THE NATIONAL ANTIMICROBIAL RESISTANCE MONITORING SYSTEM

STRATEGIC PLAN 2021-2025

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BACKGROUND

Antimicrobial resistance (AMR) has been ranked by the World Health Organization as one of the top global health challenges. Reducing human exposure to antimicrobial resistant microorganisms and their resistance determinants is key to reducing the burden of antimicrobial resistant infections, and food is a potential source of human exposure. An antimicrobial resistance monitoring system is required to track resistance among different population groups and in different settings over time, detect new resistance types, reveal the underlying determinants of resistance in different microorganisms, and measure the effectiveness of interventions.

The National Antimicrobial Resistance Monitoring System (NARMS) was established in 1996 as a collaboration of the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Department of Agriculture (USDA), the U.S. Food and Drug Administration (FDA), and state and local health departments. NARMS currently tracks resistance in enteric bacteria from humans, retail meats, and food-producing animals at the time of slaughter. Nontyphoidal *Salmonella* and *Campylobacter* are among the leading bacterial causes of foodborne illness in the United States and many other countries. Each year these two pathogens alone are estimated to cause over 2.5 million illnesses in the U.S. resulting in nearly 40,000 hospitalizations and hundreds of deaths. Whereas most *Salmonella* and *Campylobacter* infections are self-limited, some require treatment with antimicrobial agents. Emergence of antimicrobial resistance in foodborne pathogens presents a challenge for treatment of infections that warrant antimicrobial therapy.

A review of NARMS by the NARMS Review Subcommittee of the FDA Science Board was completed in 2017 and presented at the NARMS public meeting in October of that year. This review evaluated the status of the NARMS program and made recommendations for its strategic direction with an emphasis on a One Health model of monitoring. One Health is defined as a collaborative, multisectoral, and transdisciplinary approach — working at the local, regional, national, and global levels — with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment. Given the complex interplay of humans, livestock, pets, wildlife, and the environment, the adoption of a One Health approach to addressing resistance has gained acceptance worldwide. The WHO/OIE/FAO tripartite collaboration on AMR recommends that countries develop national AMR action plans, including AMR surveillance, in accord with the One Health paradigm. The updated U.S. action plan to combat antimicrobial resistance will adopt a One Health approach.

Following the NARMS Review Subcommittee recommendations to incorporate the three major domains of the One Health model (humans, animals, environment), an important theme of this strategic plan is the expansion of testing to examine resistance in animal pathogens and the environment.

For environmental monitoring, what constitutes the best sampling points will be refined over time. A good starting point is surface waters as these form the confluence points that represent differentially affected ecosystems.

During 2017-2018 a two-year pilot project was completed by the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) to evaluate the feasibility of using veterinary diagnostic laboratories to monitor the antimicrobial susceptibility of three veterinary pathogens: *Escherichia coli* and *Staphylococcus pseudintermedius* in dogs and *Salmonella enterica* in any host. Approximately 5,000 isolates from clinically sick animals were collected and tested. We plan to continue this work and include animal pathogen data in the NARMS annual reports.

In a One Health sampling design, we included the need to evaluate additional bacterial species, the development of methods to better characterize the "resistome" (*i.e.*, the complement of resistance genes in a sample), and periodic pilot projects to examine other animals and animal products for antimicrobial resistance patterns.

In addition to documenting trends in antimicrobial resistance, NARMS conducts epidemiologic and microbiologic investigations and research. Some studies examine sources, risk factors, and clinical outcomes of infections with specific bacterial types or subsets of bacteria that exhibit particular resistance patterns. Microbiologic research studies range from the genetic mechanisms of resistance and the mechanisms that permit the transfer of resistance between bacteria, to improving methods for isolation, typing, and antimicrobial susceptibility testing and novel approaches to identify antimicrobial resistance.

***Vision**: a world in which antimicrobials are effective for treating human and animal infections and the burden of antimicrobial-resistant infections is minimized*

***Mission:** to provide scientifically reliable data to help reduce the human, animal and environmental health burden caused by antimicrobial-resistant bacteria*

To accomplish its mission, NARMS currently conducts the following activities:

1. Monitors trends in antimicrobial resistance among enteric bacteria from humans, retail meats, and animals at the time of slaughter;
2. Disseminates timely information on antimicrobial resistance in pathogenic and commensal microorganisms to stakeholders in the U.S. and abroad to promote interventions that reduce resistance among foodborne bacteria;
3. Conducts research to better understand the emergence, persistence, and spread of antimicrobial resistance;
4. Provides timely antimicrobial resistance data for outbreak investigations; and
5. Provides data that assist the FDA in making decisions related to the approval of safe and effective antimicrobial drugs for animals.

NARMS ACCOMPLISHMENTS 2012-2019

In the previous NARMS Strategic Plan: 2012-2016, the goals and objectives were based largely on a 2007 NARMS program review by an External Subcommittee of the FDA Science Advisory Board. This subcommittee made recommendations related to four areas of work: 1) sampling, 2) research, 3) international activities, and 4) data management and reporting. The most important elements of each of these recommendations were achieved. One area in which NARMS has lacked efficiency is in timely data reporting, where progress is being made and which continues to be a top priority. The major activities NARMS conducted to address the previous strategic plan included:

1. Incorporation of whole genome sequencing (WGS) into NARMS testing and reporting beginning in 2013. This included the development of informatics processes to upload the WGS data in near real time into the public database at the National Center for Biotechnology Information (NCBI) Pathogen Detection site for use by stakeholders.
2. Addition of individual animal intestinal sampling at slaughter using a randomized, nationally representative scheme designed to reduce bias in estimating resistance prevalence in target organisms in 2013.
3. Analysis of more than 25,000 cecal samples and 43,000 bacterial isolates of *Salmonella, Campylobacter, E. coli* and *Enterococcus* during CY2013 to CY2019 by the USDA. During the same period, data on over 21,700 isolates from the Pathogen Reduction/Hazard Analysis and Critical Control Points (HACCP) verification program were contributed to NARMS.

4. Expansion of the geographical representativeness of retail meat testing from 11 states to 24 states and the number of annual food samples from 5,280 to 11,520.
5. Collaboration with the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) to publish data on antimicrobial resistance in select companion animal pathogens starting with the 2017 NARMS Integrated Summary report.
6. Support of pilot studies to collect antibiotic use information in livestock and poultry.
7. Targeted studies to estimate resistance in bacteria from shrimp, tilapia, and salmon.
8. Publication of crosscutting epidemiologic studies focused on the attribution of antimicrobial-resistant enteric infections to foods, food animals, and other sources, including the analysis of bacterial isolates from outbreaks.
9. Development of web-based interactive data displays and incorporation into the annual NARMS reports to make data more accessible to stakeholders. Launched NARMS Now to facilitate sharing of surveillance findings from human infections. Launched Resistome Tracker to share comprehensive data on antibiotic resistance genes identified in genomes submitted to NCBI.
10. International collaborations (*e.g.*, World Health Organization, Codex) to develop guidance documents and engage in capacity-building exercises to enhance laboratory-based surveillance of foodborne diseases and antimicrobial resistance and enhance outbreak detection and response in many countries. Contributed to various activities of the Transatlantic Task Force on AMR (TATFAR), an international initiative to share information on efforts to combat resistance.
11. Establishment of new partnerships within and outside of government to leverage resources dedicated to antimicrobial resistance to better understand antimicrobial resistance from a One Health perspective. For example, NARMS worked with EPA to identify a preliminary sampling scheme for environmental water monitoring, partnered with universities to collect retail meat data, expanded cooperation with USDA to explore animal pathogen data, and collaborated with NCBI to make NARMS data more accessible.

STRATEGIC GOALS AND OBJECTIVES

NARMS has established four strategic goals. These goals build on progress made since the last strategic plan and are dependent on the availability of resources. These goals incorporate the One Health principle of an interdisciplinary approach to human, animal and environmental health and incorporate animal pathogen and environmental testing. With these changes, NARMS is engaging experts in environmental and animal health within the partner agencies and by forming new alliances. The Environmental Protection Agency (EPA), the CDC Waterborne Disease Prevention Branch, the USDA National Animal Health Laboratory Network (NAHLN) and FDA's Veterinary Laboratory Investigation and Response Network (Vet-LIRN) have now partnered with existing NARMS agencies to design and implement one health AMR surveillance. NARMS continues to collaborate with the National Center for Biotechnology Information (NCBI) to identify AMR genes in genomic sequences and with the FDA Center for Food Safety and Applied Nutrition (CFSAN) on methods for water testing. Different agencies will focus on different aspects of the NARMS Strategic Plan according to their mission and expertise.

GOAL 1: ENHANCE SAMPLING FOR FOODBORNE PATHOGENS WITHIN A ONE HEALTH FRAMEWORK

Growing consensus around the utility of a One Health paradigm for AMR monitoring represents a major conceptual change in the structure of integrated AMR surveillance. While best practices in One Health AMR surveillance are not fully defined, generally they encompass data from human, animal, and environmental testing. NARMS plans to add animal pathogen and environmental testing data to obtain a more complete view of resistance across ecosystems.

Objective 1.1: Enhance and maintain routine resistance monitoring in select pathogens causing illness in food-producing and companion animals.

Objective 1.2: Implement geographically-representative monitoring including surface waters to establish baseline AMR data in aquatic ecosystems.

Objective 1.3: Initiate an AMR testing program for animal feed and pet food, including their ingredients, and share data in an integrated database and in NARMS reports.

Objective 1.4: Add routine testing of seafood products and imported foods and conduct pilots to explore other possible sources of resistant bacteria affecting health such as minor food-producing animal species, produce, and wildlife.

Objective 1.5: Expand NARMS to explore the diversity of antimicrobial resistance in other foodborne microorganisms.

GOAL 2: EMPLOY ADVANCED TECHNOLOGIES TO BETTER UNDERSTAND THE EVOLUTION AND SPREAD OF RESISTANCE AMONG FOODBORNE PATHOGENS

The development of advanced DNA sequencing technologies represents a major technological advancement in the science of infectious disease. It is now cost effective to determine the complete DNA sequence of a bacterium in a short time. This provides comprehensive information on bacterial traits, including their carriage of antimicrobial resistance genes. It is now possible to predict resistance (as well as phylogenetic relatedness, serotype, virulence, *etc*.) with high accuracy among pathogens from the genomic sequence alone. Metagenomics, which refers to analysis of the complete DNA sequence of a complex biological sample, is very powerful for identifying the range of resistance genes in a sample. These technologies will continue to be updated and will ultimately have a substantial impact on how NARMS conducts and reports surveillance data in the future. The use of bioinformatics for data analysis will play a larger role in NARMS as genomic data sets continue to expand rapidly.

Objective 2.1: Apply predictive resistance analytics, machine learning, and other bioinformatics tools to NARMS-related data to better understand the mechanisms, sources, and spread of resistance.

Objective 2.2: Optimize *in vitro* antimicrobial susceptibility testing to identify new resistance mechanisms.

Objective 2.3: Develop metagenomic approaches to characterize the resistome of animals, humans and environmental samples and to link resistance genes to their microbial source.

Objective 2.4: Employ long-read DNA sequencing methods to establish a reference database of fully characterized strains and their plasmids.

Objective 2.5: Conduct research to understand concomitant adaptive microbial features that might contribute to the persistence and spread of resistance (*e.g*., colonization, stress tolerance) under different selection pressures (*e.g*., heavy metals, antiseptics, *etc*.).

GOAL 3: IMPROVE DATA SHARING, COMMUNICATION, AND COLLABORATION

Given the importance of AMR among enteric pathogens to global heath, and the constant threat that resistant enteric pathogens might contribute to international epidemics, there is interagency and international interest in optimizing resources and sharing information for timely public health response.

Objective 3.1: Deposit microbiological data into public databases and post timely web-based updates that describe emergent resistance phenomena for timely response by all stakeholders.

Objective 3.2: Engage with outside partners (*e.g.*, WHO, Clinical and Laboratory Standards Institute, TATFAR, industry) to determine how resistance, whole genome sequence, and metagenomic data can be interpreted for appropriate responses.

Objective 3.3: Work with international partners to establish data quality standards, analytical protocols, and reporting formats for resistance and genome sequence information.

GOAL 4: CONDUCT RESEARCH TO ASSESS THE SOURCES AND IMPACT OF RESISTANCE AND THE EFFECTIVENESS OF PREVENTION PRACTICES FOR FOODBORNE PATHOGENS

Antimicrobial resistant enteric infections are often more difficult to treat than susceptible infections, and often require the use of second-line agents that may be more toxic, are administered intravenously and are more expensive. Antimicrobial resistant infections may persist because appropriate treatment may be inadvertently delayed until the resistance profile is known. This delay can lead to more severe illness such as bloodstream infections. Antimicrobial resistant infections can often lead to more hospitalizations and thus increased direct medical costs. Additional studies looking at the direct and indirect impact of AMR infections among animals and humans are still needed.

Sources of antimicrobial resistant enteric pathogens are often challenging to investigate but may be critical for implementing successful prevention and control strategies. Studies to assess risk factors for antimicrobial resistant infections and studies to assess preharvest practices may help to elucidate the sources of antimicrobial resistance in a variety of settings. With a limited supply of new antimicrobials and rapid emergence of resistance soon after the introduction of many antimicrobial agents, prevention strategies are crucial in reducing the impact of AMR infections. Studies looking at strategies such as vaccination, animal husbandry, and practices during processing to reduce spread of resistant organisms, may help to direct policies and strategies to reduce the burden of AMR.

Objective 4.1: Conduct studies to determine the burden and impact of antimicrobial resistance on human, animal and environmental health.

Objective 4.2: Conduct studies to determine risk factors for antimicrobial-resistant infections and to attribute infections to foods, animals, environmental and other sources.

Objective 4.3: Collaborate with partners to understand prevention practices including non-antimicrobial interventions (*e.g.*, bacteriophages, vaccines, husbandry) and their impact on resistance.

CHALLENGES AND OPPORTUNITIES

Institutional challenges include financial resource limitations, competing priorities, human resources limitations, constraints in workforce training (*e.g.*, in bioinformatics, information technology, and security), and limitations on laboratory and electronic resources needed to investigate evolving scientific issues in a timely manner. Reduced availability of isolates for microbiological testing also presents a challenge as clinical laboratories transition to testing samples using culture-independent diagnostic methods, thereby reducing the number of bacterial isolates available for surveillance purposes.

Limiting antimicrobial resistance is a priority for public health. The adoption of a One Health approach is fostering new interagency collaborations to address the resistance challenge across the human, animal and environmental domains. Similar goals are being promoted in the global arena. There is a growing consensus that AMR is best addressed through global partnerships such as the tripartite efforts of The Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Organization for Animal Health (OIE) among others. NARMS will continue to work with these partners to advance the enteric pathogen antimicrobial resistance mitigation efforts of public health authorities abroad, to better harmonize testing and reporting methods, to facilitate data sharing and collaboration across the domains of One Health.

The *NARMS Strategic Plan* is a dynamic roadmap that outlines the program's commitment to providing scientifically sound data on enteric pathogen antimicrobial resistance through sustained monitoring, research, data sharing, and collaboration. The NARMS program is critical to accomplishing the public health missions of federal and state governments. Toward accomplishing its vision for minimizing antimicrobial resistance and strengthening public health, the NARMS collaboration will continue to provide the highest quality antimicrobial resistance information for informed decision making.

LINKS TO ADDITIONAL INFORMATION

Additional information about NARMS can be found on the FDA, CDC, and USDA websites listed below. The FDA website also includes NARMS Executive Reports.

FDA:

https://www.fda.gov/animal-veterinary/antimicrobial-resistance/national-antimicrobial-resistance-monitoring-system

CDC: https://www.cdc.gov/narms/index.html

USDA:
https://www.fsis.usda.gov/wps/portal/fsis/topics/data-collection-and-reports/microbiology/antimicrobial-resistance/narms

For a review of the NARMS program commemorating its 20th anniversary, see

Karp, BE. et al. National Antimicrobial Resistance Monitoring System: Two Decades of Advancing Public Health Through Integrated Surveillance of Antimicrobial Resistance. Foodborne Pathogens and Disease, 14:10, 2017 available here: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5650714/