2016-2020 Action Plan for NP108

Action Plan: National Program 108 - Food Safety

Goal: National Program (NP) 108, *Food Safety* through research, and in collaboration with regulatory agencies, industry, academia and other stakeholder and partners, provides the means to ensure that the food supply is safe for consumers and that food and feed meet foreign and domestic regulatory requirements. Food safety research seeks ways to assess, control or eliminate potentially harmful food contaminants, including both introduced and naturally occurring pathogenic bacteria, viruses and parasites, toxins and non-biological-based chemical contaminants, mycotoxins and plant toxins. Food safety is a global issue; thus, the research program involves both national and international collaborations through formal and informal partnerships. Accomplishments and outcomes are utilized in national and international strategies delivering research results and advances to regulatory agencies, commodity organizations, industry, academia, research and extension agencies and consumers.

The safety of the food supply continues to be a visible public health issue and a national and international priority. Outbreaks of foodborne illness are still seen as a significant cause of morbidity, mortality, and chronic sequelae. The cost/burden resulting from these events can result in economic devastation both nationally and internationally. The cause of many outbreaks often remains unresolved, but issues such as intensive food production, international trade, consumption habits, travel and immigration of peoples are regarded as areas of concern.

Persistent outbreaks of major commodity-specific foods that potentially directly affect public health, regulations, industry, and trade, require our attention. A predominant focus is implementation of the Food and Drug Administration (FDA) Food Safety Modernization Act. Implementation cannot be over-estimated and consequently major changes within several Food Safety regulatory agencies, especially the United States Department of Agriculture (USDA), Food Safety Inspection Service (FSIS); and the FDA, Center for Food Safety and Nutrition and Center for Veterinary Medicine (CFSAN/CVM) have significantly impacted the Agricultural Research Service (ARS) National Food Safety Program (NP108). In the current 2011-2015 NP108 Action Plan, research efforts were redirected to problem-solving through technology development, in-line with the Office of Management and Budget (OMB) and their Program Assessment Rating Tool (PART) requirements that existed at that time.

During the past year it has become more evident that scientists nationally and internationally have very different opinions on what aspects of food safety research are critically important and there has been no consensus. Recent issues of food adulteration, examples which include adulteration of horsemeat, dioxins, olive oil, and honey, has placed a greater emphasis on traceability, food integrity, and the assurance of food supply networks. Adulteration is generally not considered a food safety issue per se but a quality issue. Regardless, European food agencies

are stressing a greater focus on food fraud, and consequently are realigning their research and regulatory surveillance programs. In addition, there is national and international concern regarding the increase in antimicrobial resistant (AMR) bacteria. There is also a greater emphasis on assisting emerging nations to develop secure food supplies; however, in most cases this is not a food safety issue. Ensuring adequate supplies of food does encompass some challenges to food safety when global climate change, water availability, and plant or animal diseases are considered.

In the development of the 2016-2020 NP108 Action Plan, the Food Safety National Program Leaders (NPLs) and Food Safety Team focused on what we believed were the most critical issues and needs. These are described as Problem Statements (1-7) under one Component, Foodborne Contaminants. The Problem Statements were formulated in part from interactions with various stakeholder groups, including: the 5-year Retrospective Review reviewers; our Federal partners and stakeholders from USDA, including FSIS, National Institute for Food and Agriculture (NIFA), Economic Research Service (ERS), and Agricultural Marketing Service (AMS); Department of Health and Human Services (DHHS), including FDA and Centers for Disease Control (CDC); commodity and professional organizations; and academia.

In developing the Action Plan, we approached the task appreciating that there are many special challenges, including: balancing stakeholder and partner needs with Program fiscal and personnel resources; ensuring that the research provides accomplishments that have impact and can be translated into practice through technology transfer; collaborating nationally and internationally and focusing on relevant issues to ensure that targeted areas are addressed; ensuring that the Program has the capability to respond when requested to unexpected needs and/or issues; and recognizing that the Action Plan remains a living document subject to review and realignment when and where required/appropriate.

Relationship of this National Program to the ARS Strategic Plan: Outputs of NP108 research support the "Actionable Strategies" associated with the performance measures outlined below from the *USDA Strategic Objective 4.3:* Protect Public Health by Ensuring Food is Safe; *REE Goal 5:* Food Safety; and the ARS Strategic Plan for 2012-2017, *Strategic Goal 1.2* - Protect food from pathogens, toxins and chemical contamination during production, processing, and preparation.

> **Performance Measure 1.2.A:** Develop detection methodologies for foodborne pathogens and technologies for the rapid and sensitive detection of toxins, chemicals, and biologics that can be implemented for improved food safety and food defense. **Target 2017:** Cumulatively, five new technologies will be developed and transferred.
>
> **Performance Measure** 1.2.B: Conduct and evaluate research that will lead to effective control and intervention strategies for the reduction of microbial, chemical, and other contaminants of the food supply, as well as elucidation of the molecular and physiological mechanisms that allow for persistence, survival, and transmission of foodborne pathogens in the populations and environment. **Target 2017:** Identify and evaluate potential control

and intervention strategies for the reduction and control of foodborne pathogens and contaminants along the food production continuum.

Component 1. Foodborne Contaminants

The production, processing, and distribution system for food in the United States is a diverse, extensive, and easily accessible system. This open system is vulnerable to introduction of contaminants through natural processes and global commerce, and by intentional means. Thus, the food supply must be protected from pathogens, toxins, and chemical contamination that cause disease or injury to humans. The ARS Food Safety Research Program seeks ways to assess and control potentially harmful food contaminants. ARS will conduct research and provide scientific information and technology to producers, manufacturers, regulatory agencies, and consumers to support their efforts to provide a secure, affordable, and safe supply of food, fiber, and industrial products.

Problem Statement 1. Population Systems

The goal of this research area is to identify and characterize the movement, structure, and dynamics of microbial populations within food-animal and plant systems, across the entire food continuum, from production through processing. At a microbial level, the diversity and complexity within environments and food matrices may alter the makeup of the populations, as well as cause change through spatial and temporal influences, or by the competitive or synergistic relationships among pathogens and commensals. Microbial populations can influence the safety of food, and the various environments in which they survive determine the success and impact of the microorganism. In turn, microorganism(s) may influence the conditions prevailing within the environment which also impacts their survival or ability to thrive. An example of identifiable area of study would include biofilms and the association of quorum sensing.

Components and emphasis for understanding and characterizing microbial populations and their environments must include epidemiology, ecology, and host-pathogen relationships. Epidemiologic studies of microbes within their environment, allows an analysis of the population therein. As such it enables the development of improved detection methods, provides a framework for integration of microbial genomic data with disease, and a mechanism to evaluate risk factors for microbial intervention and/or control. Ecologic studies determine the attributes and changes in various communities, that is, changes to populations in the same space. Such studies allow for a better understanding of the interactions and relationships, and the transmission and dissemination of pathogens and toxins in and among food producing animals and crops. Host-pathogen relationship studies provide an understanding of the acquisition of genetic traits, such as the development and movement of resistance genes; traits connected with colonization and evolution of virulence; and the role of commensals. Where appropriate, a metagenomics approach to selected research areas will be developed to determine the attributes of the ecological communities in which pathogens are found. Knowledge of the attributes, interactions and relationships within the community in which the pathogen lives is critical to the development of control and intervention strategies.

Within this Problem Statement it was critical to differentiate Food Safety from Animal Health. Certainly there will be some overlap; however, this will be addressed at the Office of National Programs level. There will be an emphasis on how pathogens persist in animals and the related environment, and this will drive mitigation and prevention strategies, as well as guidelines, policy and regulation.

Research Needs

- Improved approaches/designs for microbes based on population-based studies, monitoring of emerging pathogens, and supplying data for identified data gaps.
- Improved sampling collection protocols to maximize the probability of describing the exceedingly large number of diverse organisms that inhabit ecological communities.
- Data on the particular ecological niches or reservoirs for specific pathogens.
- Data on factors which enhance or reduce fitness characteristics related to persistent colonization, survival and growth.
- Data on the complex interactions between fungus/crop/environmental factors/production practices.
- Improved methods that allow evaluation of the impact of intervention or management strategies on microbial contamination throughout the entire food chain from field to plate.
- Data on how climate change impacts pathogen growth, persistence, pathogenicity or virulence.

Anticipated Products

- Improved epidemiological methods that allow the collection of quantitative data on the pathogen load within the food safety continuum.
- Capability to predict how environmental, nutritional, and/or biological factors influence or control the attributes and changes in ecological communities and within microbial populations.
- A foundation for developing appropriate intervention strategies based on mechanisms for transmission and dissemination of pathogens and toxins in and among food producing animals and crops.
- A risk-based framework that allows the integration of genomic data with disease outcome
- Descriptions of genetic traits associated with colonization and the evolution of virulence, including the development and movement of resistance genes, and the role of commensalism in resistance gene acquisition.

Potential Benefits/Impact

- Improves and enhances knowledge of how microbial populations in agriculture can potentially affect and impact public health.
- Delineates how microbial pathogens are transmitted and disseminated in and among food producing animals and plant crops (includes mycotoxin related research) allowing for future development of improved/alternate (environmentally compatible) intervention and/or control strategies.

- The critical factors which influence fitness characteristics related to microbial persistence colonization, survival, and growth allowing for future development of improved/alternate (environmentally compatible) intervention and/or control strategies.

Problem Statement 2. Systems Biology

Systems biology involves an integrated, multidisciplinary approach to study the complexities of biological components, a central problem to food safety. Identifying the components and players within the system allows the genetic components of bacterial, viral, and fungal pathogens and food-borne parasites, and their expression and products to be identified and directly related to the microorganisms. In order to study systems, quantitative technologies such as "omics" [genomics, proteomics, transcriptomics, metabolomics and metagenomics] combined with bioinformatics can be applied. There is an increased need for data gained from systems studies to be directly used for both pre- and postharvest food safety. For example, whole genome sequencing efforts using next generation sequencing (NGS) have increased and allowed regulatory agencies to identify and resolve outbreaks of foodborne illness (often for attribution purposes). It is recognized, however, that the use of NGS requires extensive collaborations with other researchers.

The main goal of research developed in response to this Problem Statement is to utilize omic-technologies and apply them to the study of foodborne pathogens in complex food systems. For example, research will elucidate how microbes cause disease and assess their prevalence, pathogenicity (ability to infect and cause disease) and virulence (the severity of disease). Understanding pathogenicity and virulence is critical for intervention and control strategies, modeling, and providing data for the development of risk assessments by regulatory agencies. Pathogens have the capacity to readily and rapidly adapt and evolve, so pathogenicity and release of virulence factors is an issue at all stages of the food safety continuum. The prevalence and patterns of contamination in food sectors may vary considerably and needs to be assessed and evaluated carefully. Differences in microbial prevalence, pathogenicity and their virulence are observed across different food production and processing systems, at different sampling times, and by using various methods. Contamination patterns reveal variation in the pathogenicity and virulence and the presence of persistant or sporadic strains and evidence of bacterial transfer from production environments to processing, and from processing environments to food. Continual outbreaks of industry related bacterial contamination emphasizes the continued need to examine pathogens in order to avoid public health risks.

Ongoing implemented microbial control strategies may lose their effectiveness, forcing the development of new production processes and products to maintain and improve the safety of foods. This in turn may restart the cycle of pathogen adaptation resulting from the changed environment and its stresses. Risk assessment(s) conducted by our regulatory stakeholders are also predicated on understanding the pathogen, the dose response, the behavior in foods, and any positive or negative influences that may affect virulence. Assessing the virulence of foodborne organisms and differences among serotypes/strains is critical in implementing new surveillance

and intervention strategies. A critical issue within this Statement is the need to differentiate between microorganisms that are relevant to agriculture versus food safety and public health.

Research Needs

- Whole genome sequencing (WGS) of specific pathogens to provide data for developing high resolution genotyping and molecular serotyping methods, for identifying virulence attributes, and elucidating the differences between pathogens and non-pathogens.
- Identification and characterization of pathogen virulence factors and how they interact.
- Data to determine if and/or how virulence is directly related to the infective dose.
- Data on pathogen adaptive responses to intrinsic and extrinsic food stressors such as pH, a_w, temperature, O_2, and determine their role in pathogenicity and/or persistence.
- Data to determine if resistance genes affect virulence, pathogenicity and/or persistence.
- Identification and characterization of virulence attributes and the responses of specific pathogens to their environment relative to changes in immunogenicity in the host.
- A detailed investigation of food production and processing environments for bacterial pathogens, and a determination what genetic and/or environmental factors might determine or allow certain bacterial strains to become persistent.
- Data on the impact of changing management, production and intervention practices on the incidence of parasites as it relates to foodborne risk.
- Identification and characterization of unique fungal genes for specific biological and physiological functions. For example, how mycotoxin synthesis is transcriptionally regulated during the fungal growth cycle.
- Data on the effect of climate change on mycotoxin production in food crops. How environmental stress factors interact to affect plants, fungal growth, and subsequent mycotoxin synthesis.

Anticipated Products

- Identities of the critical/required genetic components that make specific microorganisms pathogenic versus non-pathogenic, or highly versus weakly virulent.
- Principles relating regulatory mechanisms that control or impact gene expression with a microorganism's biology, for example, pathogenicity and virulence.
- Information relating how stress factors such as climate change affects pathogen gene expression.

Potential Benefits/Impact

- Provides knowledge of which genes are required for a microorganism to become a pathogen; generates data on genes that contribute to variations in pathogenicity, and how gene expression is involved in virulence and/or persistence viability in animal, plant and food systems.
- Generates data for the specific development of molecular pathogen phylogenetics, allowing for improved and faster molecular tracking, and determination and characterization (attribution) of outbreaks of foodborne illness by regulatory agencies.
- Supports development of improved risk models, and the revision of risk assessments, e.g., pathogens of low virulence may not be considered as necessary for regulatory control.

- Supports improved mitigation strategies and alternative control measures via identification of genes that code for resistance to antimicrobials and disinfectants, for toxin production; for the ability to grow in specific ecological niches; and for the ability to persist in production and/or processing environments.

Problem Statement 3. Microbial Contaminants: Technologies for Detection and Characterization

The challenge is the unequivocal detection and characterization of pathogenic microorganisms entering the food continuum (both pre- and postharvest). Detection and characterization are required at the earliest possible stage of the continuum to provide the necessary data for targeted interventions and reducing the need for recall of food products. Where possible, technologies must be developed that allow the most effective and rapid detection and characterization capabilities.

The focus of the research will be on the most promising technologies (depending on the matrix) or point of use, that is, whether the technology will be used for baseline studies, traceability and/or attribution forensics. This requires that decisions be made relative to what should be detected, and the required level of detection and characterization. It is noted that technologies that have the highest level of detection/characterization capability might not necessarily be the most practical, useful, economically viable, or easily implemented. High-through-put analysis is important, but it may be impractical. Promising technologies will be advanced through technology transfer, and where possible, and appropriate, will undergo validation through national or international bodies from academia, industry, and/or government sectors. Studies that suggest minimal outcome or impact will be terminated, and alternate approaches formulated.

Research Needs

- Sampling protocols to maximize the probability of detecting contaminants especially when combined with innovative approaches to sample processing.
- Sample recovery methods with attention to sample preparation as different matrices may present unique problems.
- Methods that do not have a sample or detection bias.
- Technologies that have applications in surveillance systems, for monitoring the food supply and for food defense.
- Technology development that has uniformity of application in both pre- and postharvest production and processing system.

Anticipated Products

- Technologies for multiple agents for trace-back and attribution, and where fiscal and personnel resources are also limited.
- Technologies with improved speed, cost effectiveness, and the capability to provide information for the determination and implementation of subsequent actions.
- Validated technologies that allow uniformity of implementation nationally and internationally.

Potential Benefits/Impact

- Provides validated technologies that have public health, regulatory [monitoring, traceability and attribution], trade, industry, and research use and a commonality of interests between stakeholders and partners.
- Allows improved response times to events, and subsequently allows for the development of mechanisms for treating foods taken out of commerce.
- Provides data to identify areas where interventions are most critically needed, thus assisting the implementation of HACCP programs by Federal agencies, and their regulated industries.
- Enables development and validation of predictive microbial models and helps fill identified data gaps.

Problem Statement 4. Chemical and Biological Contaminants: Detection and Characterization Methodology, Toxicology, and Toxinology

Toxicology examines the relationship between dose and its effects on the exposed organism, whereas ***toxinology*** deals specifically with animal, plant, and microbial toxins produced by or accumulated in living organisms, their properties and their biological significance for the organisms involved. Both kinds of studies are required to reduce risks arising from contamination of food by chemical and biological contaminants.

The regulation and control of veterinary drugs, chemical residues, heavy metals, persistent organic pollutants, and biological toxins derived from bacteria, fungi and plants are an integral component of any food safety program. To protect public health and the environment, regulations have been passed and implemented that set limits on contaminants in edible agricultural products. Compliance and enforcement of these regulations is a critical role of the ARS National Program's stakeholders that requires the availability of practical detection and characterization methods for veterinary drugs (antibiotics, beta-agonists), chemical residues (dioxins, pesticides), heavy metals (As, Pb, Cd), and organic pollutants (polybrominated diphenyl ethers). In addition to regulatory monitoring, there is a need to understand the biological effects of any inadvertent contamination by humans or animals. In addition to toxicological and toxinological studies, this Problem Statement also includes research directed towards methods for detection and identification of mycotoxins, toxicity evaluation, and mechanism of action.

Accomplishments and promising technologies within this research area will be quickly advanced through technology transfer and where appropriate, will undergo validation through national or international bodies such as the Association of Official Agricultural Chemists (AOAC). These studies require multidisciplinary approaches to meet the challenge, and accomplishments may have far reaching effects regarding food biosecurity, regulations and trade issues.

Research Needs

- Accurate, rapid, and easily used analytical detection methods: single/multiclass, single/multi-contaminant analytical methods; lab and field-based methods and instruments for analytical screening.
- Mechanism/action-based bioassays for laboratory and field use.
- Multi-task on/in-line inspection technologies that detect contaminants and quality attributes simultaneously functioning in or near real-time.
- Assays for assessing the efficacy of various processing methods to reduce or eliminate the toxicity in contaminated foods for human/animal consumption.
- Assays that have efficacy in toxico/toxinological studies.
- Intervention methods [bioremediation] to reduce bioavailability.
- Data on the fate and transport of contaminants and their derivatives in food systems and the environment for use in risk assessment by regulatory agencies.
- Provide parameters for regulatory agencies on biological residue depletion and withdrawal rates in animals.
- When requested, develop technologies that have a critical use in food defense.
- Data for use by regulatory agencies on the dose-response relationships and tissue specificity of biological toxins.
- Exposure assessment data for regulatory agencies on the relevance of biological toxins with undetermined toxicity through the use of animal models.
- Biomarker assays as a measure of exposure and disease susceptibility.

Anticipated Products

- New and validated technologies that when implemented provide tangible benefits through a more effective and efficient means of monitoring the food supply and environment where food is grown.
- Improved methods that assist researchers conducting toxico/toxinological studies.
- Toxico/toxinological data providing basic and applied knowledge on the effect of exposure to biological toxins.

Potential Benefits/Impact

- Provides technologies and data for regulatory use, and for better scientific and regulatory decision-making, reducing the likelihood of tolerance limit-errors, protection of consumers, and prevention of economic losses resulting from inappropriate regulatory actions.

Problem Statement 5. Intervention and Control Strategies

Intervention and control strategies will assist in reducing or eliminating pathogens in food animals and their derived products, seafood, and plant crops during production and processing. Reduced shedding of zoonotic pathogens by food producing animals, and contamination of seafood and plant material will subsequently help reduce the pathogen load during slaughter/ harvesting and subsequent processing and storage. Some food processing/storage technologies

have the ability to inactivate microorganisms to varying degrees; however, the intensities required can result in adverse functional and/or sensory properties, combined with a significant reduction in quality. Consequently, there remains a continued need to develop and subsequently combine new and/or innovative processing technologies. Interventions can be additive and/or synergistic, leading to improved control over pathogen growth without potential changes in food quality or reduction in nutrition. Research after an approved period that yields no outcome, or requires the purchase of expensive equipment will be terminated, and alternate approaches formulated. If alternate approaches cannot be found, the project will be redirected to another priority. Unintended or unanticipated consequences of processing intervention strategies such as changes in virulence, production of toxins, pathogen resistance, selection of resistant strains, or changes in microbial ecology should be considered for further investigation.

The challenge is that the pathogen load on a product must be significantly reduced by any processing intervention strategy to avoid the consequences in food production resulting from "dirty in, dirty out" processing. There is also the concern that during processing the initial microbial load can be reduced but recontamination occurs with different strains or serotypes present or resident within the processing environment. Such concerns are valid because there are numerous observations that the pathogens present on product prior to processing are different from those found after processing. This variation in pathogen type has significant public health concerns since those pathogens initially found on the product may not be responsible for any foodborne outbreak and/or clinical outcome.

Research should also address, where possible, the integrated lethality for an intervention process. The purpose of the process lethality determination is to provide processors with science-based validation of the effectiveness of a specific process to destroy any microorganism of concern. For example, a thermal process needs to account for many variables including the initial pathogen load, multiple pathogens, pathogen strain variability, food structure, and the heating and cooling profile of the product. In-plant validation should be conducted to verify the intervention(s). The entire lethality process is incorporated into a systems approach to developing pathogen intervention or control strategies. Problem Statement 5 addresses a wide range of food products including animals, shellfish -seafood, and plant materials. The Problem Statement also includes biocontrol technologies for food crops contaminated by mycotoxins, such a tree nuts, corn and grains.

It is critically important within these studies that for development and validation of any process intervention a common or representative core set of pathogens or surrogates be used. This is critically important in order to make the intervention research results comparable both within and external to the Program. Core sets of strains for different pathogens will be made available though the ARS bacterial culture collection. If a specific strain is not available in the collection, Office of National Programs will facilitate researchers obtaining the appropriate isolate.

Research Needs

- Interventions that prevent colonization or modulate pathogens in the gut; target specific metabolic endpoints; decrease shedding of zoonotic pathogens at the time of slaughter.

- Data on the role of transportation and lairage, slaughter/processing methods, and equipment on pathogen survival, transfer, post-harvest processing and storage.
- Data on the effect of intrinsic (pH, a_w, Eh, nutrient content, antimicrobials, structure) and extrinsic (temperature, RH, O_2) parameters in the production, processing, handling, preparation, and storage of foods. This need includes food preparation and handling for, or by food service operators and/or consumers.
- Data that elucidate the mechanism(s) of pathogen introduction, persistence/survival in shellfish.
- Production and processing intervention/control strategies for pathogen reduction in shellfish.
- For plant crops (fresh produce), obtaining data on the role of extrinsic and intrinsic factors on pathogen internalization and/or attachment; and pathogen occurrence and movement.
- For plant crops (fresh produce), obtaining data on the role and/or influence of commensals and/or non-pathogens.
- Identification of the critical control points in both production and processing of fresh produce, plant crops (grains/tree nuts) that can be mitigated through the development and implementation of intervention and control strategies.
- Biological control strategies to reduce mycotoxin production and contamination of food and feed crops such as corn/maize, cotton seeds, grains and tree nuts. Any new or modified effective biocontrol organisms and delivery systems must not introduce other toxic factors; for example, for the biocontrol of aflatoxins there should be no introduction or expression of the CPA or fusarium toxin genes.
- Data that assesses the role of chemicals that might act synergistically to enhance accepted interventions.
- Methods to prevent the growth of pathogenic and spoilage microorganisms in minimally preserved, brined, and fresh-cut foods.
- Data on the effect of single and/or combinations of intervention technologies on pathogen reduction. Validate these data through laboratory, pilot-plant processing and commercial processing facilities.
- Data on whether combinations of non-thermal technologies can be incorporated in the hurdle concept; and determine whether single or combinations of non-thermal technologies are more effective if used in combination with traditional interventions.
- Data that evaluates the outcome/impact of intervention options for small and very-small regulated plants.
- Data in intervention effectiveness to be for use in the development of Quantitative Microbial Risk Assessments (QMRAs)
- Data determining the effect of intervention technologies on sensory/quality deterioration, and accumulation of toxic chemical by-products.

Anticipated Products

- Improved intervention strategies to eliminate and/or control microorganisms in animals and their derived products, seafood and plant production, processing and storage systems. Interventions have the ability to inactivate microorganisms to varying degrees; therefore, the goal is to maximize intervention effectiveness while minimizing sensory/quality deterioration, and possible accumulation of toxic chemical by-products.
- Improved intervention strategies for various sized operations, utilizing environmentally compatible technologies.
- Improved intervention strategies focusing on the use of combinations of new or innovative technologies for (minimal) processing, thus mitigating the potential for the development of resistance.
- Improved interventions based on an understanding of their modes of action and effects on the microbial ecology of a food product, since inadequate suppression of spoilage could create an opportunity for human pathogen growth and toxin production.

Potential Benefits/Impact

- Provision of critical intervention strategy data to regulatory/action agencies, industry, and commodity organizations that allows for the development, evaluation, and implementation of Good Agricultural Practices (GAPs); Good Manufacturing Practices (GMPs) or regulations based on sound science.
- Enables methods/strategies for the evaluation of any developed interventions and controls.
- Provides production control interventions that reduce downstream contamination, which subsequently reduces disease risk.

Problem Statement 6. Predictive Microbiology/Modeling; Data Acquisition and Storage; Genomics Database

The tenet of predictive microbiology is that the behavior of any microorganism is deterministic and able to be, within limits, predicted from knowledge of the microorganism itself and the microorganism's immediate environment. However, it has been stressed by stakeholder groups that research should also include a greater emphasis on probabilistic modeling to balance the deterministic approaches. This would benefit predicting the behavior of pathogens under stressed conditions (more relevant to the food industry) where growth/inactivation is stochastic.

Behavioral predictions and models are accepted (globally) as an integral part of microbial risk assessment used to support food safety measures by both food safety regulatory bodies and industry. The Program does not develop or conduct Risk Assessments (RA), where RA is defined as the determination of a quantitative or qualitative value of risk related to a specific situation and a recognized hazard. However; the Program does conduct research and provide data when requested by our regulatory stakeholders (FSIS and FDA) for their use in conducting risk assessments.

The Program develops various modeling programs including; the **Pathogen Modeling Program** (PMP), a package of models that can be used to predict the growth and inactivation of foodborne bacteria, primarily pathogens, under various environmental conditions. In addition, the **Predictive Microbiology Information Portal** (PMIP) is geared to assist food companies (large and small) in the use of predictive models, the appropriate application of models, and proper model interpretation. The vision is that the PMIP will be the highway for the most comprehensive websites that bring together large and small food companies in contact with the information needed to aid in the production of the safest foods. The PMIP links users to numerous and diverse resources associated with models (PMP), databases (ComBase), regulatory requirements, and food safety principles.

All predictive models developed must be available for external examination, review, and utility. If predictive models are developed for internationally accepted high priority pathogen-food combinations, then they could have a major impact for food companies in the USA and other countries producing and exporting food to the USA. This will require significant interactions with risk assessors and involvement in international initiatives such as National Advisory Committee on Microbial Criteria for Foods (NACMCF), Codex Alimentarius Commission (CODEX), Food and Agriculture Organization (FAO), and the World Health Organization (WHO). Collaborations with stakeholders must be strengthened with regards to what research needs to be conducted so as to effectively utilize the inherent ARS expertise and modeling systems mechanisms.

Data acquisition and storage: ARS and international institutes, including Institute Food Research (IFR-UK) and the University of Tasmania (UTas), as well as associate members University of Querétaro, Mexico; Unilever Research, UK; Agricultural University of Athens, Greece; National Food Research Institute, Japan; Hokkaido University, Japan; and Rutgers University also developed and maintains a publically available global food safety database, **ComBase** - *a Combined dataBase for predictive microbiology* – which is the number-one web-based resource for quantitative and predictive food microbiology in the world. Its main components include a database of observed microbial responses to a variety of food-related environments and a collection of relevant predictive models. The purpose and goal of ComBase is to provide an electronic repository for food microbiology observations and to make such data and the generated predictive tools freely available and accessible to the entire food safety community. Data acquisition and use is an interdisciplinary research challenge that translates into safer products and improved public health.

Genomics as a functional and critical part of omic-technologies holds great promise for improving the early detection, prevention and control of current and emerging foodborne pathogens, thus contributing to improved food safety and consequently public health. Genomics have the potential as a partner or replacement of culture-based techniques. Food safety regulatory agencies, USDA and the FDA, have discussed and are planning to implement the increased use of genomics, in particular partial and/or whole genome sequencing (P/WGS) for both regulatory monitoring, attribution and potentially for revising risk assessments. Implementation of such a redirection requires developing a coordinated system of genomic

sequencing technology for routine testing. Critical within this issue is the development of an ARS database from our national and international sequencing/annotation efforts. For this work, a common or representative core set of bacterial pathogens or surrogates will be available. Additional data from isolates studies obtained from national and international collaborations will be incorporated. Allied to the sequencing efforts will be meta-data descriptors. This research will be part of a larger international initiative, the Global Microbial Identifier (GMI), a global, visionary taskforce including more than 30 countries who share an aim of making novel genomic technologies and informatics tools available for improved global infectious disease diagnostics, surveillance and research, by developing needs and end-user based data exchange and analysis tools for characterization of all microbial organisms and microbial communities.

Research Needs

Modeling

- Models that include an emphasis on probabilistic modeling to balance the deterministic approaches. This includes the influence of challenge strain(s); assessment of a model's performance; predictive value on extrapolation; and efficacy especially in complex food matrices where the intrinsic and extrinsic parameters may change.
- Data that examines and determines if growth/no-growth interface models predict the probability of growth occurring when a population faces more than one stressor/constraint.
- Models that have utility for risk assessment from both the producer and consumers perspective. There are distinctly different consequences of conservative (over) vs. non-conservative (under) prediction of growth or risk.
- Data that determines if changes in the microorganism(s) themselves occur, due to up/down regulation of genes; quorum sensing; or transfer of genetic information between species.
- Models that predict pathogen and non-pathogen behavior in complex food systems utilizing inactivation data. These types of studies are fundamental to developing Hazard Analysis Critical Control Point (HACCP) systems and regulations.
- Process risk models for industry that derives predictions for Critical Control Point (CCP) assessment.
- Data that demonstrates how models can be integrated more fully into supply chains, thereby increasing utility to industry and risk assessors.
- Models that determine the effects of food safety interventions, for example carcass and produce sprays; and physical and chemical interventions, for example: radio frequency, heat, cold, irradiation, and Generally Recognized as Safe (GRAS) chemicals.

Database

- Compile modeling data into a shared informational database through national/ international efforts.
- Write program code linking ComBase records to online databases. This feature will collect attributes for individual records, such as journal article title, abstract, authors, and institution.

- Data collection for specific organism-food combinations, enhance the value for the food systems community. Prioritization will be given to data needed to fill current database gaps, as well as records most sought after by ComBase customers.
- Derive and provide relevant data to regulatory agencies for use in HACCP programs, risk assessments, labeling, persistence, and issues relative to international trade.

Genomics

- Conduct sequencing and annotation efforts on pathogens of concern that fall under research efforts in various Problem Statements.
- Development of a genomic database for identification of microorganisms or development of an identifier of microorganisms as a platform for storing data.
- User friendly system to aggregate, maintain, share, mine and translate genomic data for microorganisms, for example: the identification of relevant genes or for the comparison of genomes to detect outbreaks and emerging pathogens.
- Increased focus on bioinformatics (computational biology) as more sequence data becomes available, and the complexity of both the data and questions being asked become more sophisticated.

Anticipated Products

- Predictive microbiology [models] that have validity and usefulness while addressing the limitations of the predictive ability. Studies leading to development of these models will include "real food systems" not just broth models or model food systems.
- A shared informational database done in-part through the continued development and expansion of the international collaborative project Combase. This will include data from industry/academia that pertains to "real food production/processing systems."
- A computer-based system and database to aggregate, share, mine and translate genomic data for microorganisms in real-time through a direct link using user-friendly platforms.

Potential Benefits/Impact

- Generates data on the responses of microorganisms to both defined and changing environmental conditions, and translates these data into mathematical models and user friendly software tools available on the internet at no cost. These must be readily usable by national and international regulatory and public health agencies, and industry, to assist in ensuring the safety of the food supply.
- An internet-based database ensures that data-mining and acquisition will continue to be coordinated. Genomic database and bioinformatics efforts become increasingly important so that biologists have the ability to gain information that will foster technological innovation, and an understanding of the genetic basis of foodborne microorganisms.

Problem Statement 7. Antimicrobial Resistance

The discovery of antibiotics transformed human and veterinary medicine and saved millions of lives in the United States and around the world. The rise/increase of antibiotic-resistant bacteria represents a serious threat to both animal and human health and the economy. The concern for

the development of antimicrobial resistant (AMR) bacteria has resulted in the development of both national and international strategies to address the issue. In 2014, the President signed an Executive Order, and a strategy was developed by multiple agencies to begin addressing AMR at the National level. Even though the USDA is not the lead regulatory agency for antibiotic use and AMR, USDA-ARS is an important part of the solution.

Areas of concern include detecting, measuring, and assessing the amount of AMR bacteria within the production animal populations with an emphasis on foodborne pathogens. In addition, developing alternative strategies to minimize the use of antibiotics in production animals while maintaining and improving animal health and ensuring safe food for consumers is a critical need. Currently, the role of feeding antibiotics to production animals on the development of AMR bacteria and the impact on public health is not well defined. In addition, there is a critical need for the development of alternative strategies to reduce the level of antibiotic use as well as developing mitigation strategies for foodborne AMR bacteria in food producing animals. These areas are cross-linked with Problem Statements 1 and 2 within the Action Plan

Research Needs

- Multidisciplinary approaches to understand the development, persistence, and transmission of resistant genes, and antimicrobial resistant in foodborne microorganisms.
- Improved detection methods to assess bacteria for antibiotic resistance genetic elements in foodborne pathogens.
- Methods to assist other Federal agencies in measuring and assessing AMR in food animal populations, e.g., assisting FSIS in interpreting National Antimicrobial Resistance Monitoring System (NARMS) results and provide support for USDA's National Animal Health Monitoring System (NAHMS) studies on AMR bacteria.
- Alternatives to antibiotics including management practices, pre-and probiotics, bacteriophage gene products, lytic enzymes, vaccines and other novel products to reduce their levels in food producing animals, thus reducing the need for antibiotics. The development of any practice/product must ensure practicality and potential utilization so that implementation is cost effective to the producer, readily approved by regulatory agencies and industry, and easily incorporated into any management system.
- Elucidating the ecology of foodborne AMR bacteria in terms of gene transfer, the role of the host microbiome in the development and maintenance of AMR, and the role of biofilms in the development of AMR.

Anticipated Products

- Improved detection techniques facilitating the speed, ability, and accuracy of detecting foodborne AMR bacteria in food producing animals and their products.
- Improved strategies to reduce antibiotic use and the number of AMR bacteria in the food supply.

Potential Benefits/Impact

- Provides support for both stakeholders and regulatory agencies in developing strategies to address foodborne AMR bacteria.
- Improves strategies to reduce the use of antibiotics in production animals while maintaining their health and growth efficiency. This is critical for feeding an ever growing population while also addressing a serious public and animal health concern.

Component 1 Resources

The following ARS locations have research projects addressing the 7 Problem Statements identified under Component 1

Beltsville, MD
Wyndmoor, PA
West Lafayette, IN
Peoria, IL
Ames, IA
Albany, CA
Maricopa, AZ
Clay Center, NE
Fargo, ND
College Station, TX
Fayetteville, AR
Stoneville, MS
New Orleans, LA
Dawson, GA
Athens, GA
Raleigh, NC