and how the goals and topics fit.

   We have made a more direct reference in objectives and methods to the issue of health care and drug abuse. The issue of veterans is now folded in with the sub-objective on health care infrastructure/provision, 2b. Research on health and aging issues, while it may grow out of the proposal goals, is not a central focus of NE 1079 at this time.

Reviewer #2

7. This specifically why my ratings for many areas were low, is that the approach wasn't clear, and the goals as they related to what was discussed was really a mix of too many things. There is a lot of talk about entrepreneurship and studying this issue in the goals, but there is no specific information given on how you are going to do this. Such as the social capital theory research, how are you going to test this? What data are you going to use? Why is that data set appropriate since a lot of the entrepreneurship data can be problematic in rural areas? I found the idea of looking at child care access a very interesting, important, and understudied issue, and the proposed method for obtaining this data is sound.

   We have kept the child care section in the methods section and expanded with more detail on other topics/data sources/methods. Note also that the child care section

highlights the use of spatial tools in completing the planned research (per the next comment). Specific uses of spatial tools in our proposed work are also highlighted in the methods section. Several specific data sources are now mentioned in the methods section, but of course over the five-year term of the project our work will likely expand considerably, so that both methods and data sources not mentioned in the current proposal will be used.

8. Why is adding spatial econometrics going to advance what you've already done?"

Much of the innovative work done by project members has involved spatial analysis. However, there are many ways to address spatial spillovers and our project team will use the appropriate methods as research unfolds. More details are now included in the objectives and methods sections.

9. "This proposal has a lot of talk about cross-university collaboration, which is important to these types of research, but that alone isn't sufficient justification (in my opinion)"

We have attempted to provide additional detail on past and possible future examples of how state level efforts have evolved into regional efforts. The new proposal also includes substantially more detail on the methods for the research we propose to conduct, and how working together can address the differences and similarities between rural areas and how policies, especially at the federal level, may not work if these differences are not considered.

Reviewer #3

10. The organization of the proposal itself made it very difficult to get a clear idea of what is in fact being proposed. Just as an example, p2 describes 7 (?!) areas of emphasis, with the following page tossing out 22 examples across three of those specified areas, yet with little sense of how the pieces fit into the larger context.

As noted for reviewer #1, these seven areas were actually those proposed by USDA. We have now only mentioned those that are relevant to our proposed research areas and objectives. We have also done away with the bullet list of examples as it clutters the narrative.

11. In the very next paragraphs, the document describes three very different "research areas around which to engage in the coming years: Community Resilience; Rural Entrepreneurship and Community Wellbeing; and Energy and Land Use policies in rural areas," which don't neatly match with any of the previously noted focal areas either. The section on Related, Current, and Previous Work is again a poorly organized collection of concepts and references – all of which lead to now just two Objectives. These Objectives suddenly change narrative structure to a list of Comments, again seemingly randomly tossing out some very good – but also very jumbled – sets of questions."

We have worked to shorten the justification and methods sections and to tie the objectives forward to the methods and backwards to the justification. Rural entrepreneurship is related to both the REE goals and to objective 1, as is community well-being. Energy and land use policies fits under objective 2 (Sustainable Use of Natural Resources) and objective 4 (Responding to Climate and Energy Needs). We hope our objectives and other sections now reflect all three research areas more clearly.

12. The discussion that follows finally does hew to the now manageable set of two Objectives, and finally focuses the proposal a bit. The list of Measurement of Progress is reasonable, but could use further clarity on the distinctions between the more research-oriented metrics and those for Outreach.

    We have added more detailed points to the outreach section.

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1749: Enhancing Rural Economic Opportunities, Community Resilience, and Entrepreneurship

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project with revision
2. Achievable goals/objectives:
Good
3. Appropriate scope of activity to accomplish objectives:
Fair
4. Potential for significant outputs(products) and outcomes and/or impacts:
Fair
5. Overall technical merit:
Fair
Comments
While the constituent research teams have clearly been productive with past funding, this proposal for renewal gave this reviewer substantial pause, especially for such a high-profile multistate initiative. The organization of the proposal itself made it very difficult to get a clear idea of what is in fact being proposed. Just as an example, p2 (lack of pagination doesn't help) describes 7 (?!) areas of emphasis, with the following page tossing out 22 examples across three of those specified areas, yet with little sense of how the pieces fit into the larger context. In the very next paragraphs, the document describes three very different "research areas around which to engage in the coming years: Community Resilience; Rural Entrepreneurship and Community Wellbeing; and Energy and Land Use policies in rural areas," which don't neatly match with any of the previously noted focal areas either. The section on Related, Current, and Previous Work is again a poorly organized collection of concepts and references – all of which lead to now just two Objectives. These Objectives suddenly change narrative structure to a list of Comments, again seemingly randomly tossing out some very good – but also very jumbled – sets of questions. The discussion that follows finally does hew to the now manageable set of two Objectives, and finally focuses the proposal a bit. The list of Measurement of Progress is reasonable, but could use further clarity on the distinctions between the more research-oriented metrics and those for Outreach.

Your Recommendation:
Approve/continue project with revision

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1749: Enhancing Rural Economic Opportunities, Community Resilience, and Entrepreneurship

Rate the technical merit of the project:

1. Sound Scientific approach:
Disapprove/terminate project
2. Achievable goals/objectives:
Fair
3. Appropriate scope of activity to accomplish objectives:
Fair
4. Potential for significant outputs(products) and outcomes and/or impacts:
Good
5. Overall technical merit:
Fair
Comments
From reading this proposal, I don't understand what the proposal is adding. This specifically why my ratings for many areas were low, is that the approach wasn't clear, and the goals as they related to what was discussed was really a mix of too many things. There is a lot of talk about entrepreneurship and studying this issue in the goals, but there is no specific information given on how you are going to do this. Such as the social capital theory research, how are you going to test this? What data are you going to use? Why is that data set appropriate since a lot of the entrepreneurship data can be problematic in rural areas? I found the idea of looking at child care access a very interesting, important, and understudied issue, and the proposed method for obtaining this data is sound. Why is adding spatial econometrics going to advance what you've already done? This proposal has a lot of talk about cross-university collaboration, which is important to these types of research, but that alone isn't sufficient justification (in my opinion) to continue funding this project.
Your Recommendation:
Disapprove/terminate project

Appendix G: Peer Review (Submitted)

Status: Complete

Project ID/Title: NE_TEMP1749: Enhancing Rural Economic Opportunities, Community Resilience, and Entrepreneurship

Rate the technical merit of the project:

1. Sound Scientific approach:
Approve/continue project
2. Achievable goals/objectives:
Fair
3. Appropriate scope of activity to accomplish objectives:
Excellent
4. Potential for significant outputs(products) and outcomes and/or impacts:
Excellent
5. Overall technical merit:
Excellent
Comments
It is clear that this group has continued to do great, collaborative, multi-state work that matters to communities and people. The group also attracts top talent from within the Extension system. There is no doubt in my mind that they should be awarded the opportunity to further these efforts. The methods they provide in their application are appropriate, and they have members with their expertise and experience to fully employ the methods and to accomplish whatever objects related to rural communities they choose to undertake. I always wonder if my reviewer hat it too critical, but I simply cannot figure out what their actual objectives are this time around. There is the list of seven goals at the beginning which are loosely tied to "three primary research areas" (community resilience, rural entrepreneurship and community well-being, and energy and land use policies in rural areas). They immediately lay out reasoning for land use, but don't provide an action plan or examples of planned work there.In the methods they say there are two objectives. Following their methods, they provide information about (1) rural economic opportunities and entrepreneurship and (2) resiliency of rural communities. It seems that land use got dropped, which is fine although it's not clear why or why it alone was discussed previously. But I cannot see how these two objectives tie to their seven goals, many of which are extremely important topics. It is possible that goals 1-3 fall within objective 1, but only the local foods movement is discussed related to these goals. Childcare and finance/infrastructure presumably related to goal 7, although its not clear how they promote rural-urban interdependence. Perhaps goal 7 should simply read Infrastructure and Prosperity. On community resiliency, they come back to local finance and also discuss disasters and spatial economic issues. So where do goals 4-6 (Nutrition and childhood obesity, food safety, and education and science literacy) come into play? How closely related are the goals and the two objectives? Furthermore, the application opens with concerns about an aging population, health concerns and deaths of despair, and statistics about rural veterans. Health and aging concerns are CRITICAL to many rural areas!!! But there is nothing here that addresses health and aging (other than perhaps a transfer of wealth as an economic opportunity) or veterans. Again the work this group is doing is phenomenal, and I heartily recommend that they be allowed to continue and extend it. But I'd like to see a more cohesive idea of where the project is headed and how the goals and topics fit. I'm not recommending the group revise and resubmit. I think the group and its past performance demonstrate competence needed for approved continuation, and I trust they will continue to form a clear body of collaborative and important work. But I really hope they and other projects seeking approval will, in the future, better align their goals and objectives.
Your Recommendation:
Approve/continue project

2017-18 Planning Grants Program

Northeastern Regional Association of State Agricultural Experiment Station Directors (NERA)

The Northeastern Regional Association of State Agricultural Experiment Station Directors (NERA) announces the 9th round of its competitive planning grants program. These grants will be awarded to organize agricultural experiment station scientists and research and outreach partners in the region into teams to address high priority research needs and facilitate the transfer of new research-based knowledge to appropriate audiences. To be considered, proposed programs must be 1) in experiment station mission areas, 2) cross-disciplinary, 3) multistate, and 4) address important needs of the northeast region. Proposed programs must have a clearly defined, strong core of research activities. Programs that also contain well-developed outreach or educational components or other appropriate forms of research implementation will be most competitive. Ideally, teams will focus on new and promising research collaborations or integrated research and outreach/educational activities that bring together specialists in diverse fields to apply complementary approaches to work on an important well-defined problem. The team should include scientists from a minimum of three experiment stations in the northeast. Proposals in support of programs that are forward looking or anticipatory are especially encouraged.

NERA invites applications to support teams in the major mission areas of agricultural experiment stations in the region. Applicants should consider current priorities of potential funding agencies in station mission areas (e.g., USDA-AFRI, NSF, NIH, and others) when developing proposals. For questions on whether topics are appropriate, prospective applicants can contact station directors or the NERA Executive Director (Rick Rhodes; see http://www.nerasaes.org/).

Proposals are due on **August 31, 2017**. Proposals are not to exceed **three** single-spaced pages (reasonable sized typeface and one inch margins) not including the cover page and appendices.

A planning grant review committee comprised of NERA directors will evaluate proposals and make recommendations to the full NERA membership for funding approval. Final decisions will be made by **October 1, 2017**. Applicants may apply for a maximum of **$7,000** of support and NERA expects to make **3 awards**. Funding awards will be available for a maximum of one year from the date of award notification. The funds will be administered by the Office of the NERA Executive Director and will only be used to reimburse actual expenses. Unused funds will be retained by NERA. Funds may only be used to support transportation and meeting expenses to bring teams together for planning and organizational purposes. Funds cannot be used to pay indirect costs and in general will not be awarded for salaries or wages. Planning grant funds cannot be used to support initial research or outreach activities of the proposed program.

Proposals for planning grants should include:

- Cover page (example included)
- Mission and goals of the proposed program
- Justification for the program with a focus on stakeholder needs and the potential for sustained external funding
- Activities to be engaged in by team members towards a more complete definition of the program
- Explanation of roles of team members

- Timetable for completion of the planning activities and preparation of a competitive proposal
- Budget for planning activities (travel, meeting expenses, etc.) not to exceed $7,000
- A statement on whether NERA funding will provide opportunities to leveraging additional resources
- CV of Team Leader – as an appendix (two-page maximum) demonstrating track record of leading cross-disciplinary and/or multi-institutional collaborations

The specific criteria that will be used to evaluate proposals are:
(* = required element. Other elements are preferred only.)

- Addresses an important need in the region*
- Justification demonstrates stakeholder support for the project
- Program has a strong research core*
- Substantial participation by researchers from three experiment station (minimum = 3)*
- Consistent with goals of competitive funding programs*
- Potential for sustained funding*
- Clearly defined planning activities*
- Well-developed outreach or educational components or other research implementation
- Realistic timetable*
- Team members appropriate to proposed activities*
- Team leaders with demonstrated track record*
- Potential support (funding or other) from other entities
- Well written and organized proposal that addresses all the required criteria satisfactorily*

NERA expects that an outcome of a planning grant will be a proposal submitted to a major funding agency specified in the proposal. Grant recipients will be asked to provide a written report at the end of the grant period and subsequent periodic reports on the status of resulting proposals.

In order to provide guidance and feedback from the previous rounds of grant proposals, the following reflect reviewer comments on those proposals:

- Goals not well defined
- Not clear what specific, major, or compelling issues will be addressed
- Priority not well established
- Needs not clearly justified; does this project have a clear stakeholder need or clear stakeholder support; what specific clientele will be served
- Not a strong team of AES scientists or a strong research program
- No specifics on what activities are being planned – what are the key approaches to be used
- Strategy of individual proposal development and then consolidation not clear
- Proposed collaboration not well described
- Deliverables not clear
- Potential for sustainable funding not clear

Please submit planning grant proposals as a ***single pdf file*** by close of business on **August 31, 2017** to David Leibovitz at david_leibovitz@uri.edu. (There's an underscore between david and leibovitz.)

2017-2018 NERA Planning Grants Program

Project Title: _____

_____

Team Leader Contact Information:

Name:	
Address:	
Phone:	
Fax:	
E-mail:	

Team Leader Signature:_____ Date: _____

Station Director Signature:_____ Date: _____

Team Members

Name	**Discipline**	**Institution/Agency/Other**

(Attach an additional sheet if more space is needed.)

2017-2018 NERA Planning Grants Program

Project Title: Scientists Interested In Identifying Non-antibiotic Alternative Therapies for the Treatment of Bovine Mastitis in the NE Region.

Team Leader Contact Information:

Name:	Kasey M. Moyes, PhD, Associate Professor
Address:	4127 Animal Sciences Building
	College Park, MD, 20742
Phone:	(301) – 405 - 2997
Fax:	(301) – 405 - 7980
E-mail:	kmoyes@umd.edu

Team Leader Signature: _____ **Date: __8/30/17_____**

Station Director Signature:__ **___ Date: _8/30/17**

Team Members

Name	Discipline	Institution/Agency/Other
Robert R. Peters, PhD	**Professor and Extension Dairy Specialist**	**University of Maryland Experiment Station**
Sheila Andrew PhD	**Professor and Extension Dairy Specialist**	**University of Connecticut Experiment Station**
Anne Lichtenwalner, DVM, PhD	**Associate Professor and Extension Veterinarian**	**University of Maine Experiment Station**
Ernest Hovingh, DVM, PhD	**Senior Research Associate and Extension Veterinarian**	**Pennsylvania State University Experiment Station**

(Attach an additional sheet if more space is needed.

Mission and goals of proposed program:

Goal: The aim of this proposal is to assemble a team of Northeast (NE) university research and extension experts to develop novel research and outreach projects that meet a critical need for maintaining dairy cattle health and ensuring human health and food safety in the NE region. The team leader (Dr. Kasey Moyes), tenure-track, assistant professor in the Department of Animal and Avian Sciences at the University of Maryland, has procured funding to examine the use of citral, a component of citrus oil, as a new intramammary (IMM) therapeutic for *Escherichia coli* (*E. coli*) mastitis in lactating dairy cows (i.e. Challenge Project). The researchers request funding for travel to the annual National Mastitis Council (NMC; February 2018) for the discussion of preliminary results and the generation of a competitive grant to be submitted to the US Department of Agriculture (USDA) -National Institute of Food and Agriculture (NIFA):Agriculture and Food Research Initiative (AFRI) competitive grant program (June, 2018).

The problem: One of the biggest challenges faced in the modern dairy industry is associated with the reduction in the use of IMM antibiotic therapy for the treatment of bovine mastitis [1]. Growing concerns regarding antibiotic use, the increased risk of antibiotic residues in milk and meat as well as the potential for antimicrobial resistance have all led to the examination of alternative strategies for controlling mastitis [2]. Currently, IMM antibiotic therapy is the most widely used and most effective management strategy to eliminate IMM infections and alleviate pain and suffering. Epidemiological studies have reported that recurring cases are 4.8 times more likely within the next month [3] where up to 40% of recurring cases are treated after failed therapy [4]. Therefore, non-antibiotic alternative therapies for bovine mastitis are warranted to improve therapeutic success, economic outcome and animal welfare. Coliform bacteria may cause as many as 30% to 40% of clinical mastitis cases, even for well-managed dairy herds [5, 6]. It can become responsible for some very acute, painful and potentially fatal forms of mastitis. Therefore, effective treatment for mastitis is critical to maintain overall animal health and profitability for dairy producers. The use of the citral for the treatment of *E. coli* bovine mastitis will facilitate better management strategies to enhance production efficiency, improve animal health, and develop healthy animal products for human use.

In addition, bovine mastitis is a unique disease where multiple infectious agents can trigger the inflammatory response and, therefore, the causative infectious agent is usually unknown. As a result, producers commonly treat with different combinations of antibiotics and routes of treatments that can lead to overuse of antibiotics and increase risk of residues in milk and antibiotic resistance of several mastitis-associated bacteria. The development of non-antibiotic alternative therapies for treatment of bovine mastitis in lactating dairy cows is warranted in order to help reduce future bacterial antimicrobial resistance within the dairy industry. Currently, there are no approved alternative on the US Department of Agriculture (USDA) list of treatments set by the Food and Drug Administration (FDA) indicating that alternative therapies for treatment of disease are lacking for dairy producers.

Even though antibiotics have saved millions of lives [7], there is growing interest in products from animals raised without antibiotics [8]. According to priorities within the 2014 farm bill, expanding our knowledge regarding the use of alternative therapies to treat disease, thereby reducing production costs and enhancing nutritional quality of products for human consumption while improving animal health, is a top priority. International agencies have also emphasized the need to find alternative approaches for treatment of animal disease and to identify the role of antibiotics used in animal agriculture in the emergence of antimicrobial resistance of human pathogens [9]. This study would place NE region as a leader regarding identifying alternative therapies for treatment of bovine mastitis both nationally and internationally.

Dissemination of Data: Results will be available to stakeholders via extension programs in Maryland, Connecticut, Maine and Pennsylvania, that have demonstrated well-developed outreach platforms, and results will be submitted for consideration for publication in peer-reviewed research journals most relevant to the research area. The generation of a competitive grant will be submitted.

Mission Areas: The proposed project relates to the goals of experiment stations in the NE region. This project will contribute to the sustainability of dairy farmers by providing information on non-antibiotic alternative therapies for treatment of bovine mastitis in lactating dairy cows to help reduce future bacterial antimicrobial resistance in the NE region. As land availability decreases due to the growing urban population, improving efficiency on-farm is the key to sustainability for dairy producers in the NE region and we feel that non-antibiotic alternative therapies for treatment of bovine mastitis offers improved management and production efficiency that will place the NE region at the forefront of identifying alternative therapies for treatment of disease nationally and internationally.

The focus of this proposal falls directly within the USDA-NIFA:AFRI competitive grant program. The data obtained will be used to apply for an external competitive grant evaluating the use of citral for treatment of naturally occurring bovine mastitis in the NE region. Preliminary data indicate that citral is a promising new treatment for *E. coli* bovine mastitis.

Justification Relative To Stakeholder Need and Potential For Sustained External Funding:

Relevance to Stakeholders: The current proposal is the outcome of numerous interactions with stakeholders at national and regional workshops, and group discussions with producers. Discussions with producers hoping to enhance animal health have provided us with abundant information to develop and address the research and extension needs. We will share our research results with our larger stakeholder groups through extension websites, conferences, and publications. This will allow stakeholders to review progress and outcomes of this work and to discuss important issues related to agriculture with researchers and one another on a continuing basis. Lead by scientists in the NE region, results from this project will strengthen dairy producers' capacity to improve milk quality through improving animal health and reduce future bacterial antimicrobial resistance within the dairy industry.

Addresses Needs of the NE Region: The proposed project relates to the goals of experiment stations within the NE region. This project will contribute to the sustainability of dairy farmers by providing information, via extension websites, presentation at conferences and publications in journals. Studies reported that citrus oil inhibits the growth of a wide range of microbes such as *Mycobacterium bovis* [10], *E. coli* strain O157:H7 [11], *Campylobacter jejuni* [12] and *S. aureus* [13]. Therefore, this potential therapeutic can expand to other species of interest, including poultry and humans. Coupled with more direct sales dairy farms, land availability continues to decrease in the NE region. Improving efficiency on-farm is the key to sustainability for dairy farmers in the NE region and we feel that non-antibiotic alternative therapies for treatment of bovine mastitis offers improved management and human food safety that will place the NE region at the forefront of identifying alternative therapies for treatment of disease nationally and internationally.

Potential for Sustained Funding: The focus of this proposal falls directly within the USDA-NIFA:AFRI competitive grant program. The preliminary data obtained will be used to apply for an external competitive grant evaluating the use of citral for treatment of naturally occurring bovine mastitis in the NE region where Dr. Moyes (team leader) will serve as a 'Principle Investigator 'as part of the NIFA national priority area of 'Animal Health and Production and Animal Products' with area of focus 'Animal Health and Disease (code A1221)' where Drs. Peters, Andrew, Lichtenwalner and Hovingh (team members) will serve as co-principle investigators.

Activities to be engaged in by team members toward a complete definition of the program:

Team Leader (Dr. Kasey Moyes, University of Maryland)

Project Expertise and Feasibility:

Drs. Moyes (UMD), Andrew (UCONN), Lichtenwalner (UMA) and Hovingh (PSU) are members of NMC and the NE-1048 Multi-State Regional Project that encourages and enhances multi-state, multi-disciplinary research on critical issues that have a national or regional priority. All scientists will participate with data interpretation, generation of competitive grants and the writing of manuscripts.

Roles of Team Members:

Team member, Discipline, Institution	Role on team
Kasey Moyes, Ph.D. Animal Science UMD Agricultural Experiment Station	Team Leader, project coordination and administration, research design, methods and analysis, dissemination of results via peer-reviewed publications, generation of grant.
Robert Peters, Ph.D. Animal Science UMD Agricultural Experiment Station	Team Member, research design, dissemination of results via extension and peer-reviewed publications and generation of grant.
Sheila Andrew, Ph.D. Animal Science UCONN Agricultural Experiment Station	Team Member, research design, dissemination of results via extension and peer-reviewed publications and generation of grant.
Anne Lichtenwalner DVM, Ph.D. Animal Science UME Agricultural Experiment Station	Team Member, research design, dissemination of results via extension and peer-reviewed publications and generation of grant.
Ernest Hovingh DVM, Ph.D. Animal Science PSU Agricultural Experiment Station	Team Member, research design, dissemination of results via extension and peer-reviewed publications and generation of grant.

Timetable:

Deliverables/Milestones	**2018**	**2019**		
	4Q	1Q	2Q	3Q
Discussion regarding research design for Mastitis Challenge Project	x			
Travel to NMC		x		
Discussion regarding results for Mastitis Challenge Project and generation of grant		x	x	
Submission of grant/Publication/Release to Public			x	x

Budget Request $5,785:

- Travel (n = 5): $5,485
  - Registration: $1,500
  - Lodging: $ 1,500
  - Meals: $485
  - Transportation (including airfare and hotel [2 nights]): $2,000
- Extension Outlets (extension websites and room reservation): $300

NERA Funding and Additional Opportunities:

The focus of this proposal falls directly within the USDA-NIFA AFRI competitive grant program and will attract industry professionals as well as future seed grant programs within the NE region.

CV of Team Leader:-see appendix II

Appendices I: Refence List

1. Kaneene JB, Hurd HS: **The national animal health monitoring system in Michigan. III. Cost estimates of selected dairy cattle diseases**. *Prev Vet Med* 1990, **8:**127-140.

2. Bannantine JP, Olsen SC, Kehrli ME, Jr., Stanton TB, Casas DL, Whipple DL, Zuekle KA: **High-impact animal health research conducted at the USDA's National Animal Disease Center**. *Vet Microbiol* 2013, **165:**224-233.

3. Houben EH, Dijkhuizen AA, van Arendonk JA, Huirne RB: **Short- and long-term production losses and repeatability of clinical mastitis in dairy cattle**. *J Dairy Sci* 1993, **76:**2561-2578.

4. Hillerton JE, Kliem KE: **Effective treatment of *Streptococcus uberis* clinical mastitis to minimize the use of antibiotics**. *J Dairy Sci* 2002, **85:**1009-1014.

5. Barkema HW, Schukken YH, Zadoks RN: **Invited Review: The role of cow, pathogen, and treatment regimen in the therapeutic success of bovine *Staphylococcus aureus* mastitis**. *J Dairy Sci* 2006, **89:**1877-1895.

6. Bradley A: **Bovine mastitis: an evolving disease**. *Vet J* 2002, **164:**116-128.

7. Oliver SP, Murinda SE, Jayarao BM: **Impact of antibiotic use in adult dairy cows on antimicrobial resistance of veterinary and human pathogens: a comprehensive review**. *Foodborne Pathog Dis* 2011, **8:**337-355.

8. Consumer Reports: **Meat on Drugs: The Overuse of Antibiotics in Food Animals and What Supermarkets and Consumers Can Do to Stop It.** Yonkers, NY; 2012.

9. Food and Agriculture Organization, World Health Organization, W: **Report of the joint FAO/WHO/OIE expert meeting on critically important antimicrobials.** Rome, Italy; 2007.

10. Crandall PG, Ricke SC, O'Bryan CA, Parrish NM: **In vitro effects of citrus oils against *Mycobacterium tuberculosis* and non-tuberculous Mycobacteria of clinical importance**. *J Environ Sci Health B* 2012, **47:**736-741.

11. Nannapaneni R, Muthaiyan A, Crandall PG, Johnson MG, O'Bryan CA, Chalova VI, Callaway TR, Carroll JA, Arthington JD, Nisbet DJ, Ricke SC: **Antimicrobial activity of commercial citrus-based natural extracts against *Escherichia coli* O157:H7 isolates and mutant strains**. *Foodborne Pathog Dis* 2008, **5:**695-699.

12. Nannapaneni R, Chalova VI, Crandall PG, Ricke SC, Johnson MG, O'Bryan CA: ***Campylobacter* and *Arcobacter* species sensitivity to commercial orange oil fractions**. *Int J Food Microbiol* 2009, **129:**43-49.

13. Muthaiyan A, Martin EM, Natesan S, Crandall PG, Wilkinson BJ, Ricke SC: **Antimicrobial effect and mode of action of terpeneless cold-pressed Valencia orange essential oil on methicillin-resistant *Staphylococcus aureus***. *J Appl Microbiol* 2012, **112:**1020-1033.

APPENDICES II: CURRICULUM VITAE-Dr. Kasey M. Moyes

Assistant Professor (tenure-track), Department of Animal and Avian Sciences,
University of Maryland, College Park.

EDUCATION and TRAINING

Doctor of Philosophy, University of Illinois at Urbana-Champaign
Graduation: December 22, 2008
Advisors: Dr. James K. Drackley (U of I); Dr. Juan J. Loor (U of I);
Dr. Klaus Lønne Ingvartsen (Denmark)
Major: Animal Sciences Emphasis: Nutritional Immunology of Dairy Cattle

Certificate of Business Administration, University of Illinois
Graduation: May 2005

Master of Science, University of Connecticut, Storrs, CT
Graduation: May 2004
Advisor: Dr. Sheila M. Andrew
Major: Nutrition and Milk Quality Emphasis: Dairy Cattle

Bachelor of Science, Michigan State University, East Lansing, MI
Graduation: May 2001
Advisor: David K. Beede
Major: Animal Science

RESEARCH and PROFESSIONAL EXPERIENCE

2001-2004	Graduate Research Assistant Department of Animal Science, University of Connecticut, Storrs
2004-2008	Graduate Research Assistant Department of Animal Science, University of Illinois at Urbana-Champaign
2009-2012	Post-Doctoral Research Assistant Department of Animal Science, Aarhus University, Tjele, Denmark
2012-	Assistant Professor, tenure-track, Department of Animal and Avian Sciences, University of Maryland, College Park

GRANTS: Collaborators and Affiliations

$25,485 Peters/Stahl/Moyes 12/1/15-12/31/16
MAES/ANSC
Title: Funding for telemetry equipment at the University of Maryland dairy farm to support Extension and applied research using SCR - Dairy Activity and Rumination Monitoring.

$30,500 Moyes/Peters/Johnson 1/1/13-12/31/14
MAES Integrative Research and Extension Grant
Title: Estimating and quantifying the economic impacts, production outcomes and lifestyle changes for small-to medium sized dairy farms regarding the transition from conventional to Automatic Milking Systems in the Mid-Atlantic region.

$9,850 Peters/Moyes/McCoy 6/1/12-12/31/12
MAES
Title: NC1042: Management Systems to Improve the Economic and Environmental Sustainability of Dairy Enterprises

PEER-REVIEWED PUBLICATIONS (TOTAL = 37; most relevant listed):

1. C.M. Scholte, D.C. Nelson, S. Linden, T.H. Elsasser, M. Garcia, Y. Qu and **K.M Moyes**. 2017. Short Communication: Recombinant bacteriophage endolysin, PlyC, is non-toxic and does not alter blood neutrophil response in lactating dairy cows. J. Dairy Sci. *Under review*.

2. **K.M. Moyes**, P. Sørensen and M. Bionaz. 2016. The impact of intramammary *Escherichia coli* challenge on liver and mammary transcriptome and cross-talk in dairy cows during early lactation using RNAseq. PLOSOne. 23. Doi: 10.1371/journal.pone.0157480. eCollection 2016.

3. **K.M. Moyes**, L. Ma, T. McCoy and R. Peters. 2014. A survey regarding the interest and concerns associated with transitioning from conventional to automated (robotic) milking systems for managers of small to medium-sized dairy farms. Professional Animal Scientist. 30:418-422.

4. Rezamand, P., T.A. Hoagland, **K.M. Moyes**, L.K. Silbart, and S.M. Andrew. 2007. Energy status, lipid-soluble vitamins, and acute phase proteins in periparturient Holstein and Jersey dairy cows with or without subclinical mastitis. J. Dairy Sci. 90:5097-5107.

5. Borm, A.A., L.K. Fox, K.E. Leslie, J.S. Hogan, S.M. Andrew, **K.M. Moyes**, S.P. Oliver, Y.H.Schukken, D.D. Hancock, C.T. Gaskins, W.E. Owens, and C. Norman. 2006. Effects of prepartum antibiotic therapy on udder health, milk production, and reproductive performance in dairy heifers. J. Dairy Sci. 89:2090-2098.

6. **Moyes, K. M.**, S.M. Andrew, and L.S. Hinckley. 2004. Efficacy of a re-formulated teat disinfectant for prevention of bovine mastitis. Pages 345-346 in Natl. Mastitis Counc. Ann. Mtg. Proc., Charlotte, NC. Natl. Mastitis Counc., Inc., Madison, WI.

EXTENSION PUBLICATIONS

1. **Moyes, K.M**., J.K. Drackley, J.L. Salak-Johnson, D.E. Morin, J.C. Hope, and J.J. Loor. 2008. Dietary induced negative energy balance has minimal effects on innate immunity during a *Streptococcus uberis* mastitis challenge in dairy cows during mid-lactation. Pages 12-14. Illinois Dairy Report. Univ. of Illinois, Urbana.

2. **Moyes, K.M.**, J.K. Drackley, M. Bionaz, D.M. Morin, S. Rodriguez-Zas, R.E. Everts, H.A. Lewin, and J.J. Loor. 2008. How does the mammary gland respond during the initial stages of an intramammary infection (IMI) with *Streptococcus uberis*? A genomic-level approach. Pages 15-16. Illinois Dairy Report. Univ. of Illinois, Urbana.

2017 Funding Opportunity: NEED/NERA Seed Grant Proposals

Submission date: September 8, 2017

The Northeast Extension Directors (NEED) and the Northeastern Regional Association of State Agricultural Experiment Station Directors (NERA) are seeking seed grant proposals that clearly integrate research and Cooperative Extension and will lead to the submission of a full project proposal in the competitive grant funding portfolios of the Agriculture and Food Research Initiative (AFRI), the National Science Foundation, National Institute of Health or Food and/or Drug Administration.

This opportunity supports the travel and other activities required to bring a research/Extension team together, leading to the preparation and submission of a competitively funded grant proposal. We plan to support 4 proposals at a maximum of $5,000/proposal.

Objective: **NEED and NERA intend to facilitate the coalescing of researchers and Extension personnel from regional institutions in an effort to increase success in the preparation, submission and winning of a large (e.g., >$500,000) multi-institutional, integrated research and Extension grant.**

Seed Grant Proposal Requirements: Seed grant proposals are limited to 3 pages (single-spaced, not including cover sheet), 12 pt font, 1-inch margins of narrative that should include the following elements.

- How will you use these dollars to facilitate the development of a full grant application?
- What is the problem in agriculture, food systems, or the environment that you will address in a full grant application to a funding agency? Why is it important to address the problem? (What is the justification for addressing the problem?)
- What gaps in knowledge prevent the development and implementation of solutions to this problem? What are the primary hypotheses the research will address?
- What Extension activities are needed to address the problem and achieve desired outcomes?
- With what competitive grants program(s) is this work aligned?
- Who are the team members and what roles will they play in the grant application planning process? What is the planning process timeline?

***Seed Grant Proposal Team Requirements*:** The teams must include Extension and research members from two or more Land-grant institutions in the Northeast region.

While the leadership and majority of the membership of the teams should be from Northeast states, researchers and Extension educators from other regions may participate.

***Proposal Submission*:** Please submit seed grant proposals as a **single pdf file** by the close of business on September 8, 2017 to David Leibovitz at david_leibovitz@uri.edu.

Seed Grant Proposal Evaluation: Proposals will be assessed by the Northeast's Multistate Activities Committee (MAC). The MAC is composed of members of NEED and NERA. Final decisions will be made by October 6, 2017. Final proposals will be evaluated using the following rubric:

1. *Addresses an important problem. (20%)*

- Excellent (17-20): Problem is clearly defined, stakeholders identified, stakeholder need is aligned with research and Extension activities.
- Good (12-16): Problem is defined, stakeholders not clearly defined, and/or the alignment between the need and the stakeholders not clear.
- Needs improvement (0-11): Problem is not clearly defined, stakeholders not identified.

2. *Justification (20%)*

- Excellent (17-20): Justification is clear and well-described, the research hypotheses and Extension activities are clear and well-described.
- Good (12-16): Justification is provided but lacks sufficient development or description of hypotheses and/or Extension activities to make the proposal compelling.
- Needs improvement (0-11): Justification lacks sufficient development or is not clear.

3. *Consistent with external funding programs/potential for submission of a grant proposal (20%)*

- Excellent (17-20): The proposal is aligned with external funding agencies; there is high potential that the planning effort will yield a compelling grant proposal.
- Good (12-16): The proposal describes the relationship of the planning activities with the funding intent of a granting agency, however the specifics of the alignment are not clearly defined or described.
- Needs improvement (0-11): The proposal does not clearly identify how the planning activities align with an external funding agency.

4. *Defined planning activities that clearly integrate research and Extension (20%*

- Excellent (17-20): The planning activities are clear and describe the integration between research and Extension. There is high likelihood that that the activities will lead to a compelling grant proposal.

- Good (12-16): Planning activities are described but do not clearly define the integration of research and Extension.
- Needs improvement (0-11): Planning activities do not indicate integration of research and Extension.

5. *Team Capacity*

- Excellent (17-20): The team has capacity and an excellent track record. There is a high likelihood that the team will be able to write a compelling grant proposal as a result of the work supported by the seed grant.
- Good (12-16): The team shows promise, but may not have a clear track record of success. The likelihood of a successful grant project proposal is not clear or compelling.
- Needs improvement (0-11): The team does not have sufficient breadth to support a high likelihood for writing a compelling grant proposal.

***Award Management*:** Funding up to $5,000 will be available for a maximum of one year from the date of award notification. The funds will be administered by the Offices of the NEED and NERA Executive Directors and can only be used to reimburse actual expenses. Unused funds will be retained by NEED and NERA. Funds may be used to support transportation, meeting expenses, or other well-justified activities to facilitate the planning and organizing of multi-state, integrated research and Extension grant proposals. Funds *cannot be used to pay indirect costs, salaries or wages*.

Examples of successful NEED/NERA grant applications are posted on the NERA website at http://www.nerasaes.org/planning-grants.

2017 NEED/NERA Seed Grant Proposals Cover Page

Project Title:

Team Member Name	Discipline	Affiliation (AES, CE, both, or other)	Institution/Agency/Other

(Attach an additional sheet if more space is needed.)

Team Leader Contact Information:

Name:	
Address:	
Phone:	
E-mail:	