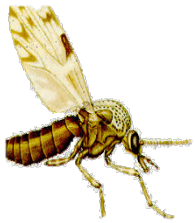
Action Plan
National Program 103
Animal Health
2022-2027

United States Department of Agriculture

Agricultural Research Service



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National Program 103
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Vision

The vision for the program is to be the leading scientific organization for agricultural animal health research worldwide.

Mission

The mission of the program is to deliver scientific information and tools to detect, control, and eradicate animal diseases that impact agriculture and public health.

Relationship of this National Program to the USDA Strategic Plan

This Action Plan outlines research that directly supports the USDA FY2018-2022 Strategic Plan by contributing to Strategic Goal 2: Maximize the Ability of American Agricultural Producers to Prosper by Feeding and Clothing the World. Specifically, it addresses the following Objectives:

Objective 2.2: Increase Agricultural Opportunities and Support Economic Growth by Creating New Markets and Supporting a Competitive Agricultural System; and

Objective 2.3: Protect Agricultural Health by Preventing and Mitigating the Spread of Agricultural Pests and Disease.

Relationship of this National Program to the USDA Science Blueprint

This Action Plan outlines research that supports Theme 1- Sustainable Ag Intensification of the 2020-2025 USDA Science Blueprint.

Additionally, this Action Plan advances OneUSDA Scientific Excellence through interconnectedness with other USDA agencies and mission areas. Research outlined in this Action Plan also supports Goal 2, Safeguarding American Agriculture, in the Animal and Plant Health Inspection Service Strategic Plan FY 2019-2023. This action plan specifically outlines research that supports: **Objective 2.1:** Prevent damaging plant and animal pests and diseases from entering and spreading in the United States to promote plant and animal health; **Objective 2.2:** Manage plant and animal pests and diseases once established in the United States to promote plant and

animal health; and **Objective 2.3:** Ensure effective emergency preparedness and response systems.

Relationship of this National Program to the USDA ARS Strategic Plan

Research outlined in this Action Plan falls under Strategic Goal Area 4, Animal Production and Protection, in the 2018-2020 ARS Strategic Plan. This action plan specifically outlines research that supports Goal 4.3: Protect and ensure the safety of the nation's agriculture and food supply through improved disease detection, prevention, and control. Research supporting ARS Goal 4.3 will further support ARS crosscutting priorities, including research projects directly addressing antimicrobial resistance and increasing the understanding of the microbiome on animal health. Further collaborations with scientists working on animal production (Goal 4.1); veterinary, medical, and urban entomology (Goal 4.4); and food safety (Goal 1.2) will be used to facilitate a systems biology approach to addressing these goals.

Performance Measure for Goal 4.3: Provide scientific information to protect animals, humans, and property from the negative effects of pests and infectious diseases. Develop and transfer tools to the agricultural community, commercial partners, and government agencies to control or eradicate domestic and exotic diseases and pests that affect animal and human health.

Introduction

Animal production is a major enterprise in the United States. Together, livestock and poultry industries employ over 5 million people and account for over half of U.S. agricultural cash receipts, often exceeding $100 billion per year. The United States has the most efficient animal production system in the world. According to the North American Meat Institute, the United States annually processes 9 billion chickens, 240 million turkeys, 32 million cattle and calves, 2.2 million sheep and lambs, and 121 million hogs. The United States is the world's third-largest producer and consumer of pork and pork products. In recent years, the United States has been either the world's largest or second largest exporter of pork and pork products. The USDA National Agricultural Statistics Service reports that the U.S. poultry industry produces 100 billion chicken eggs every year. The USDA Economic Research Service reports that cattle production is the most important agricultural industry in the United States with 27 billion pounds of beef produced in 2019, accounting for $66.2 billion in cash receipts in 2019. Overall, cattle production represents about 18 percent of the $374 billion in total cash receipts forecast for agricultural commodities in 2019.

As we advance into the 21st century, animal agriculture will continue to be critically important, not only for the United States, but for the well-being of people across the globe. The United Nations Food and Agricultural Organization has estimated that well over one billion farmers and their families are dependent on agricultural animals for their livelihood. The health of animals continues to be a priority as farmers endeavor to meet sustainable agricultural goals, lessen the impact of animal agriculture on the environment, while increasing production to feed a growing world population.

Endemic infectious diseases and pests remain the primary cause of production losses, compromising the health and welfare of farm animals. Importantly, foreign animal disease outbreaks and the emergence of new zoonotic pathogens in the last decade have devastated agricultural economies and affected the health of people worldwide. Recent examples include the 2014-2015 avian influenza outbreak in the United States resulting in the loss of 45 million birds, the spread of African swine fever to China in 2017 resulting in the loss of half the world's pig population, and the emergence of SARS-CoV-2 in Wuhan, China, in December 2019, resulting in a worldwide pandemic. The emergence of these three infectious agents alone has exposed significant gaps and vulnerabilities in the ability to effectively respond to disease outbreaks, human and animal. Investments in animal health research have never been more critical as we contemplate the threat of emerging diseases on global food security and the sustainable growth and resilience of a safe food supply for a growing world population. Enhancing the health of animals in agricultural production systems will directly impact food quality and ensure a sufficient supply of macro and micro-nutrients to meet people's basic needs. When combined with other investments in agricultural development, research-based innovations in animal health will address fundamental constraints in production and improve food insecurity by reducing risks associated with infectious diseases and pests.

Achieving results in animal health research in the 21st century will require a "One Health" approach in which research in animal, human, and environmental health are integrated through strategic collaborations across multiple scientific disciplines in the discovery of new knowledge and the development of countermeasures for preventing, treating, and controlling diseases.

The goal of National Program 103 (NP 103), Animal Health, is to protect and ensure the safety of the Nation's agriculture and food supply through improved disease detection, prevention, and control. Basic and applied research approaches will be applied to solve animal health problems of high national priority. Accordingly, the USDA-ARS Animal Health National Program fosters the alignment of research expertise and the establishment of strategic partnerships with other government, private, and university research organizations in the United States and partner countries to increase the speed of scientific discoveries. Emphasis will be given to methods and procedures to control animal diseases through the discovery and development of:

- Diagnostics
- Vaccines and vaccine platforms
- Biotherapeutics
- Alternatives to antibiotics
- Disease management systems
- Disinfectants
- Farm biosecurity measures

The Animal Health National Program prioritizes the following cross-cutting, strategic competencies:

Scientific Excellence

1. Strengthen core competencies in comparative pathology and immunology.
2. Develop core competencies in field epidemiology and predictive biology.
3. Combat antimicrobial resistant bacteria and assist stakeholders to optimize the use of antibiotics through the discovery and development of alternatives to antibiotics.
4. Lead integrated, interdisciplinary teams to support innovation and increase the resilience of animal agriculture against infectious disease incursions (supporting Grand Challenge-Synergies concepts).
5. Develop expert research laboratories recognized by the World Organization for Animal Health (OIE) and the United Nations Food and Agriculture Organization (FAO).

Capabilities

6. Establish ARS laboratories into a highly effective, highly responsive and adaptable research network, to maximize use of core competencies and resources.
7. Sustain specialized high-containment facilities to study zoonotic and high consequence transboundary and emerging diseases.
8. Maintain a cadre of scientific infectious disease expertise enabling ARS to rapidly respond to any emerging or reemerging disease.

Training

9. Sustain best-in-class training centers to attract our nation's top veterinarian researchers and animal-health scientists.

Technology Transfer

10. Sustain an effective technology transfer program to achieve the full impact of research discoveries.

The Animal Health National Program will build these strategic competencies by addressing them in the six components of this action plan. Each component includes problem statements that together define the scope of the action plan.

Importantly, this national program will also capitalize on the broad expertise across the USDA-ARS agricultural research enterprise by aligning project plans with other national programs in areas that have the potential to foster innovation and maximize sustainable production. Research components draw upon relevant expertise within NP 103, but will also espouse ARS Grand Challenges-Synergies (GCS) concepts by seeking contributions from scientists working across national programs to enable the integration of existing projects in different national programs that offer the potential for synergistic benefits; e.g., NP 101 (Animal Production), NP 104 (Veterinary, Medical and Urban Entomology), NP 106 (Aquaculture), NP 107 (Human Nutrition), NP 108 (Food Safety), NP 215 (Grass, Forage, and Rangeland Agroecosystems), and NP 303 (Plant Diseases); for example capitalizing on the microbiome research in Animal Production to enhance Animal Health outcomes, and reduce the need for

antimicrobial use, thus coordinating and integrating that expertise to develop a specific useful application of the knowledge. Projects within the research components are expected to attract additional federal, university, and industry partners at both the national and international level. The aim of these partnerships will be to strengthen component projects. Partners will bring unique skills and capabilities that will enable and enhance, the anticipated products of the component projects. A significant number of projects in the animal health research portfolio focus on the discovery of novel technologies; technology transfer strategies will be identified to maximize the impact of the research and help foster investments by the private sector in the development of these technologies.

NP 103 will also actively engage in ARS-wide investments in artificial intelligence, big data, super-computing and precision livestock management, where appropriate, to enhance the analysis of collected data and deliver novel solutions for animal agriculture's most pressing problems.

The stakeholders, partners and documents that provided critical input to inform this action plan are identified in Appendix 1 and 2. Importantly, a national survey was conducted to broadly reach out to stakeholders and partners to evaluate the success and relevance of past and current ARS Animal Health National Program activities and collect input for our next 5 year' targets. The results of this survey with the list of diseases and their ranking in terms of importance to producers (beef, dairy, poultry, pork, sheep, goats, wildlife, including captive bison and cervids), government agencies, academia, pharmaceutical industry, and scientific associations, are provided in Appendix 3, 4, 5, and 6.

The anticipated products of the animal health program are:

- Methods to detect, analyze, and effectively respond to new and emerging pathogens that threaten agriculture and public health.
- Methods and tools for producers to remain profitable while adapting farming practices to meet consumer expectations.
- Support for "One Health" initiatives through research programs that will benefit animal health, public health, and biomedical research communities, including the development of animal disease models that serve both animal and human health.
- Solutions to create and maintain a barrier to pathogens at the domestic-wildlife animal-human interfaces.
- Integrated research programs to discover genetic variations associated with disease susceptibility to increase our farmers' productivity and competitiveness.
- Enhanced United States and global food security through solutions to problems incurred by domestic and transboundary animal diseases of livestock and poultry.

Component 1: Biodefense

Biodefense research at ARS is extensively linked to the President's National Biodefense Strategy. ARS has unique and critical resources dedicated to ensuring that agricultural production is secure from the threat of foreign and emerging zoonotic animal diseases, whether the cause is due to a natural event, accidental, or deliberate exposure. These

resources include high containment Biosafety Level (BSL)-3 laboratories and BSLAg-3 animal facilities located at Orient Point, New York, Athens, Georgia, and Ames, Iowa. One new important resource will be the National Bio and Agro-Defense Facility (NBAF) that will enable for the first time the ability to conduct research on especially dangerous zoonotic BSL-4 pathogens. These critical resources are dedicated to protecting people, their animals, our food supply and the nation's agriculture economy.

Because many dangerous pathogens have the potential to rapidly spread across national borders, ARS maintains a global view of the biological threats to food and agriculture. Animal production is always threatened by diseases, naturally or deliberately introduced into a naïve healthy population of productive animals. These diseases vary in the degree of economic loss they cause, their potential to spread, and ease of control and eradication. Furthermore, each year new disease-causing agents are discovered, new pathogens emerge, known organisms mutate to unrecognized forms, and new pathways of agent introduction are created. Therefore, in the face of uncertainty and the inability to protect against every conceivable microbiological attack, the best biodefense program for countering biological threats to animal agriculture will be to enhance our ability to predict and monitor the emergence of new pathogens, and develop tools to enhance disease surveillance, prevent the spread of diseases, and increase biosecurity on farms. These are the tools that will most rapidly allow farmers to maintain, or in the case of disease most rapidly return to production.

Since many of the especially dangerous known animal pathogens are foreign and do not exist in the United States, disease research must extend to countries where the diseases exist. Partnerships with research organizations in other countries are therefore essential in implementing a biodefense research program against animal disease outbreaks. The program must include research on the ecology of the pathogen in their endemic settings to understand how a disease agent survives outside of the host, how the microorganism moves between susceptible hosts, how the pathogen affects the animal, and how it then escapes from the host. Increased research on how pathogens move between countries and between farms will allow prevention programs to enhance on-farm biosecurity and reduce the chance of pathogen introductions. In order to respond to a disease incursion, research must provide tools for accurate and continuous surveillance and vaccination programs. To ensure producers can return to full production and export their products as rapidly as possible, research must also provide the means to prove that animals are free of the disease.

To address these challenges, USDA-ARS will focus its biodefense research program on four strategic areas that directly support the National Biodefense Strategy: 1) predicting the emergence of pathogens in livestock and associated wildlife; 2) understanding the ecology of exotic, emerging, and re-emerging pathogens; 3) incidence response research; and 4) the development of veterinary medical countermeasures for early detection (diagnostics), prevention (vaccines), and treatment (biotherapeutics) of foreign and emerging animal diseases.

Strategic Area 1 consists of predicting the emergence of new pathogens by identifying the molecular determinants required to adapt to new animal hosts with an emphasis on livestock, poultry, wildlife, and humans.

Strategic Area 2 consists of field research in endemic settings to understand the ecology of animal pathogens that are exotic to the United States to determine the drivers (pathogen, host, and environment) that collectively enable their sustainability and evolution.

Strategic Area 3 falls under the incident response research program (emergency research in response to a new disease outbreak) and consists of conducting expedited animal infection studies to determine whether 1) U.S. livestock, poultry, or wildlife are susceptible to a new pathogen causing disease in humans or animals, and 2) determine if available medical countermeasures are effective, or not, against the pathogens causing the disease outbreak (i.e., do available laboratory diagnostic tests and vaccines work against an emerging pathogen).

Strategic Area 4 consists of rapidly advancing the development of new medical countermeasures to detect, prevent, or treat foreign and emerging pathogens in reservoir hosts, including the development of animal models to conduct pre-clinical testing of human and animal drugs and vaccines.

All sectors that completed the 2020 ARS Animal Health Stakeholder Survey (government, academia, industry, and livestock and poultry producers) identified research on foreign animal diseases as a national priority. Importantly, stakeholders identified each of the following foreign animal diseases as one of the 10 most important diseases that have the potential of significantly affecting animal agriculture in the United States: Foot-and-Mouth disease (67%), African swine fever (62%), avian influenza (58%), virulent New Castle disease (35%), and classical swine fever (25%), Rift Valley fever (7.7%), Peste des Petits Ruminants (7.3%) Pox viruses (Parapox, Sheeppox, Capripox) 5.5%, Crimean Congo Hemorrhagic fever (4.3%), Japanese encephalitis (4.1%), Nipah virus (3.9%), Contagious Bovine Pleuropneumonia (3.4%), Lumpy Skin disease (3.1%), and Bovine Ephemeral fever (1.1%).

All producers that completed the 2020 ARS Animal Health Stakeholder Survey (beef, dairy, pork, poultry, sheep, goats, and wildlife) also identified research on several emerging and re-emerging diseases a national priority. The following emerging animal diseases were identified as one of the 10 most important diseases that have the potential of significantly affecting animal agriculture in the United States: Bluetongue virus (17%), Epizootic Hemorrhagic disease (10%), West Nile virus (20%), Vesicular Stomatitis virus (6.8%), Egg drop syndrome (6.8%), Seneca Valley virus (5.3%), Schmallenberg virus (3.6%), and Cache Valley fever (3.5%).

Although recognized as potential threats to animal agriculture, ARS does not currently have resources to implement research for the following diseases:

- West Nile virus
- Lumpy Skin disease
- Peste des Petits Ruminants
- Heartwater
- Egg drop syndrome
- Pox viruses

- Cache Valley fever
- Schmallenberg virus
- Bovine Ephemeral fever

Problem Statement 1A: Control and eradicate foreign animal diseases
Animal health officials define an exotic or foreign animal disease as an important transmissible livestock or poultry disease believed to be absent from the United States and its territories that has the potential of resulting in significant public health or economic impact if it enters the country.

To protect the long-term health and profitability of U.S. animal agriculture, incursions of a foreign animal disease must be prevented or rapidly controlled. In the United States, disease control usually means disease eradication. Disease eradication is currently accomplished by eliminating the animal, resulting in loss of invested resources in feed and housing, loss of income to the farm community, public opposition, and environmental disruption. In addition to control costs, one of the most immediate and severe consequences of a foreign animal disease occurrence in the United States is the loss of export markets. As we move into the 21st century, many new issues and factors are affecting foreign animal disease prevention, control, management, and recovery. These factors include free trade agreements, free trade blocks, regionalization, increased international passenger travel, intensification of animal production, the constant evolution of infectious agents, and the uncertain impact of biotechnology and agroterrorism.

Current methods for rapid response to disease outbreaks caused by high consequence pathogens such as the euthanasia of infected animals and carcass disposal, are not socially, environmentally, or economically optimal. Control tools for the early identification, prevention and eradication of many foreign animal diseases don't exist or are inadequate. Further, our understanding of epidemiology, pathogenesis, and transmission is insufficient to develop effective countermeasures to prevent, control, and eradicate foreign animal disease outbreaks globally.

Priority foreign animal diseases identified as the most important in the 2020 ARS national animal health survey that will be the focus of the USDA-ARS research program include Foot-and-Mouth disease, African swine fever, avian influenza, Virulent Newcastle disease, Classical Swine fever, Rift Valley fever, and Japanese encephalitis. Other priority foreign animal diseases that ARS will also be able to include in its biodefense research program when the NBAF becomes operational in 2023 include the following BSL-4 agents Nipah virus and Crimean-Congo Hemorrhagic fever.

Research Focus:
In order to control foreign animal disease, a wide variety of agent detection platforms need to be developed and validated. Information for design of these platforms will come in part from further knowledge of pathogen genomics and proteomics and in part from understanding the evolution and genetic variability of disease agents. Although many of the foreign animal diseases have existed for years in other countries, there is still much more fundamental knowledge of these agents that is required. There remains a lack of understanding of host

range and tissue tropism, carrier state, duration and routes of shedding, transmission mechanisms (e.g. vectors, fomites, aerosols), ecology, and epidemiology (e.g., wildlife reservoirs). If these diseases should enter the United States, more effective prevention and control tools—such as suitable short-term control and recovery cost strategies need to be developed. There is also a need for vaccines that can differentiate infected and vaccinated animals (DIVA) and biotherapeutics suitable for strategic stockpiles, as well as integrated methods of disease control—including vector control associated with arthropod-borne animal diseases and animal management; all of these tools lead to a better capability to regain country disease-free status and retain economic sustainability.

Anticipated Products:

- Veterinary medical countermeasures to prevent economic losses from foreign animal diseases in agricultural and wildlife species.
- Effective countermeasures to prevent and eliminate the threat of emerging zoonotic diseases with pandemic potential in agricultural and wildlife species.
- Provide scientific information to producers and action and regulatory agencies so they can establish science-based on-farm practices that will maximize "biosecurity" to protect farms from naturally or intentionally introduced pathogens that threaten food security, farm productivity, and the trade and export of agricultural products.
- Integrated predictive modeling capability for foreign animal disease incursions and the collection of data to support these models.
- Experimental animal disease models that will serve the veterinary and public health research communities to significantly shorten the timelines for developing breakthrough medicines and disease prevention tools.
- Novel detection systems and broad-spectrum vaccines and biotherapeutics to counter the threat of emerging diseases or engineered biological weapons.
- Novel countermeasures against the natural or intentional introduction of agricultural threats, including new methods for detection, prevention, and characterization of high-consequence agents.

Potential Benefits:

- Rapid control and eradication of foreign animal diseases.
- Efficient and cost-effective means of protecting farmers and people.
- Mitigate the impact of foreign animal disease outbreaks on trade of agricultural products.
- Mitigate the impact of foreign zoonotic disease on public health and people.
- Avoid the destruction of millions of animals as a countermeasure to a foreign animal disease outbreak.
- Reduce the time needed to recover from a foreign animal disease outbreak.
- Support action and regulatory federal and state agencies in responding and controlling a foreign animal disease outbreak.

Problem Statement 1B: Predict and prevent emerging diseases

A seminal paper published in 2005, Mark Woolhouse and colleagues at the Centre for Infectious Diseases, University of Edinburgh, conducted an extensive survey of the scientific literature and reported that they had identified 1,407 human pathogens, 58% of which were zoonotic. Of the total, 177 were regarded as emerging or re-emerging. Importantly, zoonotic

pathogens were twice as likely as nonzoonotic pathogens to be in this category of emerging diseases. Recent examples of emerging zoonotic diseases include the emergence of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in 2003, pandemic H1N1nfluenza virus in 2009, Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) in 2012, and pandemic SARS-CoV-2 in 2019.

The World Health Organization has reported that 17% of all infectious diseases are vector-borne diseases transmitted by mosquitoes, ticks, lice, and flies. In a groundbreaking paper published in 2008, Peter Daszak and colleagues at the Consortium for Conservative Medicine, New York, reported that 29% of emerging diseases in the last decade were vector-borne. Recent examples of emerging vector-borne diseases outbreaks include West Nile virus in New York in 1999, Zika virus in Brazil in 2015, and Bluetongue in Northern Europe in 2006. In 2017, *Haemophysalius longicornis*, an invasive tick species was first identified in the United States and in 2019 the pathogen *Theileria orientalis* Ikeda strain was identified in infected cattle in Virginia. *H. longicornus* is a competent host for this pathogen strain, previously undetected in the United States.

Moreover, new emerging and re-emerging diseases constantly assail animal agriculture. Recent examples including Porcine Epidemic Diarrhea Virus in 2013, highly pathogenic avian influenza H5N8 in 2014-2015, and virulent Newcastle disease in 2018-2020.

The economic impact of emerging disease outbreaks can be devastating. According to the U.S. swine industry, the emergence of the 2009 pandemic H1N1 influenza virus cost industry $1.3 billion. According to the Congressional Research Service, the 2014-2015 H5 highly pathogenic avian influenza outbreak resulted in the euthanasia of 48 million birds and an economic loss of $3.3 billion.

Many factors—globalization of trade, movement of masses of people and agricultural products, changing weather patterns, rapid population growth in cities, intensive agriculture, limited genetic diversity in farm animals, changes in farm practices—are creating new opportunities for the emergence and spread of new infectious diseases. Exotic (non-native) organisms, once introduced into the United States, can escalate into an epidemic because of the absence of vaccines or effective drugs, lack of resistance in host animals, and limited resources to effectively manage the spread of such pathogens.

Priority emerging and re-emerging vector-borne animal diseases identified as the most important in the 2020 ARS national animal health survey that will be the focus of the USDA-ARS research program include Bluetongue, Vesicular Stomatitis, and Epizootic Hemorrhagic Disease.

The program will also include research on emerging zoonotic diseases such coronaviruses (e.g., SARS-CoV-2), influenza viruses (e.g., avian influenza H5N1 and H7N9, and swine influenza H1N1 and H3N2), and flaviruses (e.g., Japanese encephalitis) to increase our ability to predict the emergence of new zoonotic pathogens with pandemic potential.

Research Focus:
Our capability to rapidly identify, characterize, control, and eradicate new emerging animal pathogens is not well developed. Accordingly, emphasis will be given to filling gaps in our toolbox for predicting the emergence of new pathogens. For example, the inclusion of climatic and ecological information during disease outbreaks is nascent or rarely included in predictive models as it requires access to supercomputing capability for analysis of large data sets. The pathogen-host molecular interactome, consisting in part of protein-protein or nucleic acid-protein interactions, have yet to be deciphered. Environmental parameters that may affect virus-host molecular interactions and/or contribute to epigenetic effects is another significant gap in our knowledge base. Collectively, these gaps have resulted in the failure of models to reliably predict and forecast the emergence of new disease outbreaks. Once a new agent has been identified and isolated, there is a need to conduct whole genome sequencing of the pathogen to identify unique sequences for diagnostic discovery and field epidemiology research. Research will be conducted to identify mechanisms of disease, disease transmission, and host range specificity to determine the prevalence and emerging potential of new diseases. Emergency response research will be needed in real time when a disease outbreak occurs to minimize the impact to animal agriculture. Ultimately, good research will lead to predictors of disease emergence and disease outbreaks and the development of the appropriate intervention strategies.

Anticipated Products:
- Identification of new pathogens associated with emerging diseases.
- Identification of molecular determinants that enable emerging pathogens to infect new animal hosts, including humans.
- Integrated predictive modeling capability for emerging infectious diseases of animals and the collection of data to support these models.
- Comprehensive maps of virus-host interactions required for pathogens to adapt to new hosts.
- Three-dimensional epidemiological information, integrating metagenomics with climatic and ecological data.
- Multi-scale big-data integration models for predicting the emergence of new pandemic pathogens.
- Methods to rapidly detect and characterize the etiology of new and emerging diseases.
- Knowledge on effectiveness of existing diagnostic and control technologies to enable rapid control of the disease.

Potential Benefits:
- Availability of predictive models for early warning and rapid response to emerging diseases outbreaks.
- Advance the development of new diagnostic platforms for the early detection of emerging diseases.
- Advance the development of veterinary medical countermeasures fit for the emergence of new pathogens.
- Ability to better control emerging diseases and rapidly implement intervention strategies to respond to new disease outbreaks.

Component 1 Resources:
The following ARS locations have research projects addressing the problem statements identified under Component 1:

- Ames, Iowa
- Athens, Georgia
- Manhattan, Kansas
- Orient Point, New York
- Pullman, Washington

Component 2: Antimicrobial Resistance

Antibiotics are one of the most important medical discoveries of the 20th century and will remain an essential tool for treating animal and human diseases in the 21st century. However, antimicrobial resistance among bacterial pathogens and concerns over the prudent use of antibiotics in animals has garnered global attention. Importantly, the availability of effective medical interventions to prevent and control animal diseases on the farm is likely to impact global food security. Accordingly, more attention needs to be given to the discovery of novel technologies and strategies that can be used to prevent or treat animal diseases that commonly require the use of antibiotics.

USDA-ARS is an active participant in the President's Task Force for Combating Antibiotic Resistant Bacteria (CARB) and assisted in the development of the 2020-2025 National Action Plan (NAP). This component is in alignment with Goal 4 of the NAP to "Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines." USDA-ARS proposes to address knowledge gaps and develop effective, practical solutions that will provide stakeholders with tools to optimize the use of existing antibiotics, including the development of alternatives to antibiotics to prevent and treat animal diseases.

Additional reports that inform the USDA-ARS research program include the August 2020 report released by the American Veterinary Medical Association Committee on Antimicrobials, entitled "Antimicrobial Resistant Pathogens Affecting Animal Health in the United States." The report highlights key pathogens by commodity and identifies research and non-research needs to comprehensively address the problem. In 2015 and 2018, the OIE hosted ad hoc Groups to prioritize animal diseases for which improved vaccines would reduce the need for antibiotics. These prioritized lists include bacterial, viral and parasitic diseases, since viral and parasitic diseases can predispose to secondary bacterial infections that require antibiotic treatment. The entire NP 103 program researches many of the diseases listed in these three reports and are working towards preventive and mitigation strategies making this component cross-cutting.

All sectors that completed the 2020 ARS Animal Health Stakeholder Survey (government, academia, industry, and livestock and poultry producers) identified research on antimicrobial resistance and the development of alternatives to antibiotics a national priority. Importantly, 40% of stakeholders identified the development of alternatives to

antibiotics as one of the 10 most important issues currently affecting or that have the potential of affecting animal agriculture in the United States.

Stakeholders identified many AMR priorities that ARS does not currently have the capacity to conduct research on, including:

- Research into AMR in companion animals, including horses;
- Research into socio-economic aspects of AMR including stewardship and antibiotic selection and use.

AMR research in food-safety pathogens such as *Campylobacter*, *Escherichia coli* and *Salmonella* are addressed in the Food Safety NP 108. Alternatives to antibiotics in Aquaculture are addressed in the Aquaculture National Program NP 106. Changes to management strategies to enhance animal well-being are addressed in the Animal Production National Program NP 101.

Problem Statement 2A: Combat antimicrobial resistance through the development of Alternatives to Antibiotics

Alternatives to antibiotics to optimize the use of medically important antibiotics for animal diseases are a priority for animal health and necessary for animal well-being. ATAs are broadly defined as any substance that can be substituted for therapeutic drugs that are increasingly becoming ineffective against pathogenic bacteria, viruses, or parasites while not contributing to the development of antimicrobial resistance.

In 2012, 2016, and 2019 ARS organized three international symposia on alternatives to antibiotics in animal production in collaboration with the International Alliance for Biological Standardization (IABS), the World Organisation for Animal Health (OIE), the U.S. National Institutes of Health, the U.S Food and Drug Administration, and the European Medicines Agency. The purpose of these symposia was to highlight promising research results and novel technologies that could potentially lead to the development of alternatives to conventional antibiotics (www.ars.usda.gov/alternativestoantibiotics). Numerous promising alternative strategies have been proposed that need further investigation, including vaccines, prebiotics, probiotics, bacteriophages, bacteriophage gene products, bioactive phytochemicals, essential oils, naturally occurring bacterial lytic enzymes, animal-derived antimicrobial peptides, small interfering ribonucleic acids, immune enhancers, and recombinant and hyperimmune therapeutic antibodies.

Lastly, the mechanisms by which antibiotics enhance feed efficiency, health and weight gain in livestock and poultry production remain largely unknown; defining the mechanisms and interactions of these chemicals with the animal's physiology, microbiome and immune system will lead to the ability to rational design alternatives to antibiotics to improve animal health and production efficiency.

Research Focus:
Antibiotic resistant pathogens are prevalent in modern veterinary and human health care and new preventive and treatment strategies and technologies are needed to address them. Several

alternatives to antibiotics have been proposed and some are already commercially available as feed supplements. However, there is a critical need to understand their mechanisms of action, and ensure they are efficacious and safe. Importantly, well-controlled clinical studies are needed to determine how they may be used effectively in the field to replace antibiotics for the prevention and treatment of animal diseases, and when applicable, improved feed efficiency and weight gain.

Anticipated Products:

- Highly effective vaccines and therapeutics that could reduce the need for antibiotics in animal agriculture.
- New biotherapeutic platforms based on protective host proteins to induce and supplement an animal's innate immune response.
- Alternatives to antibiotics with defined mechanisms of action that can be used to enhance the health and well-being of animals and provides opportunities for integrating nutrition, health, and disease research.
- Validated preventive health management programs derived from the re-engineering of the gut microbiomes using specially designed feed rations and diets.

Potential Benefits:

- Provide tools to allow farmers and veterinarians to optimize the use of antibiotics in animal agriculture.
- Availability of new medical countermeasures to prevent and treat animal diseases.
- Availability of new tools fit for intensive animal production systems.
- Availability of new feed additives with defined modes of action to enhance the health of agricultural animals.
- Healthy and productive herds and flocks.

Component 2 Resources:
The following ARS locations have research projects addressing the problem statements identified under Component 2:

- Ames, Iowa
- Athens, Georgia
- Beltsville, Maryland
- East Lansing, Michigan
- Orient Point, New York
- Pullman, Washington
- Mississippi State, Mississippi
- Clay Center, Nebraska

Component 3: Endemic Bacterial Diseases

Endemic bacterial diseases cost U.S. farmers and poultry producers through production losses and costs of treating sick animals, every day. With increased scrutiny on the use of antibiotics

in food producing animals, some farmers and producers are changing their management practices to never use antibiotics which makes the need for improved diagnostic, preventive and treatment strategies all the more pressing for controlling these challenging diseases. Several bacterial diseases that are a part of this component are zoonotic, meaning that they pass from animals to humans and thus also pose a public health risk. Brucellosis and Tuberculosis are two of these diseases and are also part of targeted control and eradication programs into which the U.S. government has invested millions of dollars. Priority diseases include but are not limited to Brucellosis, Mycobacterial diseases, Anaplasmosis, *Coxiella burnetti*, Spirochete diseases, Mycoplasma respiratory disease, *Mannheimia hemolytica*, *Pasturella multocida*, Avian Pathogenic *Escherichia coli* (APEC) and others.

For the purposes of this action plan, the endemic bacterial diseases are grouped by 1) Zoonotic Bacterial Diseases 2) Respiratory Bacterial Diseases and 3) Production-Related Bacterial Diseases.

Stakeholders representing the livestock and poultry industries that responded to the 2020 ARS animal health national survey identified research to prevent and mitigate the impact of endemic bacterial diseases as a national priority. The following endemic bacterial diseases were identified as one of the 5 most important diseases that have the potential of significantly affecting animal agriculture in the United States: 34% of beef producers identified anaplasmosis, 77% of dairy industry - mastitis, 55% of the dairy industry - digital dermatitis, 20% of government representatives – bovine tuberculosis and 25% of government representatives – brucellosis.

ARS will continue to work with other government partner agencies such as USDA-APHIS and HHS CDC to inform their efforts for control of these diseases in animal and human populations.

Stakeholders identified many priorities that ARS does not currently have the resources to conduct research on, including:

- Bacterial diseases of turkeys such as *Ornithobacterium rhinotracheale, Bordetella avium,* and Clostridial diseases (Gangrenous dermatitis);
- Bacterial diseases of horses such as *Streptococcus equi* and *Burkholderia mallei* (Glander's);
- *Streptococcus equi* subspecies *zooepidemicus* in swine causing high mortality in cull sows and feeder pigs;
- Liver abscesses of cattle- *Fusobacterium necrophorum;*
- Infectious keratoconjunctivitis (Pink eye)- *Moraxella* spp. and *Mycoplasma* spp.,
- *Chlamydia psittaci*- Psittacosis; and
- Biothreat agents such as Anthrax, *Francisella tularensis* (Tularemia), Plague (*Yersinia pestis*) and *Burkholderia mallei.*

Problem Statement 3A: Mitigate the consequences of zoonotic bacterial diseases

In developing countries, zoonotic diseases stand out as the most prevalent and important threat to public health. Zoonoses also have a negative impact on commerce, travel, and economies worldwide. In industrialized nations, zoonotic diseases are particularly concerning

to the agricultural sector. Priority diseases include those that are especially difficult to diagnose and cause substantial morbidity and mortality, resulting in significant economic costs to producers when they persist or reemerge. Because many determinants of zoonotic diseases lie outside the purview of the human health sector, agriculture and the animal health community must play an important role in preventing these diseases from propagating in domestic animals, starting with proper surveillance systems. Over the years, USDA has invested significant resources in attempts to eradicate endemic zoonoses from livestock populations in the United States (e.g., brucellosis and tuberculosis). However, their persistence in wildlife reservoirs continues to pose challenges. Moreover, some zoonotic agents have been identified as having the potential to be used for bioterrorism. Effective countermeasures are needed to eliminate zoonotic agents at their animal source and protect our Nation from these important public health threats.

The ARS zoonotic bacterial diseases research program focuses on brucellosis, leptospirosis, tuberculosis, and Q-fever with the strategic goal of developing countermeasures to diagnose and prevent disease transmission in domestic livestock and wildlife reservoir hosts and to provide subject matter expertise to federal and state agencies tasked with control programs for these diseases.

Research Focus:

Brucellosis

USDA-ARS research will focus on the development of rationally designed Brucellosis vaccines for both livestock and wildlife species. This will include emphasis on delivery platforms that are conducive to vaccination of wildlife species and may allow for oral remote delivery or extended antigen release. Research will also focus on improved diagnostic development to delineate between brucella species as well as be used in a multitude of livestock and wildlife species. Basic research in antigen discovery, comparative immunology, genomics and transcriptomics are critical to the successful development of efficacious vaccines and diagnostics.

Leptospirosis

USDA-ARS research will focus on the characterization of circulating leptospires to inform vaccine and diagnostic development. This will include characterizing emerging spirochete strains associated with field outbreaks, and culturing leptospires under different conditions to assess antigenic differences. There is a need to determine *Leptospira* gene expression changes under improved culture conditions and in multiple infection models to design vaccines that are effective in multiple hosts. Improved diagnostic tools will support molecular epidemiology studies to understand the ecology of *Leptospira* species and the emergence of new serovars and ultimately lead to better disease control.

Tuberculosis

USDA-ARS research will focus on the need to develop efficacious vaccines that can work in livestock and wildlife. It will also work on the development of improved diagnostic tests with an emphasis on next generation technologies that could allow for remote or continuous disease surveillance. There is a continued need to characterize *Mycobacterium bovis*

infections, pathogenesis, and immune responses in domestic livestock and relevant wildlife reservoir hosts.

Q-Fever

There is a need to develop new technologies for diagnosing and mitigating the risk of *Coxiella burnetii* transmission from ruminant livestock that are effective, economically-feasible and ecologically responsible.

Anticipated Products:

- Scientific information to inform and assist regulatory and public health partners in establishing science-based management strategies in support of eradication and outbreak control programs.
- Effective vaccine platforms to prevent and control zoonotic bacterial diseases in livestock and relevant wildlife reservoir hosts.
- Diagnostic and intervention strategies for wildlife reservoirs of zoonotic bacterial diseases that will enable control and eradication.
- Knowledge of the pathogenesis of *Brucella* species to identify mechanisms of protective immunity in different host species.
- Scientific information on the protective immune responses to spirochete antigens in large and small animal disease models.
- The transcriptome and antigenic expression of pathogenic *Leptospira* species to identify differentially expressed genes to characterize virulence traits for selection of vaccine candidates.
- Scientific information on the molecular pathogenesis of *Mycobacterium bovis* infections.
- Improved sensitive and specific diagnostic platforms amenable to the rapid screening of large cattle herds for bovine tuberculosis.
- Host genetic tools to prevent or reduce ruminant shedding of *Coxiella burnetii*.

Potential Benefits:

- Targeted surveillance and control programs that eliminate new sources of infection and increase our ability to eradicate brucellosis and bovine tuberculosis in the United States.
- Ability to conduct vaccine discovery research and develop new diagnostic platforms to protect against Leptospirosis.
- Decreased incidence of and protection from spirochete-associated zoonoses.
- Ability to safeguard individuals with potential exposure *Coxiella burnetti*-containing aerosols.
- Enhanced production and distribution of livestock products.
- Enhanced and retained access of United States-grown livestock to domestic and foreign markets.
- Protection for the United States and trading partners from the agricultural, ecological, and economic threat posed by animal and human disease.

Problem Statement 3B: Mitigate respiratory bacterial diseases of livestock species
Across species of agricultural importance, respiratory disease is one of the most common causes of morbidity and mortality. The National Animal Health Monitoring System's (NAHMS) Beef Feedlot 2011 study found that an estimated 21.2% of beef cattle (2.29 million) placed in feedlots were affected by respiratory disease. The total cost for treating 2.29 million cattle for respiratory disease is, estimated to be USD $54.12 million, not including production losses due to morbidity and mortality. In the 2013 NAHMS study, 21.5% of layer farms had issues with respiratory disease. Antibiotic usage for prevention and therapy of respiratory disease is widespread and very costly to producers and is not sustainable. Respiratory disease complexes are polymicrobial and often include concurrent viral infections. This problem statement will focus on the bacterial causes of respiratory disease and Component 4 will address the viral components. There will be overlap and collaboration between projects addressing bacterial and viral components of respiratory disease.

The list of infectious agents that cause bacterial respiratory disease in cattle is extensive and ARS will focus on *Mannheimia hemolytica, Pasteurella multocida,* and *Mycoplasma bovis.*

The list of infectious agents that cause bacterial respiratory disease in swine is extensive and includes *Glasserella parasuis, Streptococcus suis*, *Mycoplasma hyopneumoniae*, *Bordetella bronchiseptica*, and *Pasteurella multocida*.

ARS will focus on *Mycoplasma* species causing respiratory diseases in poultry, sheep, and bison.

Research Focus:
Cattle, Swine, and Bison
There is a need to characterize the pathogenesis of polymicrobial infections associated with respiratory disease of cattle and swine. There is a need to define mechanisms and virulence factors, such as biofilm formation used by respiratory pathogens to cause disease and identify and characterize changes in gene expression of both the host and bacterial respiratory pathogens during the infection. There is also a need to characterize the mechanisms of development of antimicrobial resistance in these pathogens as well as detail changes in the microbiome after administration of antibiotics.

Poultry
There is a continued need to characterize the pathogenesis of *Mycoplasma* species in order to develop improved diagnostics and vaccines for disease control programs. There is also a need to better understand the epidemiology of infection to support the implementation of control programs.

Sheep
In addition to the cost to the sheep and goat industry of morbidity and mortality associated with respiratory diseases, there is the additional concern about transmission of respiratory diseases from domestic to wild sheep populations. Research needs include defining the

pathogenesis of important bacterial pathogens, developing diagnostic tests that accurately identify different bacterial species, identifying the host range of the bacterial species, defining and comparing the immune responsiveness of domestic and wild sheep in respiratory disease; defining the role of host genetics in susceptibility/resistance to respiratory disease and defining the role of management practices on infectious agent transmission and respiratory disease outcome.

Anticipated Products:

- New knowledge of pathogen interactions that lead to polymicrobial infections and respiratory disease complexes in livestock species of agricultural importance.
- Vaccines for preventing and treating respiratory diseases.
- Determine the important immune responses necessary for limiting bacterial respiratory disease in livestock species.
- Identify the genetic determinants of respiratory disease susceptibility.
- Identify mechanisms of development of antimicrobial resistance in swine respiratory pathogens and perturbations to the microbiome due to antibiotic administration.
- Identify mechanisms of disease transmission between livestock and associated wildlife species.

Potential Benefits:

- Ensure an economically viable and safe food supply through alternatives to antibiotics, including vaccines, to prevent and treat respiratory diseases.
- Ability to equip regulatory agencies with the knowledge required to elucidate risk of disease transmission between sheep and bighorn sheep.
- Ability to allow sheep ranchers to continue their livelihoods by having strategies to diagnose, prevent, and mitigate shedding.
- Enhanced economic base of the veterinary biomedical commercial enterprise.

Problem Statement 3C: Diagnose and mitigate strategies for production related bacterial diseases

Production-related bacterial diseases are often insidious and are associated with intensive management practices of high-producing animals. As such, there are multiple factors that may predispose an animal to develop these diseases. These diseases affect American farmers daily through production losses, treatment costs and often premature culling of animals. It is estimated that Anaplasmosis costs producers $300 million annually and Johne's disease costs producers between $200 and $1500 million annually.

The ARS production bacterial diseases research program focuses on Johne's disease, Mastitis, Digital dermatitis, Anaplasmosis and Avian Pathogenic *E.coli* (APEC) with the strategic goal of developing diagnostics and countermeasures to prevent disease in domestic livestock.

Research Focus:
Much of this research overlaps with Component 2: Antimicrobial Resistance since effective mitigation and intervention strategies will allow for farmers and veterinarians to optimize antibiotic use.

Genomic and proteomic analyses of *M. paratuberculosis* (MAP) are needed to identify immunogens that may be differentially expressed in subclinical and clinical stages of disease. In concert with studies in microbial genomics, studies on host immune responses are needed during the different stages of disease to ascertain potential mechanisms to control infection with MAP.

There is a need to develop alternatives to antibiotic and immunologic-based strategies to prevent and control bovine mastitis. Functional genomics studies are needed to understand the genetic differences between animals that are more resistant to infection with common mastitis pathogens.

Historically, Anaplasmosis has been controlled using in-feed tetracyclines. Restrictions on the use of antibiotics in feed makes this a non-sustainable control measure. Producers require better vaccines and vaccine platforms, and basic research to characterize the immune responses of animals that can be used to identify correlates of protection as well as disease resistance and disease tolerance in order to develop effective, sustainable control strategies.

Digital Dermatitis is one of the leading causes of lameness in dairy cattle. It is treated with antibiotic footbaths or administration of systemic antibiotics. In order to develop more sustainable treatments for this disease, alternatives to antibiotics need to be developed through basic research to understand disease pathogenesis, development of reliable animal models and partnerships to develop and test new antibiotic alternatives. Sequencing of lesion material to identify all causative pathogens is also needed.

Avian Pathogenic *E.coli* causes collibacillosis and is one of the most commonly occurring and economically devastating bacterial diseases of poultry worldwide. Improved vaccines and vaccine platforms are needed in addition to elucidating molecular determinants of pathogenesis, strain variation, and tissue tropisms. In concert with animal production and engineering scientists, there is a need to investigate management strategies that may help prevent further infections.

Anticipated Products:

- Understanding of the pathogenesis of priority endemic production diseases such as Johne's, mastitis, digital dermatitis, Anaplasmosis and APEC for the development of improved diagnostics, therapeutics and vaccine platforms.
- Understanding of host immune responses that determine host resilience to control different stages of disease for the development of targeted therapeutics.
- New biotherapeutic platforms/immune stimulators based on protective host proteins to induce and supplement the host's immune response.
- Define bacterial pathogenesis with the outcome of new targets for intervention of persistent or chronic infections.

Potential Benefits:

- Ability to prevent and treat production-related diseases in order to ensure an economically viable and safe food supply.

Component 3 Resources:
The following ARS location has research projects addressing the problem statements identified under Component 3:

- Ames, Iowa
- Pullman, Washington
- Mississippi State University, Mississippi
- Clay Center, Nebraska

Component 4: Endemic Viral Diseases

Preventing and controlling endemic viral diseases are critical to ensure the health, well-being, and productivity of farm animals throughout their production cycle. The aim is to mitigate the threat that endemic diseases pose to farm animals to ensure agricultural production is secure, sustainable, and efficient to provide American consumers a healthy, safe, and affordable food supply. Endemic viral diseases are especially challenging because of their rapid spread and impact on sustainable production. For the purpose of this action plan, priority endemic diseases that most impact animal agriculture in the United States are classified as either respiratory diseases or production diseases.

Viral respiratory diseases are separated from production diseases in this action plan because of their significant economic impact, high level of prevalence in intensive management systems, their propensity to favor secondary bacterial infections, and challenges in preventing them despite the implementation of the best on-farm biosecurity measures. Most respiratory diseases present themselves as disease complexes involving several primary and secondary viral and bacterial pathogens, complicating control and prevention strategies. The vast majority of the economic impact of these diseases is due to the hidden cost of sub-clinical disease where animals are infected but show no apparent disease symptoms. Livestock and poultry that develop respiratory diseases have notable decreases in growth performance. Even with the majority of livestock and poultry being vaccinated for a number of primary pathogens associated with respiratory disease today, lesions are still prevalent at slaughter and their impact on weight gain and carcass quality is significant. Respiratory diseases continue to be a major problem today, in spite of decades of using control measures such as antibiotics and vaccines.

Production diseases are inherently linked to the type of production system used in animal farming (e.g., intensive versus extensive), the agricultural product (meat, dairy product, wool, or eggs), and the types of animals selected, including their genetic and phenotypic characteristics. Some of the common production diseases associated with intensive management systems include oncogenic viruses associated with poultry and dairy production, avian reoviruses associated with arthritis and tenosynovitis in poultry, and enteric viruses that affect poultry and pork production.

Stakeholders representing the livestock and poultry industries that responded to the 2020 ARS animal health national survey identified research on respiratory and production viral diseases

a national priority. Because of the sheer number of pathogens involved in respiratory and production diseases and the ability of many pathogens to cross the species barrier, ARS will use available resources to focus strategically on priority viral respiratory pathogens associated with the bovine, porcine, and poultry. Emphasis will be given to the design of experimental animal disease models to test newly discovered technologies and countermeasures, with the eventual goal of validating them under field conditions through strategic partnership with industry.

Producers that completed the 2020 ARS Animal Health Stakeholder Survey (beef, dairy, pork, poultry, sheep, goats, and wildlife) ranked the following endemic viral diseases as the most important diseases that have the potential of significantly affecting animal agriculture in the United States:

Beef - Viral Diarrhea Virus (BVDV) 61%, Bovine Respiratory Syncytial Virus (BRSV) 48%, Infectious Bovine Rhinotracheitis (IBR) 44%, Bovine Leukemia 4.3%.

Dairy – Bovine Viral Diarrhea Virus (BVDV) 67%, Bovine Leukemia 56%, Infectious Bovine Rhinotracheitis (IBR) 56%, Bovine Respiratory Syncytial Virus (BRSV) 33%, Malignant Catarrhal Fever (MCF) 11%.

Swine - Porcine Reproductive and Respiratory Syndrome (PRRS) 100%, Swine Influenza Virus (SIV) 75%, Porcine Coronavirus (PEDV/PDCoV) 75%, and Porcine Circovirus 50%.

Poultry – Infectious Bronchitis Virus (IBV) 47%, Marek's Disease Virus (MDV) 47%, Infectious Laryngotracheitis (ILT) 40%, Reoviruses 33%, Infectious Bursal Disease (IBD) 27%, low virulent Newcastle Disease 13%, Avian Leukosis 13%, Avian Pneumovirus (APV) 6.7%. None of the poultry producers identified Reticuloendotheliosis virus (REV) and Poult Enteritis Mortality Syndrome (PEMS) as important diseases.

Sheep - Bovine Viral Diarrhea Virus (BVDV) 19%, Bovine Respiratory Syncytial Virus (BRSV) 15%, Infectious Bovine Rhinotracheitis (IBR) 15%, Malignant Catarrhal Fever (MCF) 7.4%.

Goats – Goat producers did not identify any endemics viral diseases of importance but did identify the following emerging diseases - discussed under Problem Statement 1B - as important: Bluetongue 50%, West Nile Virus (33%), and Vesicular Stomatitis (17%).

Wildlife (includes captive bison and cervids): Malignant Catarrhal Fever (MCF) 50%, Bovine Viral Diarrhea Virus 50%, and Bovine Respiratory Syncytial Virus (BRSV) 25%.

The following endemic viral diseases will not be included in the ARS Animal Health National Program because they were either identified as low priority by producers or ARS has insufficient resources to implement the research:

- Avian Leukosis
- Avian Pneumovirus
- Bovine Leukemia

- Infectious Bronchitis Virus
- Newcastle Disease (Low virulent)
- Poult Enteritis Mortality Syndrome (PEMS)
- Reticuloendotheliosis virus

Problem Statement 4A: Prevent respiratory viral diseases of livestock and poultry
Respiratory diseases are the single most costly adverse event facing producers today. Animals raised in intensive management systems are especially vulnerable to the introduction and rapid spread of respiratory pathogens. Many of these respiratory pathogens work in concert to form co-infections that result in a respiratory disease complex comprised of primary viral pathogens and secondary bacterial infections. Although improvements in genetics, housing, equipment, and disease surveillance has allowed continued improvements in disease prevention, industry has historically depended on vaccination programs and preventive feed medication. However, with fast industry growth and market maturity new challenges have risen in animal agriculture. As discussed under Problem Statement 2A, a key challenge for producers today is the loss of effective antibiotics due to antimicrobial resistance and the inevitable restrictions imposed by regulatory agencies to preserve medically important antibiotics for human use. This has drawn attention to the need for alternatives to antibiotics, including improved vaccines to effectively control primary viral respiratory pathogens that often trigger the use of antibiotics to treat secondary bacterial infections. The assessments conducted by the OIE in 2015 and 2018 by infectious diseases experts clearly demonstrate the need for effective vaccines to prevent respiratory viral pathogens like Bovine Viral Diarrhea, Porcine Reproductive and Respiratory Syndrome, and swine influenza. Each of these infectious agents contribute on their own to significant economic losses, but also the aberrant use of antibiotics in cattle, pig, and poultry production.

Recent National Animal Health Monitoring System (NAHMS) surveys confirm that respiratory disease continues as the leading cause of morbidity and mortality in U.S. cattle feedlots and is the most common cause of weaned dairy heifer mortality. Economists working on the USDA National Institute of Food and Agriculture (NIFA)-funded Bovine Respiratory Disease Consortium Coordinated Agricultural Project used the national estimate of 16% incidence of bovine respiratory disease (BRD) in feedlots and calculated that more than 4 million feedlot cattle were affected by the disease in 2013 alone. Based on the cost of treating BRD-affected cattle, they estimated BRD cost $254 per head in 2013, or more than $1 billion annually. Death losses to BRD are estimated to be just under 400,000 head for beef cattle, and the number reaches 1.1 million head when you include dairy calves. This represents the single largest variable cost of cattle production for cattle producers. The nature of cattle production and marketing in the United States produces an exceptional challenge to efforts directed at disease control. Movement of cattle from cow-calf operations to stockers to feed yards increases stress and provides high levels of exposure to numerous infectious agents. Countermeasures, such as vaccines or biotherapeutics, must therefore be deployed rapidly and need to be highly effective. A variety of vaccines to a number of respiratory pathogens are commercially available and widely used to mitigate the effects of several significant viral pathogens, though additional viruses, not present in current vaccines are playing a role in disease pathogenesis. Increasing our understanding of disease threats and the discovery of

countermeasures specifically designed to control and prevent disease introductions are critical to sustain the efficiency of the U.S. cattle industry.

According to previous NAHMS surveys, respiratory disease was the single greatest cause of mortality in swine, accounting for 28.9 percent of nursery deaths and 39.1 percent of deaths in grower/finisher pigs. The National Pork Board has consistently listed the porcine respiratory disease complex (PRDC) as a top research priority. The list of viral infectious agents that cause respiratory disease in swine is extensive and includes porcine reproductive and respiratory syndrome virus (PRRSV), swine influenza virus (SIV), porcine circovirus type 2 (PCV2), and porcine respiratory coronavirus (PRCV). PRRSV alone has been estimated to cost the U.S. swine industry $664 million per year. Although any one of these pathogens can potentially cause disease on its own, more serious and chronic respiratory disease result in significant economic loss when infection with multiple pathogens occurs.

Endemic respiratory viral pathogens have also had a significant impact on the profitability of commercial poultry production. The incidence, prevalence, and etiology of poultry respiratory disease pathogens are typically dependent on the specific industry segment and, with respect to chickens, the genetic line used in broiler production. Thus, the broiler, layers, and turkey producers report different respiratory disease pathogens as being the most important in their industry. High-impact respiratory disease pathogens for the broiler industry include Infectious Bronchitis virus and Infectious Laryngotracheitis virus; the layer industry has concerns with avian influenza and infectious bronchitis virus; whereas the turkey industry has concerns with turkey rhinotracheitis and influenza viruses, either of avian or swine origin.

Endemic viral respiratory pathogens also impact small ruminant production such as sheep and goats, as well as the captive cervids and bison industries. Although these smaller producers (in comparison to the larger cattle, swine, and poultry industries) have unique pathogens that impact their respective industries, they also have endemic pathogens that are shared with cattle, such as bovine viral diarrhea virus. Importantly, some pathogens may cause subclinical infections in one breed but may cause significant disease and loss in another, as exemplified by malignant catarrhal fever virus that has very little effect in the sheep reservoir host but can transmit from sheep to bison with dire outcomes.

Research Focus:
The research program on respiratory viral diseases will focus on the scientific gaps that remain in our understanding of respiratory disease complexes and the ecological and host interactions that lead to disease and production losses. With the current emphasis on reduced usage of antibiotics in livestock and poultry operations, new research approaches are needed to design effective disease prevention and control programs that will facilitate proper planning, careful attention to health management, and the discovery of effective countermeasures.

<u>Bovine</u>
The focus of the program will be the bovine respiratory disease complex. Although emphasis will be given to BVDV (identified as the most important respiratory pathogen by cattle producers in the 2020 ARS survey) other respiratory viruses will be included to either

decipher their involvement in the bovine respiratory disease complex or as stand-alone primary respiratory pathogens. Specific needs include improved diagnostic tests to enable the rapid detection of respiratory viral pathogens on farm premises; characterize the pathogenesis of respiratory diseases associated with polymicrobial infections; identify the mechanisms of disease transmission of respiratory pathogens in relevant beef and dairy production systems; epidemiological field studies to identify reservoirs of respiratory pathogens; characterize host responses to respiratory infections, including mechanisms of immune evasion and protective immunity; and develop new innovative prevention and control strategies for bovine respiratory diseases.

Swine

The focus of the program will be the porcine respiratory disease complex. Emphasis will be given to the two most important respiratory pathogens identified by producers in the 2020 ARS survey: PRRSV and SIV. Similarly, to what was described for bovine, other respiratory viruses may be included to either decipher their involvement in the porcine respiratory disease complex or as stand-alone primary respiratory pathogens. Specific needs also include improved diagnostic tests to enable the rapid detection of respiratory viral pathogens on farm premises; new innovative vaccines designed to provide better cross-protection against heterologous viral strains and prevent the shed and spread of respiratory pathogens. Special emphasis will also be given to supporting SIV surveillance programs and predicting the emergence of zoonotic SIV strains.

Poultry

The focus of the research will be on individual respiratory pathogens that have been identified as the most important by poultry producers in the 2020 ARS survey. Emphasis will be placed on Infectious Laryngotracheitis (ILT), an acute highly contagious herpesvirus infection of chickens characterized by severe dyspnea, coughing, and rales that may reach 50 percent mortality. The frequency of ILT has continued to increase over the past several years with the majority of cases occurring in areas with a large amount of unvaccinated broiler flocks in close proximity to vaccinated commercial egg-layers. Current vaccines only reduce the risk of disease in exposed birds. They do not prevent infection of vaccinated birds, which can still be a source of ILT virus to susceptible birds for a long period of time. Some vaccine strains may also be shed from vaccinated birds and cause disease in susceptible unvaccinated contact birds. Most of the ILT outbreaks in the United States cause milder clinical signs and are associated with “vaccine-like” strain virus. There is therefore a need to discover novel vaccine platforms that are highly efficacious and safe.

Small Ruminants and Captive Cervids

The focus of the research will be on ruminant respiratory viral pathogens that are common to both cattle and small ruminants. Emphasis will be place on BVD, a viral disease which infects mainly cattle, but can also infect sheep, goats, and deer. There is a need to develop prevention and control strategies specifically designed for use in small ruminants and captive cervids.

Bison (American Buffalo)

The focus of the research will be on Malignant catarrhal fever (MCF), a disease syndrome primarily of ruminant species, caused by a member of an expanding group of gammaherpesviruses. These viruses exist in nature as asymptomatic infections in well-adapted

ruminants that act as reservoir hosts. MCF is a global problem and can have a significant economic impact on highly disease-susceptible hosts, such as domestic cattle in Africa, Bali cattle in south Asia, farmed deer in New Zealand, and bison in North America. MCF in North America is predominantly caused by ovine herpesvirus 2 (OvHV-2), which is carried by sheep. The disease has emerged as a significant threat to American bison due to their high disease-susceptibility and it has also posed serious problems in cattle, especially in congregated livestock. The inability to co-graze bison, cattle, or other clinically susceptible species with sheep due to the risk of MCF has seriously affected the use of rangelands. There is a need to develop effective control strategies to mitigate the economic losses induced by MCF virus in clinically susceptible species.

Anticipated Products:

- Discovery of determinants of virulence and characterization of mechanisms of infection.
- Identify mechanisms of immune evasion and protective immunity.
- Drug and vaccine delivery systems that target the ruminant respiratory tract.
- Diagnostic platforms that can be used to develop rapid on-site tests.
- Highly effective vaccines that induce targeted immune responses to prevent colonization of the respiratory tract and prevent shedding and disease transmission.
- Identify changes in gene expression underlying immune responses to infection with respiratory pathogens.
- Discovery of determinants of virulence and characterization of mechanisms of infection.
- Scientific information on microbial genetic variations associated with differences in virulence and disease transmission.
- Scientific information on the characteristics of aerosol spread of priority respiratory pathogens in relevant animal production systems.
- Scientific information on pathogen interactions that lead to polymicrobial infections and respiratory disease complexes.
- Diagnostics platforms that can be used to develop pen-side tests.
- Highly effective vaccines that induce cross-protection against heterologous strains of highly mutable RNA viruses to prevent colonization of the respiratory tract and prevent shedding and disease transmission.

Potential Benefits:

- Improved diagnosis, control, and prevention of endemic respiratory diseases that will benefit the beef, dairy, pork, poultry, small ruminants, and captive cervids and bison industries.
- More predictable costs and better potential returns to farmers, making the business of animal production sustainable.
- Ability of U.S. farmers to remain competitive and profitable.

Problem Statement 4B: Enhance the control of viral diseases in intensive production systems

Although livestock and poultry production in the United States is considered one of the most productive and efficient worldwide, some viral pathogens are inherently linked to certain

intensive production systems. If not properly controlled, these viral pathogens will not only affect the health and well-being of farm animals during their production cycle but can negate any production efficiencies gained through genetic selection, feed efficiency, and management. Based on the 2020 ARS survey, priority production viral diseases that have been selected for this action plan include Marek's Disease, Avian reoviruses, Infectious Bursal Disease, and Porcine Epidemic Diarrhea Virus.

Marek's Disease is perhaps the most insidious virus the poultry industry faces. The continued circulation of Marek's Disease viruses in commercial flocks lead to shifts in viral virulence or the emergence of new subgroups through mutation and/or recombination. Depending on the virus, control measures consist of either blanket vaccination of all commercial birds or diagnostic testing procedures to ensure breeder flocks remain virus free. These control measures cost the U.S. poultry industry in excess of $200 million for vaccination and $20 million in diagnostic tests annually—a conservative estimate. More importantly, these viruses have been evolving for more than 50 years, continually rendering the latest control measures ineffective.

Avian reoviruses are also ubiquitous among poultry flocks. Although infection is usually present without disease, reoviruses may occasionally be involved in several disease syndromes of which viral arthritis and tenosynovitis in chickens is the most important, particularly in broiler breeds. In turkeys, Arthritis Reovirus was recognized as a newly emerging disease in 2011 associated with arthritis and tenosynovitis in commercial turkeys. Research indicates that Turkey Arthritis Reovirus is distinct from the recently identified novel reovirus causing arthritis in chickens. The combined efforts of breeder vaccination, commercial farm biosecurity and flock management once appeared to be controlling Turkey Arthritis Reovirus but recent research suggest that the reovirus has mutated and continues to affect the turkey industry.

Infectious Bursal Disease commonly known as Gumboro disease is one of the most prevalent diseases in broiler chickens. The Infectious Bursal Disease virus is a highly contagious and suppresses the immune system of chickens. The effect of Infectious Bursal Disease-induced immunosuppression facilitates secondary pathogens to invade and exacerbate their pathogenesis and may also affect the effectiveness of vaccines used to prevent common viral and bacterial poultry diseases. Infectious Bursal Disease-infected flocks have higher mortality, poorer feed conversion ratio, and decreased meat production.

Porcine Epidemic Diarrhea Virus (PEDV) was first reported in the United States in 2013. The National Pork Producers Council (NPPC) estimated the introduction of this novel coronavirus in the United States resulted in the loss of 10 percent of the country's pigs. As a result of reduced volumes of available pig and hog supplies, reductions in annual returns occurred for packers, processors, distributors, and retailers. In addition, pork consumers who experienced reduced-supply-induced pork-price increases were harmed directly by higher prices paid for pork and indirectly as prices of competing meats were also strengthened by PEDV. Although the severity of the disease is variable and dependent on the epidemiologic status of the herd, morbidity rates can reach 100 percent in both suckling pigs as well as feeder and grower pigs. Mortality rates are extremely high in suckling pigs, reaching 50 to 80 percent, though both

higher and lower rates have been reported. While the prevalence of PEDV in U.S. swine herds has been significantly reduced, the persistence of this production endemic disease emphasizes the critical need for research to improve current disease control and elimination strategies.

Research Focus:
There is a need to evaluate genomic information from the chicken genome project and from sequencing the genomes of avian tumor viral strains to identify the genes and gene products associated with mechanisms of disease. There is a need to research genomic information to enable the selection of poultry for improved health traits, including disease resistance and good responders to vaccinations. There is a need to implement genomics-based research programs to identify and decipher genetic and biological determinants of virulence, immune evasion mechanisms, and the emergence of new tumor viral strains. There is a need to identify host genetic determinants that influence viral tumorigenicity and protective immunity.

Marek's Disease
Although significant success in the control of Marek's Disease (MD) has been achieved with vaccines that prevent tumor development, one of which became the first vaccine ever developed to prevent a cancer, but current vaccines do not block viral infection and spread. Scientists speculate that vaccine selection pressures have resulted in new highly virulent viral strains, which reportedly cause greater than 50 percent mortality in certain unvaccinated flocks. Continued reports of periodic MD outbreaks in vaccinated flocks worldwide - with increasing reports of vaccination breaks and emergence of more virulent pathotypes - point to the need for new strategies to control this re-emerging viral disease to prevent devastating losses in commercial layer and broiler flocks.

Avian Reovirus
Avian reoviruses are immunosuppressive pathogens that belongs to the *Orthoreovirus* genus in the *Spinareovirinae* subfamily of the *Reoviridae* family. Avian reoviruses are distributed worldwide in chickens, turkeys and other bird species and are ubiquitous in poultry farms. Some strains can lead to severe diseases, causing huge economic losses. The association between viral arthritis and Avian Reovirus has been conclusively determined. Confirmation requires rigorous diagnosis and sometimes challenge studies. The inherent variability of the Avian Reovirus genome makes them mutate and recombine at high rates. Since 2011, the poultry industry has been facing consequences of the emergence of Avian Reovirus variants. The variants of Avian Reovirus have been linked to a rise in clinical cases of tenosynovitis in poultry in the United States. Hundreds of clinically relevant Avian Reovirus associated with a history of leg problems, poor performance and lack of uniformity have been isolated from broiler chickens and their breeders. There is an urgent need to improve diagnostic methods for the early detection of Avian Reovirus on poultry farms and the development of cost-effective vaccines that are cross-protective against relevant reovirus strains. Similarly, control measures are also needed for Turkey Arthritis Reovirus.

Infectious Bursal Disease
Infectious Bursal Disease Virus (IBDV) belongs to the *Birnaviridae* family. Infectious Bursal Disease Virus replicates in differentiating lymphocytes of the Bursa of Fabricius, causing the

immunosuppressive and often fatal condition called infectious bursal disease (IBD) or Gumboro. IBDV consists of two serotypes, 1 and 2. Serotype 1 viruses are infectious for chickens, differing in their pathogenicity and are classified as avirulent, classical, variant and very virulent strains. Variant and very virulent IBDV strains have been isolated from disease outbreaks despite the presence of high levels of maternal antibody to classic strains of IBDV. The use of an appropriate vaccine is vital for effective protection and hence there is a need for differentiation and identification of local IBDV isolates for selection of an appropriate vaccine strain. While several vaccines for IBDV exist, there are issues with vaccine application, maternal antibody interference, emergence of variant strains, and a short window of opportunity to vaccinate.

Porcine Epidemic Diarrhea Virus

Porcine Epidemic Diarrhea Virus (PEDV) is a member of the family *Coronaviridae.* Different strains of PEDV exist with virulence dependent upon the spike (S) gene sequence. Current PEDV vaccines have been shown to reduce morbidity and mortality in piglets. However, molecular phylogenic studies of coronaviruses demonstrate a great deal of diversity in antigenic variants, which may lead to limited vaccine cross-protection against infection with different strains. Thus, it is important to continue to survey novel PEDV variants that may emerge locally or globally through antigenic drift or recombination events. There is a need to improve vaccines that prevent mortality and clinical disease in newborn piglets, the age group most seriously affected by the disease, as well as viral shedding. As lactogenic immunity is the primary mechanism of protection, efforts to enhance the levels of antibodies in the milk to improve passively acquired maternal immunity, and the duration of such immunity are needed. Importantly, research on next-generation vaccines that are highly efficacious and can be developed rapidly for the prevention of future outbreaks of emerging coronavirus viruses are needed.

Anticipated Products:

- Quantify genetic variations in the immune response to viral pathogen infection.
- Scientific information on how the interplay between specific host and viral genes, and the variation within these genes, leads to disease susceptibility or resistance.
- Simple molecular tests to pathotype emerging field strains of viral production pathogens, including Marek's Disease, Infectious Bursal Disease, Reoviruses, and Coronaviruses.
- Identification of molecular predictors of virulence shifts responsible for the pathogenesis of production viral pathogens.
- Scientific information on the ecology of viral production pathogens that drive their evolution and adaptation in U.S. poultry and swine production systems.
- New and improved diagnostic methods to support the surveillance and monitoring of production viral pathogens in poultry and swine production.
- Safe and effective vaccines with mass vaccination capability that convey protection against production viral pathogens in defined host animal genotypes.

Potential Benefits:

- Improved diagnosis, control, and prevention of endemic production diseases that will benefit poultry and swine production.

- Sustainable intensification of poultry and swine production in the United States.

Component 4 Resources:
The following ARS locations have research projects addressing the problem statements identified under Component 4:

- Ames, Iowa
- Athens, Georgia
- Beltsville, Maryland
- East Lansing, Michigan

Component 5: Parasitic Diseases

Parasites represent a diverse groups of organisms that live on a host (ectoparasites) or within a host (endoparasites) and are responsible for hundreds of insidious diseases ranging from enteric diseases to vector-borne hemoparasitic infections. The livestock industries are severely affected by these parasitic diseases, which cause significant losses in animal production due to lower weight gain, anemia, diarrhea, and death from parasites. For example, the control of nematode infections in cattle costs beef producers over $1 billion per year. Moreover, many parasites are invasive and exotic to the United States and impact international trade. Most importantly, the emergence of drug resistant parasites against many commonly used pharmaceutical drugs has huge economic implications. To further complicate control, the populations of parasites may change with the climate changes anticipated with global warming.

All sectors that completed the 2020 ARS Animal Health Stakeholder Survey (government, academia, industry, and livestock and poultry producers) identified research on parasites as a national priority. Importantly, all producers except for swine identified intestinal parasites as the most important issue currently affecting their industry.

Stakeholders identified many priorities that ARS does not currently have the resources to conduct research on, including:

- Parasitic diseases of turkeys such as *Histomonas meleagridis* and *Heterakis gallinarum*
- Gastrointestinal parasitic diseases of horses

Problem Statement 5A: Improve diagnostic and mitigation strategies for gastrointestinal (GI) parasitic diseases
Gastrointestinal parasites of most species of domestic animals were until recently considered a minor health problem to their host. With the development of efficacious anti-parasitic drugs and strategies, most producers were confident that their parasite problems were controlled. In addition, the species of parasites impacting domestic agricultural animals had been stable for a long time. With the concern about global climate change, however, producers are worried that new parasites will enter the United States animal populations.

Currently, drug resistance has emerged as the single most important problem confronting the control of parasites in livestock worldwide. The use of drugs continues to be the primary treatment against parasites, but the intensive use of these products has resulted in some degree of resistance to the majority of the drugs currently available. A survey conducted by the Food and Agriculture Organization (FAO) of the United Nations and the World Animal Health Organization (OIE) determined that more than 20 percent of the countries surveyed reported problems with drug resistant parasites.

The availability of effective drugs to control parasitic diseases in cattle, small ruminants and poultry in the United States is no less important. Helminthic diseases of cattle and sheep are rising in prevalence due to the ever-increasing incidence of drug resistance in parasitic nematodes. Developing control measures against nematodes will require knowledge of the species composition and the ability to differentiate closely related helminths. Selective pressures on parasite populations (e.g. drugs, climate change, and wildlife host introductions) will continue to alter the composition of parasites on pasture-fed cattle and sheep. Coccidial disease in poultry continues to be an issue for U.S. poultry producers and with the increased scrutiny on the use of in-feed ionophores that are commonly used to treat coccidia, gaining a greater understanding of the disease and development of novel prevention and treatment strategies are critical. For both ruminants and poultry, understanding the intestinal microenvironment will be critical in developing novel control strategies such as vaccines to control parasites. Researchers will also investigate the host response to the parasite to determine the role genetics of the host and parasite play in maintaining infestation and clearing the parasites. The application of classical and molecular tools to rapidly and reliably identify drug resistant parasites, the host's immune response, and the genomics of the host and parasite will be critical to managing and controlling parasitic diseases in the face of potential climate change and increased drug-resistance.

Research Focus:
There is a need to define the mechanisms of anti-helminthic resistance to drugs such as Ivermectin and Fenbendazole used to treat nematodes of small ruminants and cattle. There is a need to elucidate the genetics of the immune response to parasites at both the host and parasite level to enable the development of novel intervention strategies to reduce resistance to drugs by parasites. There is a need to define the interactome of the gut to include the transcriptome, proteome, microbiome and metabolome during a parasite infection in order to identify perturbations that may allow for the rationale design of treatment alternatives.

Anticipated Products:
- Scientific information on cases of drug resistance related to parasite species; e.g., *Haemonchus contortus, H. placei, Cooperia punctata, C. oncophora, Ostertagia ostergii, Nematodirus helvetianus*, and *Trichostrongylus*.
- Scientific information on drug resistance and development of control strategies for *Eimeria* species that infect poultry.
- Quantify genetic and environmental effects on variation in host and parasite drug resistance.
- Molecular probes to better define parasite species in the field to enable tracking of their range changes due to climate change.

- Molecular markers of drug resistance based on mode of action and measure the allele frequency of parasite genes involved in drug resistance.
- Scientific information on patterns of gene flow in nematode populations to manage drug resistance in different production systems to reduce the impact of drug resistance on productivity.
- Novel control strategies such as vaccines and natural anti-parasiticides to control parasites.

Potential Benefits:

- Reduction in the incidence and effects of nematode infections in cattle and sheep.
- Preventive and therapeutic strategies to safeguard poultry from parasites.
- Slowing the development of resistance in animal parasites.

Problem Statement 5B: Prevent spread of Hemoparasitic diseases of livestock

Hemoparasitic diseases result in significant export and production problems for the U.S. cattle and equine industries and continue to be a national priority for these industries.

Babesia species are protozoan parasites of domestic and wild animals. They belong to the subclass commonly referred to as "piroplasms" due to the pear-like shaped merozoites that live as small intra-erythrocytic parasites. They commonly infect mammals, particularly cattle, sheep, goats, horses, pigs, dogs, cats, and occasionally man. *Babesia* has an unusual life cycle in that they include one-host ticks, belonging to the genus *Rhipacephalus.* The parasites are passed to the eggs and hence to the larval stages, a process that is known as transovarian transmission.

Babesia bovis and *B. bigemina* are important causative agents of bovine babesiosis in tropical and subtropical regions of the world, while *B. divergens* is more common in temperate climates. Babesiosis was a significant problem in the southern United States until the 1940's when it was controlled by eradication of the tick vectors through intensive acaricide dipping of cattle. However, the number of tick vectors present in the buffer zone along the Rio Grande, in Mexico, and in U.S. territories has been increasing as have the number of ticks found outside the quarantine zones. Of additional concern is that some of the ticks have acaricide resistance. The increasing presence of these ticks poses a threat for reemergence into the United States, as evidenced by occasional outbreaks of babesiosis in the border region. There is a threat of reintroducing bovine babesiosis, a tick borne, hemoparasitic protozoal disease, into the United States from Mexico for the following reasons: 1) the USDA-APHIS surveillance program involves ticks only 2) between one and two million cattle are moved north across the Mexican border each year, a percentage of which are Babesia carriers, 3) acaracide resistant ticks increasingly occur in northern Mexico and southern United States, 4) there is an increase in the number of wild ungulates along the border that serve as hosts for multiple tick populations, and these and some cattle are not treated for ticks, and 5) there is no babesiacidal drug or vaccine approved for use in the United States.

The lack of diagnostics and a vaccine for control of babesiosis leaves U.S. cattle vulnerable to babesiosis upon reintroduction. It is estimated that the first year cost of controlling vector

ticks alone, should they be introduced, into the United States, is over $1.3 billion. In the United States, most of the hundreds of reported cases of babesiosis have been caused by *Babesia microti*, a parasite of small mammals transmitted by *Ixodes scapularis* (deer ticks); these ticks also transmit *Borrelia burgdorferi* (the cause of Lyme disease) and *Anaplasma (Ehrlichia) phagocytophila*.

Two products from research that would alleviate this threat are safe and effective anti-tick and babesia vaccines and diagnostic assays capable of handling large numbers of samples for use in surveillance. Babesia vaccine development requires the characterization of the protective immune mechanisms, the identification of protective antigens from the parasites, and the development of effective delivery systems. Babesial parasites have a complex life cycle including sexual stages in tick vectors and asexual reproduction during the erythrocytic stage in the mammalian host. Ideally, an effective anti-babesial vaccine will include parasite antigens of known function that will induce immune responses that prevent disease in the mammalian host and block transmission from tick vectors.

Equine piroplasmosis is another important tick-borne protozoal hemoparasitic disease that has tremendous impact on the movement of horses across international borders. Equine piroplasmosis has historically been exotic to the United States. A recent outbreak that appears to have originated in Texas spread to at least 14 states to date prior to obtaining control. Piroplasmosis is difficult to diagnose, as it can cause variable and nonspecific clinical signs. The symptoms of this disease range from acute fever to anemia and jaundice, sudden death, or chronic weight loss, to poor exercise tolerance.

Equine piroplasmosis results from infection by the protozoa *Babesia caballi* or *Theileria equi* (phylum Apicomplexa), two organisms that may infect an animal concurrently. *B. caballi* and *T. equi* are transmitted by both adult and nymphal ticks. These diseases are spread by ticks in the genera *Dermacentor*, *Hyalomma*, and *Rhipicephalus* and up to 50 percent of infected animals may die. Recently, new variant strains of *Babesia* species and tick reservoirs have been identified for this disease in the Western Hemisphere. Equine piroplasmosis can also be spread by contaminated needles and syringes. Intrauterine infection of the foal is fairly common, particularly with *T. equi*. After recovery, horses may become carriers for long periods of time.

In cattle, there are both endemic and exotic species of Theileria. *Theileria parva* is the causative agent of East Coast Fever and *Theileria annulata* causes tropical theileriosis. In 2019, the *Theileria orientalis* Ikeda strain was found in Virginia cattle for the first time along with discovery of its vector the exotic *Haemaphysalis longicornis* tick. As of August 2020, the tick has been identified in 14 eastern states and while the disease has not yet spread outside of Virginia, the presence of the tick, similarities in clinical presentation with endemic diseases, animal movement and lack of effective vaccines or treatments suggest it will spread.

Due to the close interaction of these diseases with their tick vectors, collaborations with National Program 104: Veterinary, Medical and Urban Entomology will continue and be supported.

Research Focus:
Research is needed to improve diagnostics that differentiate exotic from endemic pathogens, control and elimination strategies including vector-related contributions to reduce disease risks from these important hemoparasites in areas within the United States where disease is endemic or being reintroduced. There is a need to characterize parasite antigen structures associated with high transmission efficiency.

Anticipated Products:
- Knowledge related to pathogenesis of hemoparasites and immune responses associated with clearance and persistent infections.
- Vaccines that prevent production losses from clinical disease and transmission.
- Improved diagnostics to detect variant species of hemoparasites.
- Scientific information on the effectiveness of current chemotherapeutics for *Babesia caballi, Theileria* and variant piroplasma species in clearing persistent infections.

Potential Benefits:
- Data-driven decision making for import/export restrictions and regulatory programs such as Cattle Fever Tick Programs.
- Ability to block vector borne disease transmission.
- Novel treatment strategies.

Component 5 Resources:
The following ARS locations have research projects addressing the problem statements identified under Component 5:

- Pullman, Washington
- Beltsville, Maryland

Component 6: Transmissible Spongiform Encephalopathies (TSEs)

Transmissible spongiform encephalopathies (TSEs) include several fatal diseases of people and animals involving degeneration of the nervous system and brain function. TSEs are caused by agents known as prions, or what appear to be primarily infectious proteins that cause normal protein (cellular-prion protein PrP^{c}) molecules to convert into an abnormally structured form (disease-prion protein PrP^{sc}) that can include inducement of the formation of proteinaceous deposits and plaques in the brain. TSEs include Creutzfeldt-Jakob disease (CJD), the primary human prion disease; Scrapie of sheep and goats; Chronic Wasting Disease (CWD) of deer, elk, and moose; and Bovine Spongiform Encephalopathy (BSE), also called “mad cow,” which is the cause of variant CJD (vCJD) in people and the only TSE known to have crossed the species barrier from animals to people.

Our understanding of TSEs continues to evolve with ongoing research efforts. TSEs are progressive but long developing diseases. In humans, for example, incubation periods from

the time of contact with an infectious prion may be decades long. Consequently, completion of research plans in natural hosts may require several years. Improvements have been made with the development of experimental rodent models to shorten the time required to obtain experimental results, but the relevance of any findings in mouse models remains uncertain unless confirmed and validated in natural hosts. In 2004, the Institute of Medicine of the *National Academies* published a report entitled: Advancing Prion Science, Guidance for the National Prion Research Program. Several federal agencies have directed resources to implement recommendations in the report, including HHS-NIH, USDA-ARS, HHS-FDA, HHS-CDC, DoD, and EPA. Although significant scientific advances have been made, the research conducted to date has yet to deliver many of the concrete solutions needed to safeguard people and animals from these devastating diseases. A critical concern is the potential for environmental, genetic, or iatrogenic events to lead to new variant TSEs that are infectious and zoonotic.

The White House Office of Science and Technology Policy (OSTP) Interagency Working Group (IWG) on Prion Science identified the following research priorities to maximize the impact of the National Prion Research Program:

- Identification of the nature and origin of prion agents
- Studies on the pathobiology of prion strains
- Research on the determinants of transmissibility and epidemiology
- Development of diagnostics, detection, and surveillance

These interrelated priorities represent areas with critical gaps in our knowledge base. They were selected with the aim of establishing strategic collaborations that will produce benefits by aligning core competencies across Federal agencies. Especially notable are the potential benefits to be derived from collaboration between animal health and human-biomedical research.

All sectors that completed the 2020 ARS Animal Health Stakeholder Survey (government, academia, industry, and livestock and poultry producers) identified research on TSEs a national priority. Importantly, stakeholders identified the following TSEs as one of the 10 most important diseases that have the potential of significantly affecting animal agriculture in the United States: Chronic Wasting Disease (29%), Bovine Spongiform Encephalopathy (18%), and Scrapie (11%).

Producers that completed the 2020 ARS Animal Health Stakeholder Survey (beef, sheep, goats, and wildlife) also identified TSEs as one of the top five diseases currently affecting their commodity. The following TSEs were ranked by producers as one of the top five diseases, as follows:

Chronic Wasting Disease: Wildlife, including captive cervids (80%), sheep (15%), and beef (4.3%).

Bovine Spongiform Encephalopathy: Beef (8.7%).

Scrapie: Sheep (56%), goats (17%), beef (4.3%).

Although recognized as important, ARS does not currently have resources to implement research for the following priority:

- Identification of the nature and origin of prion agents.

Problem Statement 6A: Determine pathobiology of prion strains

Important gaps remain in our basic understanding of the pathobiology of animal prion diseases. One critical need is understanding the tissue tropism and dissemination of prions and resolving the variations seen in different animal species. Proving especially problematic is that the normal prion protein is widely expressed, particularly on neurons in the brain, and is found on cell surfaces but its function is unclear. Another enigma of TSEs is that different strains are found within the same animal species. Importantly, there is evidence that atypical strains have emerged and there is a need to investigate the transmissibility of atypical Scrapie strains, such as the Nor98-like Scrapie.

Research Focus:

It is widely assumed that the oral route of infection is important in the pathogenesis of naturally occurring TSEs of livestock and cervids; however, basic research is needed to understand the mechanisms of transmission of TSE agents from the initial site of entry to the central nervous system. A notable feature of prion diseases is a lack of detectable immune responses and inflammation during the course of a prion infection, even though immune system cells may carry prions to target tissues. To date, research in animals suggests that prion accumulation may be largely influenced by the host species affected rather than the TSE involved. An investment in comparative pathology, which has not received much experimental attention, is needed to advance research programs in epidemiology and diagnostic discovery.

Anticipated Products:

- Scientific information on the mechanisms responsible for the development of multiple TSE strains within a host species.
- Scientific information on the manner in which prions enter the nervous system from peripheral sites of exposure such as a host's gastrointestinal tract, nasal mucosa, skin, and eyes.
- Scientific information on the mechanisms by which prion spread within the nervous system.
- Scientific information on the mechanisms that control prion disease incubation times.
- Elucidate the mechanisms of prion neuropathogenesis.
- Determine prion distribution in goats infected with Scrapie.
- Scientific information on prion distribution in sheep infected with atypical Scrapie.

Potential Benefits:

- Understanding the pathobiology of prion disease and tissue distribution in susceptible animal species is paramount to inform the development of detection methods and ability to develop countermeasures to protect against animal prion diseases.

Problem Statement 6B: Reveal genetics of prion disease susceptibility

Prion diseases have stimulated intense scientific scrutiny since it was first proposed that the infectious agent was devoid of nucleic acid. Despite this finding, host genetics has played a key role in understanding the pathobiology and clinical aspects of prion diseases through the effects of a series of polymorphisms and mutations in the prion protein gene. The advent of vCJD confirmed a powerful human genetic susceptibility factor, as all patients with clinical disease have an identical genotype at the polymorphic codon 129 of the prion gene. The alternative variant at codon 129 is not protective, however, and abnormal prions have been found in lymphoid tissues of individuals of other prion genotypes after exposure to transfused blood products from patients who later succumbed to the disease. Familial forms of prion diseases are also known to be inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the altered gene from one affected parent. In some people, familial forms of prion disease are caused by a new mutation in the prion gene. Although such people most likely do not have an affected parent, they can pass the genetic change to their children. Familial Creutzfeldt-Jakob disease (fCJD), Gerstmann-Sträussler-Scheinker (GSS) syndrome, and fatal familial insomnia (FFI) represent the core phenotypes of genetic prion disease.

Genetic studies in animals have uncovered similar polymorphisms and mutations in the prion protein gene. Genetic information has led to the discovery of genotypes with relative susceptibility and resistance to Scrapie in sheep. Current Scrapie control programs in the United States and Europe are based on the elimination of susceptible genotypes from the breeding pool. However, a significant portion of Scrapie resistance in sheep is not explained by the currently known resistance allele coding R, at codon 171, and codon A at codon 136. Less is known in cervids and CWD. In addition, recent evidence indicates that some forms of BSE may be genetic in nature. The 2006 U.S. H.-type atypical BSE cow had a polymorphism at codon 211 of the bovine prion gene, resulting in a glutamic acid to lysine substitution (E211K). This substitution is analogous to a human polymorphism associated with the most prevalent form of heritable TSE in humans, and it is considered to have caused BSE in 2006 in a U.S. case that was determined to be atypical BSE.

Research Focus:

The functional genomics of disease resistance are not completely understood, and recent research suggests genetic variations may lead to different clinical outcomes. There is a need to look more broadly at the genome of livestock species to identify markers associated with resistance to Scrapie in sheep and goats and CWD in cervids.

In the case of Scrapie, the sheep genome may help identify other alleles that may explain why some QR and RR sheep genotype are susceptible, allowing these sheep to be classified as susceptible and removed from the farm. This will make genotype testing a more effective control tool. This research area is aimed at utilizing powerful computational biology and bioinformatic approaches, along with traditional animal breeding experiments, to steadily improve our understanding of mechanisms of genetic disease resistance.

Our understanding of Scrapie genetic resistance in goats is not as advanced as sheep Scrapie, and there is a need to identify markers for genetic resistance in goats. This will enable the use

of markers identified to develop resistant lines of high production meat and milk goats in cooperation with industry. The USDA eradication program is increasing its focus on goats and it is critically important to provide other options to goat producers besides whole herd depopulation, with the hope that premises contamination does not result in reinfection. Scrapie eradication in the United States will not be achieved unless it is eradicated from sheep and goats.

Anticipated Products:

- Identification of genetic variations associated with disease susceptibility.
- Scientific information on the correlation between host genotypes and the phenotypes of prion agents.
- Identification of genetic factors controlling susceptibility of goats to Scrapie.
- Scientific information to evaluate the effectiveness of disease resistance breeding programs in sheep.
- Scientific information to evaluate sheep ARR/ARR genotype for resistance to different TSE strains.
- Determine whole genome associations with TSE susceptibility or resistance in sheep, goats, and cervids.
- Determine the effects of the PRNP genotype on current diagnostic test assay accuracy in sheep and goats with Scrapie.

Potential Benefits:

- The identification of genetic markers associated with disease susceptibility and resistance.
- Ability to develop prion disease control programs by selecting farm animals that are resistant to prion diseases.
- Ability to enhance surveillance programs for animals known to be genetically susceptible to prion diseases.

Problem Statement 6C: Diagnose, detect, and prevent prion diseases

Important gaps remain in our arsenal of diagnostic tools for early detection and countermeasures to prevent disease outbreaks, transmission, and spread. Current diagnostic tests were validated for use only on post-mortem samples; simple, sensitive, cost-effective ante mortem tests have yet to be developed. Because there is no detectable immune response or inflammation during the course of TSE infection, direct tests are needed to confirm a diagnosis. At present, only highly infected tissues, such as brain material or lymph tissue, are suitable for providing accurate diagnosis.

There is also a need to determine what level of environmental contamination can lead to infections in animals, and then develop a test for determining if this level of contamination exists on farm premises.

Significant gaps also remain for inactivating TSEs in farm settings. Currently the methods available for prion inactivation are not very effective in soil and other organic material. This is problematic as most contaminated bedding is either buried, left as is, or tilled in the soil relying on exclusion or dilution. Research studies have shown that prions last a very long

time when bound to soils or water and may be taken up by plants. Development of a cost-effective method of prion inactivation to non-transmissible levels is needed.

Research Focus:
Diagnostic approaches currently in use include techniques such as immunohistochemistry (IHC), Western blot, and enzyme-linked immunosorbent assays (ELISA). IHC is one of the original tests developed and is considered the gold standard, but it is more labor intensive and time consuming than the other two, whereas the Western blot and particularly ELISA tests are more efficient for the initial screening of large numbers of samples. Another method is the Conformation-Dependent Immunoassay (CDI), currently a research technique that claims to discriminate between normal prion and the abnormal prion on the basis of its shape, but this has yet to be validated as a diagnostic test in animals. New technologies and methods have been described using protein misfolding cyclic amplification techniques (PMCA), similar in concept to gene/DNA amplification, which effectively increases the concentration of prions in normal or pathological conformations. There is a critical need to improve diagnostics methods for surveillance, including the discovery of an ante mortem test for early detection and implementation of intervention strategies. There is also a critical need to develop tools for inactivating TSEs in farm settings, especially the inactivation of TSEs present in organic material.

Anticipated Products:
- TSE diagnostic test capable of detecting low levels of abnormal prions (i.e., key step to enable the development of an ante mortem test that can identify disease during the early stages of incubation).
- Improved live animal and post mortem tests for Scrapie.
- Develop a sensitive, high-throughput assay suitable for use in veterinary diagnostic laboratories for detection of PrP-Sc in sheep with classical scrapie.
- Develop a live animal test for the early detection of CWD in white tail deer.
- Validation of existing biopsy-based TSE tests in goats, deer, and elk.
- Standardize sampling and assay protocols for screening environments for CWD and Scrapie prions.
- Rapid biochemical methods for strain typing.
- Determine the suitability of a sensitive, high-throughput assay for detection of PrP-Sc (Nor98) in brain, peripheral tissues, and placentas from Sheep with Nor98.
- Validated murine models for strain typing.
- Improved diagnostics for TSEs in bodily fluids, including blood and other readily available samples in host species.
- Technologies to distinguish infectious prions from normal cellular prion proteins.
- A sensitive, high-throughput assay suitable for use in veterinary diagnostic laboratories for detection of PrP-Sc in sheep with classical scrapie.
- Effective chemicals with anti-prion properties that can safely be used in farm environments.

Potential Benefits:
- Effective surveillance programs based on early detection of animal prion diseases.
- Deployment of animal prion disease prevention measures.

Component 6 Resources:
The following ARS locations have research projects addressing the problem statements identified under Component 7:

- Albany, California
- Ames, Iowa
- Pullman, Washington

Appendix 1: Meetings with livestock and government stakeholders that informed the development of this action plan

- National Cattleman's Beef Association
- American Association of Swine Veterinarians
- National Pork Board
- National Pork Producer's Council
- United States Animal Health Association/ American Association of Laboratory Veterinary Diagnosticians (AAVLD) Executive Board
- National Bison Association
- Texas Cattle Feeders
- National Milk Producers Federation
- American Association of Avian Pathologists
- National Horse Council
- American Association of Equine Practitioners
- National Turkey Federation
- American Sheep Industry
- American Goat Federation
- North American Deer Farmers Association
- American Veterinary Medical Association
- Animal Plant Health Inspection Service (APHIS)
- Centers for Disease Control (CDC)
- Department of Homeland Security (DHS)
- Environmental Protection Agency (EPA)
- NIFA Animal Health Stakeholder Webinars - October and November 2016

Appendix 2: Scientific and government stakeholder input that informed this action plan

1. National Biodefense Strategy
2. Combating Antimicrobial Resistant Bacteria (CARB) National Action Plan
3. "Antimicrobial Resistant Pathogens Affecting Animal Health in the United States."
4. United States Animal Health Association (USAHA) Resolutions
5. 2015 Report of the meeting of the OIE AD HOC group on prioritization of diseases for which vaccines could reduce antimicrobial use in animals (poultry, swine, aquaculture)
6. 2018 Report of the meeting of the OIE AD HOC group on prioritization of diseases for which vaccines could reduce antimicrobial use in cattle, sheep and goats.
7. Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses (STAR-IDAZ)
8. DISCONTOOLS - Research gaps for improving infectious disease control in animals

Appendix 3: Heatmap of responses across all survey respondents to the 10 most important diseases currently affecting or that have the potential of affecting animal agriculture in the United States (n=413):

Disease	All	Consultant	Government Agency	Other	Private Sector	Producer	Scientific Association	Trade Association	University
Foot-and-Mouth Disease Virus (FMDV)	66.8	80.0	70.2	55.6	66.0	55.7	77.8	83.3	66.1
African Swine Fever (ASF)	62.0	56.0	84.5	33.3	78.0	30.7	88.9	56.7	65.3
Avian Influenza (AI – High Path and Low Path)	58.4	40.0	81.0	66.7	68.0	35.2	66.7	53.3	59.3
Antimicrobial Resistance	49.2	48.0	46.4	44.4	44.0	39.8	77.8	46.7	59.3
Development of Alternatives to Antibiotics	39.7	36.0	38.1	55.6	38.0	38.6	44.4	36.7	42.4
Newcastle Disease (Virulent/Exotic)	34.6	12.0	52.4	44.4	38.0	22.7	33.3	26.7	35.6
Porcine Reproductive and Respiratory Syndrome	30.8	32.0	25.0	33.3	46.0	18.2	44.4	26.7	37.3
Chronic Wasting Disease (CWD)	29.1	20.0	42.9	33.3	8.0	33.0	22.2	26.7	28.0
Bovine Viral Diarrhea Virus (BVDV)	25.9	48.0	13.1	11.1	22.0	26.1	0.0	23.3	35.6
Classical Swine Fever Virus (CSFV)	24.9	24.0	42.9	22.2	34.0	6.8	66.7	16.7	21.2
Swine Influenza Virus (SIV)	24.9	20.0	28.6	33.3	40.0	10.2	55.6	30.0	23.7
Porcine Coronavirus (PEDV/PDCoV)	23.7	20.0	28.6	22.2	32.0	8.0	44.4	26.7	27.1
Mastitis - Bovine	21.3	32.0	6.0	22.2	26.0	23.9	0.0	13.3	29.7
Intestinal parasites of ruminants	21.1	24.0	8.3	11.1	18.0	40.9	0.0	23.3	17.8
Brucellosis	20.6	20.0	32.1	0.0	8.0	28.4	0.0	30.0	12.7
Bovine Tuberculosis	20.3	12.0	31.0	22.2	8.0	26.1	22.2	33.3	11.9
M. paratuberculosis (Johne's Disease)	18.9	4.0	10.7	22.2	16.0	31.8	11.1	16.7	20.3
Bovine Spongiform Encephalopathy (BSE)	17.9	16.0	10.7	11.1	20.0	25.0	11.1	36.7	13.6
Anaplasmosis – Bovine	15.0	20.0	17.9	11.1	4.0	17.0	11.1	26.7	12.7
Mycoplasma bovis	14.8	40.0	2.4	22.2	18.0	14.8	0.0	16.7	16.9
Bovine Respiratory Syncytial Virus (BRSV)	13.1	8.0	6.0	11.1	8.0	19.3	0.0	10.0	18.6
West Nile virus	13.1	8.0	9.5	11.1	6.0	20.5	0.0	16.7	14.4
Avian Coccidiosis	12.8	8.0	1.2	11.1	32.0	21.6	11.1	20.0	5.9
Mannheimia haemolytica	12.3	28.0	4.8	22.2	14.0	11.4	0.0	10.0	15.3
Vesicular Stomatitis Virus (VSV)	12.1	8.0	22.6	11.1	10.0	6.8	0.0	6.7	12.7
Infectious Bovine Rhinotracheitis (IBR)	11.4	16.0	3.6	22.2	6.0	19.3	0.0	10.0	12.7
Necrotic enteritis (NE)	11.4	8.0	2.4	22.2	38.0	9.1	11.1	6.7	9.3
Bluetongue Virus (BTV)	11.1	12.0	10.7	0.0	6.0	17.0	11.1	13.3	9.3
Scrapie	10.9	4.0	7.1	0.0	2.0	27.3	11.1	13.3	6.8
Coxiella burnetii (Q-fever)	10.7	8.0	16.7	0.0	6.0	13.6	22.2	10.0	6.8
Leptospirosis	10.4	16.0	6.0	11.1	2.0	20.5	0.0	13.3	8.5
Infectious Bronchitis Virus (IBV)	9.9	4.0	4.8	33.3	14.0	17.0	0.0	0.0	9.3
Pasteurella multocida	8.7	24.0	2.4	11.1	10.0	17.0	0.0	3.3	5.1
African Horse Sickness	8.5	8.0	21.4	22.2	2.0	2.3	11.1	6.7	5.9
Marek's Disease Virus (MDV)	8.5	8.0	2.4	0.0	18.0	12.5	22.2	0.0	7.6
Mycoplasma gallisepticum (MG)	7.7	12.0	4.8	22.2	10.0	10.2	0.0	6.7	5.9
Rift Valley Fever Virus	7.7	4.0	14.3	0.0	6.0	1.1	11.1	3.3	11.0
Avian Pathogenic *E.coli* (APEC)	7.5	0.0	2.4	0.0	24.0	10.2	0.0	3.3	5.9
Digital dermatitis- cattle	7.5	24.0	2.4	11.1	4.0	9.1	0.0	6.7	8.5
Infectious Laryngotracheitis (ILT)	7.3	8.0	4.8	22.2	8.0	9.1	11.1	3.3	6.8
Peste des petits ruminants (PPR)	7.3	8.0	10.7	0.0	10.0	4.5	0.0	0.0	8.5
Toxoplasmosis	7.3	4.0	4.8	0.0	2.0	15.9	11.1	6.7	5.9
Porcine Circovirus	7.0	20.0	3.6	0.0	14.0	2.3	22.2	6.7	6.8
Mycoplasma hyopneumoniae	6.8	12.0	1.2	11.1	10.0	5.7	22.2	10.0	6.8
Streptococcus suis	6.8	12.0	1.2	22.2	8.0	8.0	11.1	3.3	7.6
Babesiosis - Bovine	6.5	12.0	10.7	0.0	2.0	1.1	0.0	3.3	10.2
Epizootic Hemorrhagic Disease (EHD)	6.1	0.0	8.3	0.0	2.0	10.2	11.1	6.7	4.2
Reoviruses	5.8	4.0	3.6	11.1	10.0	6.8	0.0	10.0	4.2
Bovine Leukemia Virus	5.6	12.0	2.4	0.0	2.0	6.8	11.1	6.7	6.8
Pox viruses (Parapox, Sheeppox, Capripox)	5.6	8.0	1.2	0.0	2.0	13.6	0.0	10.0	3.4
Infectious Bursal Disease (IBD)	5.3	4.0	2.4	0.0	6.0	9.1	11.1	3.3	5.1
Newcastle Disease (Low virulent/Endemic)	5.3	8.0	8.3	0.0	6.0	4.5	0.0	0.0	5.1
Seneca Valley Virus	5.3	0.0	9.5	11.1	6.0	0.0	22.2	6.7	5.1
Trichinellosis	4.8	0.0	3.6	11.1	2.0	9.1	0.0	10.0	3.4
Crimean Congo Hemorrhagic Fever	4.4	4.0	10.7	11.1	0.0	0.0	0.0	3.3	5.1
Ehrlichia ruminantium (Heartwater)	4.4	4.0	10.7	0.0	2.0	1.1	22.2	0.0	3.4
Mycoplasma ovipneumoniae	4.4	0.0	4.8	0.0	2.0	9.1	0.0	3.3	3.4
Histomoniasis	4.1	4.0	0.0	11.1	10.0	4.5	0.0	6.7	3.4
Histophilus somni	4.1	8.0	1.2	11.1	6.0	2.3	0.0	0.0	6.8
Japanese Encephalitis virus	4.1	4.0	6.0	11.1	0.0	1.1	11.1	6.7	5.1
Fusobacterium necrophorum	3.9	4.0	1.2	11.1	2.0	5.7	0.0	6.7	4.2
Gangrenous dermatitis	3.9	0.0	0.0	0.0	8.0	8.0	11.1	6.7	1.7
Nipah virus	3.9	4.0	9.5	0.0	0.0	0.0	11.1	0.0	5.1
Malignant Catarrhal Fever (MCF)	3.6	0.0	3.6	0.0	0.0	5.7	0.0	10.0	3.4
Schmallenberg Virus	3.6	4.0	8.3	0.0	2.0	3.4	0.0	3.3	1.7
Contagious Bovine Pleuropneumonia (CBPP)	3.4	4.0	2.4	11.1	2.0	3.4	0.0	6.7	3.4
Piroplasmosis - Equine	3.4	4.0	6.0	0.0	0.0	1.1	0.0	3.3	5.1
Egg Drop Syndrome	3.1	0.0	1.2	0.0	2.0	6.8	11.1	0.0	3.4
Lumpy Skin Disease	3.1	0.0	3.6	11.1	0.0	1.1	0.0	3.3	5.9
Actinobacillus suis	2.7	4.0	1.2	0.0	0.0	6.8	0.0	3.3	1.7
Lawsonia intracellularis	2.7	4.0	0.0	11.1	8.0	0.0	11.1	0.0	3.4
Theileria spp.	2.4	4.0	4.8	0.0	0.0	1.1	0.0	6.7	1.7
Poult Enteritis Mortality Syndrome (PEMS)	1.9	0.0	2.4	0.0	4.0	0.0	0.0	3.3	2.5
Avian Pneumovirus (APV)	1.7	4.0	0.0	0.0	0.0	3.4	0.0	3.3	1.7
Atrophic Rhinitis (*Bordetella bronchiseptica*)	1.5	0.0	0.0	0.0	0.0	5.7	0.0	0.0	0.8
Avian Leukosis Virus (ALV)	1.5	0.0	0.0	0.0	2.0	4.5	0.0	0.0	0.8
Cache Valley Fever	1.5	0.0	2.4	0.0	0.0	3.4	0.0	0.0	0.8
Actinobacillosis (Wooden Tongue)	1.0	0.0	0.0	0.0	0.0	3.4	0.0	0.0	0.8
Bovine Ephemeral Fever	0.7	0.0	1.2	0.0	0.0	1.1	0.0	3.3	0.0
Brachyspira hyodysenteriae	0.7	0.0	0.0	11.1	0.0	0.0	0.0	0.0	1.7
Glaesserella parasuis	0.7	4.0	0.0	0.0	0.0	1.1	0.0	0.0	0.8
Ornithobacterium rhinotracheale (ORT)	0.7	0.0	0.0	0.0	0.0	1.1	0.0	6.7	0.0
Reticuloendotheliosis virus (REV)	0.2	0.0	0.0	0.0	2.0	0.0	0.0	0.0	0.0

Appendix 4: Heatmap of responses across the producer commodity groups to the 10 most important diseases currently affecting or that have the potential of affecting animal agriculture in the U.S. (n=88)

Disease	All Producers	Beef	Dairy	Sheep	Goats	Poultry	Pork	Wildlife
Foot-and-Mouth Disease Virus (FMDV)	55.7	52.2	88.9	74.1	50.0	33.3	100.0	20.0
Intestinal parasites of ruminants	40.9	39.1	11.1	81.5	83.3	13.3	0.0	40.0
Antimicrobial Resistance	39.8	47.8	33.3	59.3	50.0	20.0	0.0	40.0
Development of Alternatives to Antibiotics	38.6	39.1	33.3	55.6	66.7	26.7	25.0	20.0
Avian Influenza (AI – High Path and Low Path)	35.2	30.4	11.1	25.9	50.0	93.3	0.0	40.0
Chronic Wasting Disease (CWD)	33.0	30.4	0.0	66.7	16.7	20.0	0.0	100.0
M. paratuberculosis (Johne's Disease)	31.8	26.1	33.3	59.3	66.7	13.3	0.0	40.0
African Swine Fever (ASF)	30.7	39.1	11.1	25.9	0.0	33.3	100.0	40.0
Brucellosis	28.4	43.5	22.2	40.7	0.0	13.3	25.0	60.0
Scrapie	27.3	8.7	0.0	74.1	66.7	20.0	0.0	0.0
Bovine Tuberculosis	26.1	17.4	88.9	25.9	33.3	6.7	0.0	40.0
Bovine Viral Diarrhea Virus (BVDV)	26.1	60.9	66.7	18.5	0.0	0.0	0.0	40.0
Bovine Spongiform Encephalopathy (BSE)	25.0	43.5	66.7	18.5	0.0	6.7	25.0	0.0
Mastitis - Bovine	23.9	17.4	88.9	25.9	50.0	20.0	0.0	0.0
Newcastle Disease (Virulent/Exotic)	22.7	8.7	11.1	7.4	33.3	80.0	25.0	20.0
Avian Coccidiosis	21.6	4.3	0.0	25.9	33.3	80.0	0.0	0.0
Leptospirosis	20.5	34.8	44.4	18.5	33.3	0.0	25.0	0.0
West Nile virus	20.5	13.0	0.0	44.4	33.3	20.0	0.0	0.0
Infectious Bovine Rhinotracheitis (IBR)	19.3	43.5	55.6	14.8	0.0	0.0	0.0	0.0
Bovine Respiratory Syncytial Virus (BRSV)	19.3	47.8	33.3	14.8	0.0	0.0	0.0	20.0
Porcine Reproductive and Respiratory Syndrome (PRRS)	18.2	21.7	0.0	14.8	16.7	6.7	100.0	20.0
Anaplasmosis – Bovine	17.0	43.5	22.2	14.8	0.0	0.0	0.0	0.0
Infectious Bronchitis Virus (IBV)	17.0	21.7	22.2	7.4	0.0	46.7	0.0	0.0
Pasteurella multocida	17.0	8.7	11.1	22.2	33.3	20.0	25.0	20.0
Bluetongue Virus (BTV)	17.0	17.4	0.0	22.2	50.0	0.0	0.0	60.0
Toxoplasmosis	15.9	13.0	0.0	44.4	16.7	13.3	0.0	0.0
Mycoplasma bovis	14.8	13.0	33.3	14.8	33.3	13.3	0.0	20.0
Pox viruses (Parapox, Sheeppox, Capripox)	13.6	0.0	0.0	25.9	16.7	20.0	25.0	20.0
Coxiella burnetii (Q-fever)	13.6	4.3	0.0	37.0	33.3	6.7	0.0	0.0
Marek's Disease Virus (MDV)	12.5	4.3	0.0	3.7	16.7	46.7	25.0	0.0
Mannheimia haemolytica	11.4	17.4	0.0	14.8	33.3	0.0	0.0	0.0
Swine Influenza Virus (SIV)	10.2	4.3	11.1	7.4	0.0	13.3	75.0	20.0
Avian Pathogenic *E.coli* (APEC)	10.2	0.0	0.0	3.7	16.7	46.7	0.0	0.0
Epizootic Hemorrhagic Disease (EHD)	10.2	8.7	0.0	14.8	0.0	6.7	0.0	60.0
Mycoplasma gallisepticum (MG)	10.2	0.0	0.0	0.0	16.7	46.7	0.0	20.0
Digital dermatitis- cattle	9.1	17.4	22.2	7.4	16.7	0.0	0.0	0.0
Infectious Bursal Disease (IBD)	9.1	8.7	22.2	3.7	0.0	26.7	0.0	0.0
Infectious Laryngotracheitis (ILT)	9.1	0.0	11.1	3.7	0.0	40.0	0.0	0.0
Mycoplasma ovipneumoniae	9.1	4.3	0.0	18.5	33.3	6.7	0.0	0.0
Necrotic enteritis (NE)	9.1	0.0	0.0	7.4	0.0	40.0	0.0	0.0
Trichinellosis	9.1	26.1	0.0	11.1	16.7	0.0	0.0	0.0
Streptococcus suis	8.0	8.7	11.1	7.4	16.7	6.7	25.0	0.0
Porcine Coronavirus (PEDV/PDCoV)	8.0	13.0	0.0	0.0	0.0	0.0	75.0	20.0
Gangrenous dermatitis	8.0	0.0	0.0	14.8	16.7	13.3	0.0	0.0
Bovine Leukemia Virus	6.8	4.3	55.6	0.0	0.0	0.0	0.0	0.0
Classical Swine Fever Virus (CSFV)	6.8	4.3	0.0	3.7	0.0	0.0	100.0	20.0
Vesicular Stomatitis Virus (VSV)	6.8	8.7	0.0	11.1	16.7	0.0	25.0	0.0
Actinobacillus suis	6.8	4.3	0.0	14.8	16.7	0.0	0.0	0.0
Egg Drop Syndrome	6.8	0.0	0.0	3.7	0.0	40.0	0.0	0.0
Reoviruses	6.8	0.0	0.0	0.0	0.0	33.3	0.0	20.0
Malignant Catarrhal Fever (MCF)	5.7	0.0	11.1	7.4	0.0	0.0	0.0	40.0
Mycoplasma hyopneumoniae	5.7	0.0	0.0	7.4	0.0	0.0	50.0	20.0
Atrophic Rhinitis (Bordetella bronchiseptica)	5.7	4.3	0.0	7.4	16.7	6.7	25.0	0.0
Fusobacterium necrophorum	5.7	8.7	0.0	3.7	0.0	0.0	0.0	40.0
Newcastle Disease (Low virulent/Endemic)	4.5	0.0	11.1	0.0	16.7	13.3	0.0	0.0
Avian Leukosis Virus (ALV)	4.5	0.0	0.0	3.7	16.7	13.3	0.0	0.0
Histomoniasis	4.5	0.0	0.0	3.7	0.0	20.0	0.0	0.0
Peste des petits ruminants (PPR)	4.5	0.0	0.0	14.8	0.0	6.7	0.0	0.0
Schmallenberg Virus	3.4	0.0	11.1	3.7	0.0	0.0	25.0	0.0
Actinobacillosis (Wooden Tongue)	3.4	4.3	0.0	3.7	0.0	0.0	0.0	0.0
Avian Pneumovirus (APV)	3.4	8.7	0.0	0.0	16.7	6.7	0.0	20.0
Cache Valley Fever	3.4	4.3	0.0	11.1	0.0	0.0	0.0	0.0
Contagious Bovine Pleuropneumonia (CBPP)	3.4	4.3	0.0	7.4	0.0	0.0	0.0	0.0
Porcine Circovirus	2.3	0.0	0.0	0.0	0.0	0.0	50.0	0.0
Histophilus somni	2.3	4.3	0.0	0.0	0.0	0.0	25.0	0.0
African Horse Sickness	2.3	4.3	0.0	0.0	0.0	0.0	0.0	0.0
Bovine Ephemeral Fever	1.1	0.0	11.1	0.0	0.0	0.0	0.0	0.0
Glaesserella parasuis	1.1	0.0	0.0	0.0	0.0	0.0	25.0	0.0
Babesiosis - Bovine	1.1	0.0	0.0	0.0	16.7	0.0	0.0	0.0
Ehrlichia ruminantium (Heartwater)	1.1	0.0	0.0	3.7	0.0	0.0	0.0	0.0
Japanese Encephalitis virus	1.1	4.3	0.0	0.0	0.0	0.0	0.0	20.0
Lumpy Skin Disease	1.1	4.3	0.0	0.0	0.0	0.0	0.0	20.0
Ornithobacterium rhinotracheale (ORT)	1.1	0.0	0.0	0.0	0.0	6.7	0.0	0.0
Piroplasmosis - Equine	1.1	4.3	0.0	0.0	0.0	0.0	0.0	0.0
Rift Valley Fever Virus	1.1	0.0	0.0	3.7	0.0	0.0	0.0	0.0
Theileria spp.	1.1	4.3	0.0	0.0	0.0	0.0	0.0	0.0
Brachyspira hyodysenteriae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Crimean Congo Hemorrhagic Fever	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lawsonia intracellularis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Nipah virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Poult Enteritis Mortality Syndrome (PEMS)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Reticuloendotheliosis virus (REV)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Seneca Valley Virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Appendix 5: Heatmap of responses across all survey respondent of the five most important diseases for the commodity they work with most frequently (n=413):

Disease	All	Consultant	Government Agency	Other	Private Sector	Producer	Scientific Association	Trade Association	University
Antimicrobial Resistance	23.7	24.0	21.4	33.3	20.0	13.6	33.3	40.0	28.8
African Swine Fever (ASF)	23.0	24.0	38.1	22.2	32.0	3.4	44.4	20.0	22.0
Foot-and-Mouth Disease Virus (FMDV)	21.5	20.0	29.8	11.1	14.0	11.4	44.4	36.7	22.0
Avian Influenza (AI – High Path and Low Path)	19.4	8.0	44.0	22.2	20.0	8.0	11.1	13.3	14.4
Bovine Viral Diarrhea Virus (BVDV)	16.5	24.0	4.8	11.1	12.0	19.3	0.0	26.7	22.0
Mastitis - Bovine	16.0	20.0	4.8	22.2	22.0	13.6	0.0	10.0	24.6
Intestinal parasites of ruminants	15.3	8.0	7.1	0.0	4.0	45.5	0.0	13.3	7.6
Porcine Reproductive and Respiratory Syndrome	13.6	16.0	6.0	11.1	32.0	4.5	44.4	20.0	13.6
M. paratuberculosis (Johne's Disease)	12.1	0.0	9.5	11.1	4.0	21.6	11.1	6.7	14.4
Mannheimia haemolytica	11.1	16.0	2.4	11.1	12.0	11.4	0.0	13.3	16.1
Mycoplasma bovis	11.1	24.0	2.4	33.3	12.0	8.0	0.0	6.7	16.9
Bovine Respiratory Syncytial Virus (BRSV)	10.9	4.0	2.4	0.0	10.0	12.5	0.0	13.3	18.6
Development of Alternatives to Antibiotics	10.4	8.0	2.4	11.1	14.0	13.6	11.1	6.7	13.6
Avian Coccidiosis	9.9	4.0	2.4	11.1	32.0	11.4	11.1	6.7	6.8
Brucellosis	9.4	12.0	25.0	0.0	2.0	5.7	0.0	10.0	5.1
Anaplasmosis – Bovine	9.0	16.0	4.8	0.0	6.0	10.2	0.0	16.7	10.2
Classical Swine Fever Virus (CSFV)	8.2	12.0	14.3	11.1	10.0	2.3	33.3	0.0	6.8
Porcine Coronavirus (PEDV/PDCoV)	8.2	4.0	8.3	11.1	22.0	3.4	11.1	10.0	5.9
Infectious Bovine Rhinotracheitis (IBR)	7.7	4.0	2.4	0.0	6.0	13.6	0.0	10.0	9.3
Scrapie	7.7	0.0	9.5	0.0	2.0	18.2	0.0	10.0	3.4
Swine Influenza Virus (SIV)	7.5	8.0	13.1	11.1	10.0	1.1	33.3	6.7	5.1
Chronic Wasting Disease (CWD)	7.3	4.0	13.1	0.0	0.0	9.1	0.0	10.0	5.9
Infectious Bronchitis Virus (IBV)	7.3	4.0	1.2	22.2	16.0	6.8	11.1	0.0	9.3
Necrotic enteritis (NE)	7.0	4.0	0.0	11.1	30.0	3.4	11.1	3.3	5.9
Infectious Laryngotracheitis (ILT)	6.8	8.0	4.8	0.0	10.0	9.1	11.1	3.3	5.9
Bluetongue Virus (BTV)	6.1	4.0	7.1	0.0	0.0	11.4	11.1	6.7	4.2
Pasteurella multocida	6.1	4.0	4.8	11.1	10.0	9.1	0.0	3.3	4.2
Digital dermatitis- cattle	5.8	12.0	0.0	11.1	6.0	9.1	0.0	0.0	7.6
Newcastle Disease (Virulent/Exotic)	5.8	4.0	8.3	11.1	8.0	3.4	11.1	3.3	5.1
Coxiella burnetii (Q-fever)	5.6	4.0	7.1	0.0	0.0	6.8	0.0	10.0	5.9
Bovine Tuberculosis	5.3	8.0	7.1	0.0	0.0	3.4	0.0	13.3	5.9
Bovine Leukemia Virus	4.8	8.0	2.4	11.1	0.0	3.4	11.1	0.0	9.3
Mycoplasma gallisepticum (MG)	4.6	8.0	4.8	11.1	2.0	5.7	0.0	6.7	3.4
Porcine Circovirus	4.4	12.0	1.2	0.0	10.0	2.3	11.1	3.3	4.2
Epizootic Hemorrhagic Disease (EHD)	3.9	0.0	6.0	0.0	0.0	5.7	11.1	6.7	2.5
Babesiosis - Bovine	3.6	4.0	6.0	0.0	2.0	0.0	0.0	3.3	5.9
Leptospirosis	3.6	4.0	3.6	0.0	2.0	6.8	0.0	3.3	2.5
Avian Pathogenic *E.coli* (APEC)	3.4	8.0	3.6	11.1	4.0	5.7	0.0	0.0	0.8
Fusobacterium necrophorum	3.4	4.0	0.0	11.1	4.0	6.8	0.0	3.3	2.5
Marek's Disease Virus (MDV)	3.4	4.0	1.2	0.0	6.0	5.7	0.0	0.0	3.4
Toxoplasmosis	3.4	4.0	0.0	0.0	0.0	8.0	0.0	0.0	5.1
West Nile virus	3.4	0.0	9.5	11.1	2.0	1.1	0.0	3.3	1.7
Mycoplasma ovipneumoniae	2.9	0.0	3.6	0.0	2.0	4.5	0.0	6.7	1.7
Newcastle Disease (Low virulent/Endemic)	2.9	0.0	6.0	0.0	6.0	1.1	0.0	0.0	2.5
Reoviruses	2.9	0.0	1.2	11.1	10.0	2.3	0.0	3.3	1.7
Vesicular Stomatitis Virus (VSV)	2.9	4.0	7.1	0.0	0.0	0.0	0.0	3.3	3.4
Histophilus somni	2.7	0.0	0.0	11.1	4.0	0.0	0.0	0.0	6.8
Mycoplasma hyopneumoniae	2.7	4.0	0.0	0.0	6.0	0.0	0.0	6.7	4.2
African Horse Sickness	2.2	0.0	3.6	0.0	0.0	0.0	11.1	3.3	3.4
Bovine Spongiform Encephalopathy (BSE)	2.2	0.0	3.6	0.0	0.0	2.3	0.0	13.3	0.0
Gangrenous dermatitis	2.2	4.0	0.0	0.0	8.0	3.4	0.0	0.0	0.8
Seneca Valley Virus	2.2	0.0	8.3	0.0	0.0	0.0	0.0	3.3	0.8
Infectious Bursal Disease (IBD)	1.9	4.0	0.0	0.0	4.0	1.1	0.0	0.0	3.4
Trichinellosis	1.9	0.0	1.2	0.0	0.0	5.7	0.0	3.3	0.8
Histomoniasis	1.7	0.0	1.2	0.0	4.0	2.3	0.0	3.3	0.8
Rift Valley Fever Virus	1.7	0.0	4.8	0.0	0.0	0.0	0.0	0.0	2.5
Streptococcus suis	1.7	4.0	0.0	0.0	2.0	1.1	0.0	3.3	2.5
Cache Valley Fever	1.5	0.0	0.0	0.0	0.0	3.4	0.0	3.3	1.7
Ornithobacterium rhinotracheale (ORT)	1.5	0.0	2.4	0.0	2.0	2.3	0.0	3.3	0.0
Piroplasmosis - Equine	1.5	0.0	3.6	0.0	0.0	0.0	0.0	3.3	1.7
Pox viruses (Parapox, Sheeppox, Capripox)	1.5	4.0	1.2	0.0	0.0	3.4	0.0	0.0	0.8
Lawsonia intracellularis	1.2	4.0	0.0	11.1	4.0	0.0	0.0	0.0	0.8
Malignant Catarrhal Fever (MCF)	1.2	0.0	0.0	0.0	0.0	0.0	0.0	13.3	0.8
Nipah virus	1.2	0.0	4.8	0.0	0.0	0.0	0.0	0.0	0.8
Avian Leukosis Virus (ALV)	1.0	0.0	1.2	0.0	2.0	1.1	0.0	0.0	0.8
Ehrlichia ruminantium (Heartwater)	1.0	0.0	3.6	0.0	0.0	0.0	0.0	0.0	0.8
Glaesserella parasuis	1.0	0.0	0.0	0.0	0.0	1.1	0.0	0.0	2.5
Japanese Encephalitis virus	1.0	0.0	1.2	0.0	2.0	0.0	0.0	3.3	0.8
Lumpy Skin Disease	1.0	0.0	1.2	0.0	0.0	1.1	0.0	0.0	1.7
Peste des petits ruminants (PPR)	1.0	4.0	0.0	0.0	0.0	2.3	0.0	0.0	0.8
Actinobacillosis (Wooden Tongue)	0.7	0.0	0.0	0.0	0.0	1.1	0.0	0.0	1.7
Contagious Bovine Pleuropneumonia (CBPP)	0.7	0.0	0.0	0.0	0.0	1.1	0.0	3.3	0.8
Crimean Congo Hemorrhagic Fever	0.7	4.0	2.4	0.0	0.0	0.0	0.0	0.0	0.0
Theileria spp.	0.7	0.0	1.2	0.0	0.0	1.1	0.0	0.0	0.8
Actinobacillus suis	0.5	0.0	0.0	0.0	0.0	0.0	0.0	3.3	0.8
Avian Pneumovirus (APV)	0.5	0.0	0.0	0.0	0.0	1.1	0.0	3.3	0.0
Brachyspira hyodysenteriae	0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.7
Egg Drop Syndrome	0.5	0.0	0.0	0.0	2.0	0.0	11.1	0.0	0.0
Bovine Ephemeral Fever	0.2	0.0	1.2	0.0	0.0	0.0	0.0	0.0	0.0
Poult Enteritis Mortality Syndrome (PEMS)	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8
Schmallenberg Virus	0.2	0.0	1.2	0.0	0.0	0.0	0.0	0.0	0.0
Atrophic Rhinitis (*Bordetella bronchiseptica*)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Reticuloendotheliosis virus (REV)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Appendix 6: Heatmap of responses across producer commodity groups of the five most important diseases for the commodity they work with most frequently (n=88):

Disease	All Producers	Beef	Dairy	Sheep	Goats	Poultry	Pork	Wildlife
Intestinal parasites of ruminants	45.5	43.5	11.1	85.2	83.3	26.7	0.0	80.0
M. paratuberculosis (Johne's Disease)	21.6	17.4	11.1	48.1	50.0	13.3	0.0	0.0
Bovine Viral Diarrhea Virus (BVDV)	19.3	52.2	55.6	0.0	0.0	0.0	0.0	0.0
Scrapie	18.2	4.3	0.0	55.6	16.7	26.7	0.0	0.0
Antimicrobial Resistance	13.6	21.7	0.0	22.2	0.0	6.7	25.0	0.0
Development of Alternatives to Antibiotics	13.6	8.7	22.2	25.9	16.7	0.0	0.0	0.0
Infectious Bovine Rhinotracheitis (IBR)	13.6	34.8	44.4	3.7	0.0	0.0	0.0	0.0
Mastitis - Bovine	13.6	0.0	77.8	11.1	33.3	6.7	0.0	0.0
Bovine Respiratory Syncytial Virus (BRSV)	12.5	39.1	22.2	0.0	0.0	0.0	0.0	0.0
Bluetongue Virus (BTV)	11.4	17.4	0.0	14.8	16.7	0.0	0.0	60.0
Avian Coccidiosis	11.4	0.0	0.0	7.4	0.0	53.3	0.0	0.0
Foot-and-Mouth Disease Virus (FMDV)	11.4	21.7	0.0	14.8	0.0	6.7	50.0	0.0
Mannheimia haemolytica	11.4	21.7	11.1	11.1	16.7	0.0	0.0	0.0
Anaplasmosis – Bovine	10.2	34.8	11.1	3.7	0.0	0.0	0.0	0.0
Chronic Wasting Disease (CWD)	9.1	4.3	0.0	14.8	0.0	0.0	0.0	80.0
Digital dermatitis- cattle	9.1	8.7	55.6	7.4	0.0	0.0	0.0	0.0
Infectious Laryngotracheitis (ILT)	9.1	0.0	11.1	0.0	0.0	46.7	0.0	0.0
Pasteurella multocida	9.1	8.7	11.1	18.5	0.0	6.7	0.0	0.0
Avian Influenza (AI – High Path and Low Path)	8.0	0.0	0.0	0.0	16.7	46.7	0.0	0.0
Mycoplasma bovis	8.0	13.0	33.3	0.0	0.0	0.0	0.0	20.0
Toxoplasmosis	8.0	4.3	0.0	25.9	0.0	6.7	0.0	0.0
Coxiella burnetii (Q-fever)	6.8	0.0	0.0	14.8	33.3	0.0	0.0	0.0
Fusobacterium necrophorum	6.8	8.7	0.0	3.7	0.0	0.0	0.0	60.0
Infectious Bronchitis Virus (IBV)	6.8	0.0	11.1	3.7	0.0	26.7	0.0	0.0
Leptospirosis	6.8	17.4	11.1	3.7	0.0	0.0	0.0	20.0
Avian Pathogenic *E.coli* (APEC)	5.7	0.0	0.0	0.0	16.7	33.3	0.0	0.0
Brucellosis	5.7	13.0	0.0	3.7	0.0	6.7	0.0	20.0
Epizootic Hemorrhagic Disease (EHD)	5.7	4.3	0.0	0.0	0.0	0.0	0.0	100.0
Marek's Disease Virus (MDV)	5.7	0.0	0.0	7.4	0.0	26.7	0.0	0.0
Mycoplasma gallisepticum (MG)	5.7	0.0	0.0	0.0	0.0	26.7	0.0	20.0
Trichinellosis	5.7	21.7	0.0	0.0	0.0	0.0	0.0	0.0
Mycoplasma ovipneumoniae	4.5	0.0	0.0	11.1	16.7	0.0	0.0	0.0
Porcine Reproductive and Respiratory Syndrome	4.5	0.0	0.0	0.0	0.0	0.0	100.0	0.0
African Swine Fever (ASF)	3.4	0.0	0.0	0.0	0.0	0.0	75.0	0.0
Bovine Leukemia Virus	3.4	0.0	33.3	0.0	0.0	0.0	0.0	0.0
Bovine Tuberculosis	3.4	4.3	22.2	0.0	0.0	0.0	0.0	0.0
Cache Valley Fever	3.4	4.3	0.0	11.1	0.0	0.0	0.0	0.0
Gangrenous dermatitis	3.4	0.0	0.0	3.7	0.0	13.3	0.0	0.0
Necrotic enteritis (NE)	3.4	0.0	0.0	0.0	0.0	20.0	0.0	0.0
Newcastle Disease (Virulent/Exotic)	3.4	0.0	0.0	0.0	0.0	20.0	0.0	0.0
Porcine Coronavirus (PEDV/PDCoV)	3.4	0.0	0.0	0.0	0.0	0.0	75.0	0.0
Pox viruses (Parapox, Sheeppox, Capripox)	3.4	0.0	0.0	7.4	0.0	6.7	0.0	20.0
Bovine Spongiform Encephalopathy (BSE)	2.3	8.7	0.0	0.0	0.0	0.0	0.0	0.0
Classical Swine Fever Virus (CSFV)	2.3	0.0	0.0	0.0	0.0	0.0	50.0	0.0
Histomoniasis	2.3	0.0	0.0	0.0	0.0	13.3	0.0	0.0
Ornithobacterium rhinotracheale (ORT)	2.3	0.0	0.0	0.0	0.0	13.3	0.0	0.0
Peste des petits ruminants (PPR)	2.3	0.0	0.0	7.4	0.0	0.0	0.0	0.0
Porcine Circovirus	2.3	0.0	0.0	0.0	0.0	0.0	50.0	0.0
Reoviruses	2.3	0.0	0.0	0.0	0.0	13.3	0.0	0.0
Actinobacillosis (Wooden Tongue)	1.1	4.3	0.0	0.0	0.0	0.0	0.0	0.0
Avian Leukosis Virus (ALV)	1.1	0.0	0.0	0.0	0.0	6.7	0.0	0.0
Avian Pneumovirus (APV)	1.1	0.0	0.0	0.0	16.7	6.7	0.0	0.0
Contagious Bovine Pleuropneumonia (CBPP)	1.1	4.3	0.0	0.0	0.0	0.0	0.0	0.0
Glaesserella parasuis	1.1	0.0	0.0	0.0	0.0	0.0	25.0	0.0
Infectious Bursal Disease (IBD)	1.1	0.0	11.1	0.0	0.0	0.0	0.0	0.0
Lumpy Skin Disease	1.1	0.0	0.0	3.7	0.0	0.0	0.0	0.0
Newcastle Disease (Low virulent/Endemic)	1.1	0.0	0.0	0.0	0.0	6.7	0.0	0.0
Streptococcus suis	1.1	0.0	0.0	0.0	0.0	0.0	25.0	0.0
Swine Influenza Virus (SIV)	1.1	0.0	0.0	0.0	0.0	0.0	25.0	0.0
Theileria spp.	1.1	4.3	0.0	0.0	0.0	0.0	0.0	0.0
West Nile virus	1.1	0.0	0.0	3.7	0.0	0.0	0.0	0.0
Actinobacillus suis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
African Horse Sickness	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Atrophic Rhinitis (*Bordetella bronchiseptica*)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Babesiosis - Bovine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Bovine Ephemeral Fever	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Brachyspira hyodysenteriae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Crimean Congo Hemorrhagic Fever	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Egg Drop Syndrome	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ehrlichia ruminantium (Heartwater)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Histophilus somni	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Japanese Encephalitis virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lawsonia intracellularis	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Malignant Catarrhal Fever (MCF)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mycoplasma hyopneumoniae	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Nipah virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Piroplasmosis - Equine	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Poult Enteritis Mortality Syndrome (PEMS)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Reticuloendotheliosis virus (REV)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Rift Valley Fever Virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Schmallenberg Virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Seneca Valley Virus	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Vesicular Stomatitis Virus (VSV)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0