NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

Progress Report

Fiscal Year 2021

Prepared by the United States Task Force for Combating Antibiotic-Resistant Bacteria

Contents

The Task Force for Combating Antibiotic-Resistant Bacteria

The Department of Health and Human Services (HHS) and its following components:

AHRQ	Agency for Healthcare Research and Quality
ASPE	Office of the Assistant Secretary for Planning and Evaluation
ASPR	Administration for Strategic Preparedness and Response
BARDA	Biomedical Advanced Research and Development Authority within ASPR
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare & Medicaid Services
FDA	and Drug Administration
NIH	National Institutes of Health
OGA	Office of Global Affairs

The United States Department of Agriculture (USDA) and its following components:

APHIS	Animal and Plant Health Inspection Service
ARS	Agricultural Research Service
FAS	Foreign Agriculture Service
FSIS	Food Safety and Inspection Service
NIFA	National Institute of Food and Agriculture
OCS	Office of the Chief Scientist

The Department of Defense (DoD) and its following components:

DHA	Defense Health Agency
GEIS	Global Emerging Infections Surveillance
IDCRP	Infectious Disease Clinical Research Program
MIDRP	Military Infectious Diseases Research Program
MRSN	Multidrug-Resistant Organism Repository and Surveillance Network
PVC	Pharmacovigilance Center
WRAIR	Walter Reed Army Institute of Research

Department of the Interior (DoI)
Department of State (DoS)
Environmental Protection Agency (EPA)
United States Agency for International Development (USAID)
Department of Veterans Affairs (VA)

Background

Pathogens that have evolved to be resistant to the drugs currently used to treat infections are an ongoing threat to public health, animal health, food production, and national security. A recent analysis estimated that 1.2 million deaths globally were caused by antibiotic-resistant (AR)[1] bacteria in 2019, making this threat a leading cause of death for people of all ages worldwide. Domestically, the CDC estimates that more than 2.8 million Americans suffer from AR infections each year and that more than 35,000 Americans die.

The U.S. government is pursuing a National Strategy for Combating Antibiotic-Resistant Bacteria (CARB), which takes a One Health approach to five goals:

Goal 1: Slow the emergence of resistant bacteria[2] and prevent the spread of resistant infections.

Goal 2: Strengthen national One Health surveillance efforts to combat resistance.

Goal 3: Advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria.

Goal 4: Accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines.

Goal 5: Improve international collaboration and capacities for antibiotic-resistance prevention, surveillance, control and antibiotic research and development.

The federal CARB Task Force, co-chaired by DoD, USDA, and HHS, was established to facilitate and monitor implementation of the National Strategy. In 2015, the CARB Task Force translated the CARB National Strategy into a five-year National Action Plan for CARB (2015 Plan). Under the 2015 plan, the U.S. government established critical infrastructure and programs that improved antibiotic use in humans and animals, dramatically increased awareness of AR threats in real time, drove innovation in diagnostics and treatment options, and solidified global partnerships and action.

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[1] The 2020 CARB National Action Plan follows the framework of CDC's 2019 AR Threats Report and uses the term "antibiotic" to describe antibacterial and antifungal drugs, which kill bacteria and fungi, respectively. CDC is currently transitioning to use the term "antimicrobial resistance," abbreviated as AR, to describe the phenomenon of resistance among the bacterial and fungal pathogens. In this report, the acronyms AR and AMR are both used to refer to antimicrobial resistance.

[2] Although tuberculosis (TB) falls outside the scope of the CARB Strategy and National Action Plan, certain TB activities are reported here because they represent critical near-term public health activities that will support progress to reduce the burden of drug-resistant TB in the United States. Otherwise, U.S. government activities to address drug-resistant TB domestically and internationally are managed through efforts such as the U.S. National Action Plan for Combating Multidrug-Resistant TB.

These actions have had an impact: prior to the COVID-19 pandemic, deaths from AR infections in the United States decreased. However, CDC has found a reversal of this progress as antibiotic use and AR infections surged significantly in U.S. hospitals during the first year of the pandemic, including an alarming 15 percent increase in both resistant hospital-onset infections and deaths. There are still too many deaths from AR infections both in the United States and globally;[3] the health, economic, social, and development burden of AR infections remains too high; new forms of resistance continue to emerge; and new strategies are needed to prevent, treat, and limit the spread of infections. Therefore, the U.S. government reaffirmed its commitment to addressing the threat of AR bacteria by publishing a National Action Plan for CARB for 2020 through 2025 (2020 Plan). The 2020 plan maintains the five goals of the National Strategy and builds on progress since 2015 with new objectives and targets to be met in the next five years.

The CARB Task Force has developed this report to document progress toward these goals during fiscal year (FY) 2021. This report includes highlights of agency activities as well as a comprehensive list of progress toward each target in the 2020 plan. The report also describes challenges encountered during this period and updates to targets where relevant. The CARB Task Force will continue to report annually on progress toward the goals of the 2020 plan.

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[3] Approximately 254,000 children under five years of age die from AMR per year (approximately one child every two minutes), and of these children, 99.65% are in low- or middle-income countries.

Highlights of Progress in Fiscal Year 2021

The Intersection of CARB and Pandemic Preparedness

CMS continued to take actions that ensured the health and safety of Medicare/Medicaid beneficiaries, including focused infection control surveys to assess compliance with CMS's infection prevention and control (IPC) requirements. COVID-19 reporting requirements for hospitals and critical access hospitals (CAHs) (85 FR 85866) and nursing homes (86 FR 62240) have proven instrumental for data-driven decision-making and response efforts at federal, state, and local levels. Similarly, CMS requirements for COVID-19 vaccinations have ensured that all residents, clients, and staff members receive education about the benefits and potential risks associated with the COVID-19 vaccines so that each of them can make an educated decision on whether to be vaccinated. During FY 2021, CMS was actively engaged in the development of the interpretive guidelines for the long-term care (LTC) and hospital IPC and antibiotic stewardship program (ASP) requirements. However, due to the ongoing public health emergency of COVID-19, the guidance was issued in FY 2022, and additional details will be included in the next report.

CDC's significant earlier investments to build foundational capacity to prevent, detect, and respond to AR across the United States proved critical to supporting the response to COVID-19 early in the pandemic, particularly in state and local health departments. This critical foundation included activities to track infections, respond to outbreaks, and prevent healthcare-associated infections (HAIs) while also building strong local relationships between public health and health care facilities that facilitate the implementation of actionable prevention strategies locally. CDC's AR Solutions Initiative continues to support this work, while empowering AR and HAI experts nationwide who pivoted to provide infection control expertise to healthcare facilities during the pandemic. Leveraging lessons learned from the more than 2,200 HAI and AR-related outbreak consultations conducted in 2019, state and local health departments performed more than 14,000 outbreak consultations, many in long-term care facilities, to stop the spread of COVID-19.

In addition, CDC's National Tuberculosis Molecular Surveillance Center utilized Antimicrobial Resistance Laboratory Network (AR Lab Network) sequencing capacity to quickly sequence more than 4,700 SARS-CoV-2 genomes in 2020 to support contact tracing and help stop the virus from spreading, while simultaneously supporting rapid AR detection and response. Although public health laboratories were diverted to support SARS-CoV-2 testing and pandemic response efforts, the AR Lab Network was able to maintain critical AR testing by coordinating to resolve pandemic-related challenges. These collaborations display the flexibility of the AR Lab Network and how CDC's AR investments can be quickly adapted during a crisis.

Globally, CDC's investments in IPC to prevent the spread of AR were leveraged to support the COVID-19 response. CDC and partners trained nearly 20,000 healthcare workers in more than 30 countries to help make healthcare facilities safer. Although these responses demonstrate the value of foundational investments in public health infrastructure, responding to the COVID-19 threat drew resources away from the continuing threat of AR, as described in the Common Challenges and Barriers section below.

DoD's Global Emerging Infections Surveillance Branch (GEIS) supports a globally positioned network of DoD laboratories and was uniquely poised to rapidly respond to new and emerging threats during the COVID-19 pandemic. In 2020, the GEIS Network quickly integrated SARS-CoV-2 testing and whole-genome sequencing

(WGS) by leveraging its existing and robust network of influenza and respiratory surveillance partners. The network rapidly expanded to be a global leader in SARS-CoV-2 detection and characterization, providing critical information on the distribution of variants of concern to the DoD and other U.S. Government entities. GEIS partners sequenced almost 18,000 SARS-CoV-2 samples. Data are aggregated and distributed weekly to DoD leaders and decision-makers through products developed by GEIS and the Integrated Biosurveillance Branch. Accomplishments and lessons learned from this effort include the rapid incorporation of new laboratory workflows, sample and data sharing agreements, and standardization of data feeds, and these lessons are being implemented across broader surveillance activities. For example, the Antimicrobial Resistant Infections Focus Area is developing similar programmatic workflows and data reporting methods to improve aggregation and communication of data related to AR organisms collected by the GEIS network.

ASPR/BARDA partnered with CDC's Emerging Infections Network (EIN) to gain an understanding of bacterial infections in hospitalized COVID-19 patients. The EIN is a provider-based sentinel network of infectious disease physicians that is supported by the CDC under a cooperative agreement with the Infectious Diseases Society of America. BARDA surveyed EIN clinicians and found that unresolved bacterial infections, including those that were treated unsuccessfully or deaths that occurred during antibiotic treatment, were a significant contributor to mortality in critically ill COVID-19 patients, thereby underscoring the risk posed by unresolved healthcare-associated bacterial infections during events that place a strain on the U.S. healthcare system (Figure 1).
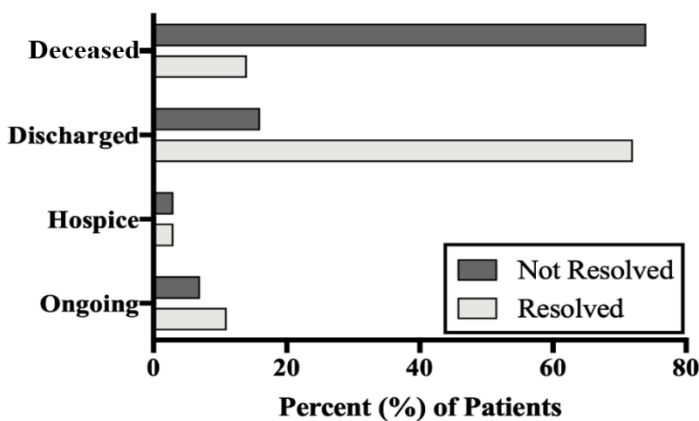

Figure 1. Patient outcome based on resolution of bacterial infection after antibiotic treatment. Among patients with resolved bacterial infections, 14% died and 72% were discharged as recovering. For patients with unresolved bacterial infections, 74% died and 16% were discharged as recovering. At least 91% of the patients who died with an unresolved bacterial infection were still receiving antibiotic treatment at the time of their death.
Jacobs AC, Khosrowshahi L, Risi G, Beekmann S, Polgreen PM, COVID-19 Study Team, Albrecht M. Impact of bacterial infections and antibiotic use on hospitalized COVID-19 patients: An Emerging Infections Network Survey. *COVID*. 2022;2(5):649-659.

Scientists with **FDA's** Center for Biologics Evaluation and Research (CBER) leveraged their ongoing CARB-related work to develop a [screening tool to assess SARS-CoV-2 RNA shedding in stool](#). Prior to the COVID-19 pandemic, FDA/CBER scientists had explored fecal microbiota transplantation (FMT), an emerging therapy to address recurrent or refractory *Clostridioides difficile* infection, multidrug-resistant organism (MDRO) colonization, and further development of antimicrobial resistance (AMR). Building on this work, FDA/CBER researchers developed and implemented a novel tool to assess viral RNA shedding in stool of individuals who are COVID-positive, or living with someone who has tested COVID-positive, to inform regulatory decisions regarding FMT stool donor exclusion and re-inclusion.

As a multisectoral development agency with a global presence, **USAID** promotes a holistic One-Health approach to AR by strengthening health systems and health ecosystems. Working with host governments and partner countries, USAID leveraged AR investments to rapidly support the COVID-19 response, maintained investments in AMR capacity building, and advanced critical services (e.g., water, sanitation, and hygiene; immunization) that underpin efforts to address both COVID-19 and AMR. For example, to limit COVID-19

transmission and protect healthcare workers and patients, USAID partners assisted countries to design tools to assess and track IPC improvements in healthcare facilities; established and operationalized IPC coordination committees; developed and disseminated IPC guidance for healthcare workers, health facility workers, patients, family members, caregivers, and visitors; and trained health managers and health providers. Recognizing the critical role that AMR capacities and communities played in enabling rapid responses to COVID-19, USAID continues to assess opportunities to strengthen country capacities in AMR as underpinnings of adaptive, responsive, and resilient health systems able to effectively scale for health emergencies.

As chair of the Global Health Security Agenda Antimicrobial Resistance Action Package (GHSA AMR AP) for FY 2021, **OGA** ensured that AR remained high on the agenda despite the COVID-19 pandemic. Relevant discussions included GHSA members' experiences in combating AMR during the COVID-19 pandemic, as well as the importance of prioritizing and investing in prevention to combat COVID-19 and AMR. OGA invited environmental experts to these meetings to present their work and to facilitate a forum for members to connect, communicate, and collaborate on AMR environmental issues. OGA also invited the United Nations Environmental Programme (UNEP) for the first time to present their work on the environmental dimensions of AMR, including providing guidance to inform national and global AMR strategies and their connection to pandemic preparedness.

Equity Issues Related to CARB

Many risks for AR infections and inappropriate antibiotic prescribing and use are tied to the social determinants of health—the environmental conditions in which people are born, live, learn, work, play, worship, and age—that affect a wide range of health, functioning, and quality-of-life outcomes and risks. Because of this, AR infections also bear disproportionate harms for vulnerable populations and communities underserved by the healthcare system. Social, economic, and environmental factors contribute to heath disparities and AR threats such as: higher incidence of *C. difficile* infections in low-income communities; increased incidence of *Salmonella* in children aged five or younger and older adults living in higher poverty areas; and more common *Campylobacter* infections with decreased susceptibility to ciprofloxacin in low- and middle-income countries. Prolonged illnesses, higher cost, and greater potential side effects associated with second-line and last-resort treatments also contribute to the social and economic burden of AR.

In addition, health disparities are reflected in antibiotic prescribing use and trends. For example, children who receive care from a pediatrician vs. other healthcare professionals (e.g., family practice provider, nurse practitioner) are more likely to receive appropriate antibiotic therapy. Variability in the quality of antibiotic stewardship programs and activities and access to stewardship expertise may also exacerbate or create health inequities.

AHRQ renewed and strengthened its emphasis on research benefiting AHRQ's priority populations representing underserved communities in two ways. First, AHRQ's Policy on the Inclusion of Priority Populations in Research was updated with an expanded definition of priority populations. Second, AHRQ updated language for prospective Notices of Funding Opportunities (NOFOs) to indicate that investigators should specifically consider AHRQ priority populations and health equity in their applications. This updated language was included in AHRQ's reissue of its two CARB NOFOs, published in October 2021.

CDC is addressing AR and health equity as a part of the agency's CORE Health Equity Science and Intervention Strategy, a CDC-wide strategy to increase equity across public health. This strategy includes systematically expanding the collection of disparities- and equity-focused data; characterizing health inequities related to key bacterial pathogens across incidence, infection outcome, and antibiotic resistance at a geospatial level; supporting states' efforts to address health disparities related to AR pathogens and antibiotic use through infection control and patient safety efforts; addressing educational needs that impact diverse frontline healthcare workers' ability to protect themselves and their patients from infections; and addressing disparities in the quality of long-term care.

CDC is also prioritizing research and action to fully understand potential disparities related to AR through programs like Project Firstline, which addresses infection prevention and control training gaps for healthcare workers from diverse educational and training backgrounds; the AR Lab Network, which is working to include and analyze patient demographic data alongside laboratory test results; and the National Healthcare Safety Network (NHSN), which provides patient demographic data for analyses that can drive improvements in healthcare quality. NHSN data has also been used to inform vaccination and infection prevention strategies across healthcare settings while integrating health equity and antibiotic stewardship principles into its programs and activities. For example, the federal Office of Rural Health Policy used NHSN's data to monitor the overall effectiveness of its Medicare beneficiaries' quality improvement program that serves disproportionately affected populations. In addition, CDC continues to integrate stewardship principles, such as its Core Elements of Antibiotic Stewardship, into healthcare policies and practices to enhance CDC's targeted prevention initiatives domestically and globally.

As outlined in its newest Framework for Health Equity and National Quality Strategy, **CMS** is taking steps to measure the impact of its policies on health equity; develop sustainable solutions that close gaps in health and healthcare access, quality, and outcomes; and invest in solutions that address health disparities, including those driven by infections. To reduce the disparities in long-term care facilities, for example, CMS has directed the Quality Innovation Networks–Quality Improvement Organizations to provide technical assistance for infection prevention. The technical assistance includes working directly with facility administrators to review infection control procedures and conducting infection prevention training for staff. Similarly, under the American Indian/Alaska Native Healthcare Quality Initiative, CMS has assisted IHS facilities in identifying, tracking, and reducing healthcare disparities related to patient safety and harms, such as the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) and *C. difficile.*

Further Highlights of Agency Progress toward the CARB Goals

FDA's Center for Veterinary Medicine (CVM) made multiple advances to foster stewardship of medically important antibiotics in animals. The agency announced a potential revised process and criteria for ranking antibiotic drugs for animals based on their importance in human medicine. They are also working to understand how animal drug sponsors could voluntarily make changes to the approved uses for certain medically important antibiotic drugs, so as to establish a defined duration of use for indications that currently lack such a definition. FDA also finalized Guidance for Industry #263 to outline the process for animal drug sponsors to voluntarily change the approved marketing status of certain medically important antibiotic drugs from over-the-counter (OTC) to prescription (Rx). Once the marketing statuses change in June 2023, these drugs will only be used in animals under the supervision of a licensed veterinarian. To provide additional information to relevant stakeholders, CVM published Frequently Asked Questions for Farmers and Ranchers

and awarded an education and outreach contract to develop information on AR and to highlight the importance of stewardship and veterinary involvement. Finally, in 2021, four veterinary colleges initiated projects funded by FDA's Veterinary Laboratory Investigation and Response Network (Vet-LIRN) to develop tools and educational materials for supporting antibiotic stewardship (AS) in animals. These projects explore education about AR in companion animals, laboratory-supported AS, sequencing capabilities to address nosocomial infections in veterinary facilities, and an evaluation of veterinary students' selection of antibiotic products in animal treatment.

DoD/WRAIR conducts near real-time biosurveillance through the MRSN, which has now expanded to the 15 largest DoD hospitals throughout the United States and Europe. This service no longer depends on human pattern detection to identify possible outbreaks or transmission events, but rather employs systematic genomic comparison of newly received MDROs to a repository of >95,000 historical bacterial clinical isolates from throughout the military healthcare system (MHS). As a result, possible MDRO transmission events are now identified as soon as isolates are received and processed, and the affected military treatment facility (MTF) is immediately notified of the number of patients involved, bacterial information, and the ward/intensive care units (ICUs) impacted. In the context of its global health mission, DoD supported the evacuation of individuals from Afghanistan in support of Operation Allies Refuge and Operation Allies Welcome. As part of this effort, evacuees who required inpatient medical or surgical care were admitted to MTFs. Targeted proactive biosurveillance performed by the MRSN documented high rates of MDROs among these patients compared to the general U.S. population. Rapid detection of these MDROs using whole-genome sequencing enabled effective prevention of the spread of these dangerous bacteria in healthcare settings. This effort led to updated guidance on MDRO screening in recently evacuated individuals across the entire MHS, and CDC concurrently issued guidance to health departments in states housing Operation Allies Welcome evacuees, so that civilian hospitals would be aware of high rates of MDRO colonization and ensure appropriate infection prevention and control. Finally, in 2021, WRAIR created a One Health branch to expand multidisciplinary efforts to combat health threats that may impact military readiness occurring at the human, animal, and environmental interface. A One Health AMR focus group was formed, and its first project is a pilot study funded by DoD's GEIS branch to implement AMR bacterial surveillance in working military dogs.

USDA/APHIS published two dashboards to reach broader audiences and make antimicrobial use (AMU), stewardship, and resistance data more accessible and interactive. First, the National Animal Health Monitoring System (NAHMS) developed an online data dashboard that visually portrays the results of national studies. An example of this new approach to reporting is the NAHMS Antimicrobial Use and Stewardship on U.S. Swine Operations 2017 study. Second, the National Animal Health Laboratory Network (NAHLN) AMR Pilot Project now provides near real-time updates that monitor AMR profiles in animal pathogens routinely isolated from veterinary clinics and diagnostic laboratories across the United States. Scientists at the Wildlife Services National Wildlife Research Center (NWRC) continue to conduct research on the role of wildlife in disseminating AMR at the wildlife-agriculture interface, which includes developing novel laboratory diagnostics in wildlife samples, conducting experimental infections with AMR bacteria in peridomestic wildlife species to determine host capabilities, and conducting field studies to examine the transmission potential of wildlife to agricultural operations and their capability to move AMR across the landscape.

USDA/FSIS expanded microbiological sampling of National Antimicrobial Resistance Monitoring System (NARMS) samples to include evaluation of gut contents from sheep, goat and lamb, and veal for *Salmonella,*

Campylobacter, Enterococcus, and *Escherichia coli*. In addition, FSIS evaluated cattle mesenteric lymph nodes for the presence of *Salmonella*, and characterized *Enterococcus* and *E. coli* isolated from *Siluriformes* fish (e.g., catfish). FSIS also specifically added isolation and characterization of carbapenem-resistant *Enterobacterales* (CRE) and exploration of microbial AMR diversity to a subset of NARMS samples.

EPA is soliciting research proposals to investigate the extent to which the level of AR in the environment is due to AR present in raw sewage, the proliferation of AR during treatment, subsequent gene transfer in the environment, or other nonwastewater-related pathways (e.g., natural development, animal husbandry, or exposure of intestinal flora to antibiotics). These proposals will also help prioritize AR genes and microbes to be monitored, evaluate removal of prioritized AR genes and microbes through wastewater treatment plants, and define loads discharged into the environment, thereby informing future national-scale wastewater surveys. Investigation of the effect of wastewater sources on the persistence of AR bacteria and their genes in the environment is supported by an existing EPA-led interagency national-scale survey of receiving waters.

DoD's WRAIR Experimental Therapeutics (ET) Branch leads the DoD's CARB working group (CARB WG), collaborating with partners to develop novel antimicrobial candidates to combat the threat of MDR infections in combat wounds and sepsis. During 2021, the DoD CARB WG advanced 23 projects through optimization of lead molecules from novel chemical classes, generation of drug potency data, and, when appropriate, evaluation of FDA-approved antibiotics for additional clinical indications. ET's high-throughput *in vitro* antibacterial screening capability using MDR, militarily relevant strains from MRSN clinical bacterial isolates is central to accelerating discovery of promising drug candidates for this program. ET also supports key animal models to evaluate drug candidates for safety, pharmacokinetics, and efficacy.

ASPR/BARDA continued to be a major driver of antibacterial development by awarding 14 new projects across the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) and Advanced Research and Development portfolios to support the treatment, prevention, and diagnosis of AR bacterial infections, and supporting the development of the antibiotic NUZYRA® (omadacycline) from Paratek Pharmaceuticals toward approval for treatment of infections caused by *Bacillus anthracis* as well as procurement of NUZYRA® as a potential medical countermeasure for postexposure prophylaxis and treatment of anthrax.

NIH's National Institute of Allergy and Infectious Diseases (NIH/NIAID) launched two innovative programs to increase understanding of mechanisms of resistance and the host immune response and to stimulate development of preventive approaches and novel treatments, including antibiotics and nontraditional therapeutics. Given that past screenings of several large chemical libraries have not yielded novel antibiotic compounds, NIH/NIAID established the [Chemistry Center for Combating Antibiotic-Resistant Bacteria (CC4CARB)](#) to oversee the design, synthesis, and management of external investigator-submitted libraries of chemical compounds specifically targeting gram-negative bacteria. The resulting CC4CARB compound library will be publicly available and will contain a broad range of both novel and resynthesized known drug scaffolds that may provide useful research tools, chemical probes, or early chemical starting points to fuel drug discovery. NIH/NIAID also created a new collaborative research program, the CARB Interdisciplinary Research Units (CARBIRUs), supporting three multidisciplinary research centers focused on discoveries that can be translated into new antibacterial products and strategies to combat CDC-designated AR threats. CARBIRU researchers are investigating alternative treatment and prevention strategies, including antibodies, receptor

blocking analogs, bacteriophages, and defined microbial consortia, as well as poorly understood resistance mechanisms.

USDA/ARS funded 11 one-year mini proposals through an internal funding call to address AR and antibiotic alternatives research. These projects include supporting the development of vaccines against bovine respiratory disease, using machine learning to predict coselection of AR in *Salmonella* and *Enterococcus*, and controlling fire blight disease in the pome fruit (e.g., apples, pears) industry with antibiotic alternatives. ARS scientists published 78 peer-reviewed journal articles relating to AR and/or alternatives to antibiotics (ATA) in FY 2021. Examples of impactful work include ARS researchers helping to develop an oral antibiotic alternative that fights poultry coccidiosis, which costs the global poultry industry $3.5 billion annually. ARS also developed a hoof balm to protect cattle from a bacterial infection causing hoof lesions.

USDA/NIFA A1366 Agriculture and Food Research Initiative program supported research, education, and extension activities to decrease AR across the food chain. Among the funded projects, Mississippi State University has been studying bacteria that live on healthy catfish. Fish are raised with feed containing antibiotics to control fish disease, making catfish farming possible.

During the United Kingdom's Group of 7 (G7) presidency in 2021, the United States supported AMR as a priority issue in the finance, climate and environment, and health tracks. **OGA** supported and negotiated these efforts on behalf of the U.S. government, including as members of G7 working groups to develop and promote economic incentives and shared valuation principles regarding reimbursement for antibiotics. OGA also represented U.S. equities and negotiations on strengthening the antibiotic manufacturing and distribution pipeline and bolstering global manufacturing requirements with respect to the environment.

In late 2021, **CDC** launched the Global Antimicrobial Resistance Laboratory and Response Network (Global AR Lab & Response Network), a comprehensive, One Health network that spans nearly 50 countries and works with more than 20 organizations worldwide to build laboratory capacity to detect AR organisms; prevent infections in healthcare settings, the community, and the environment through proven IPC practices; strengthen collaborative global antibiotic stewardship activities to improve quality of care and respond to emerging AR threats; and apply new and innovative ways to respond to AR. This network identifies risk factors driving the emergence and spread of AR across healthcare and sexually transmitted, fungal, enteric, and invasive bacterial and respiratory pathogens, while responding on the ground to these threats.

New and Updated Items in the CARB National Action Plan, 2020-2025

Given their experiences during FY2021, the CARB Task Force has adopted several new and updated targets for the CARB National Action Plan for 2020-2025.

Item	Original	Update	Rationale
Target 1.4.2.2	New target	Promote equity across public health by incorporating efforts to understand and address health disparities in antibiotic resistance, including through CDC's CORE Health Equity Science and Intervention Strategy, an agency-wide strategy that includes tailored prevention efforts and materials. *CDC will report on this target.*	New activity
Target 2.1.1.3	New target	Increase laboratory capacity for colonization screening to ≥25 CDC Antimicrobial Resistance Laboratory Network laboratories to detect and respond to existing and emerging pathogens, such as CRE and *Candida auris* that can be exacerbated by COVID-19, and other novel threats by 2025. *CDC will report on this target.*	New activity
Target 2.3.4.2	New target	Pilot collection of AR data from wastewater surveillance by 2023. *CDC will report on this target.*	New activity
Target 2.1.2.1	Increase percentage of isolates with test results and uploaded sequence data.	Increase numbers of isolates each year with test results and uploaded sequence data.	For many relevant pathogens, tracking numbers of isolates is more appropriate than tracking percentages.
Target 2.2.3.1	Establish mechanisms for sharing food and animal isolates by 2021.	*CDC removed from the list of departments and agencies reporting on this target.*	CDC does not collect food or animal isolates.

Item	Original	Update	Rationale
Target 2.2.4.1	Identify suitable storage solutions that will satisfy access requirements by 2021.	Identify suitable storage solutions that will satisfy access requirements by 2022.	Implementation delayed due to the COVID-19 pandemic response.
Target 2.4.1.1	Explore interagency collaborations to examine options for increased reporting to CDC's National Healthcare Safety Network (NHSN) Antibiotic Resistance Module.	Explore interagency collaborations to examine options for increased reporting to CDC's National Healthcare Safety Network (NHSN) Antimicrobial Use Option.	Edited for clarity and consistency with Goal 2, Objective 4.
Target 3.1.1.1	Support 10 new antibiotic resistance-related diagnostics projects across the U.S. government by 2021, through funding or scientific or technical support.	Support 10 new antibiotic resistance-related diagnostics projects across the U.S. government annually through 2025, through funding or scientific or technical support.	Date changed because this is an ongoing activity.
Goal 4 Activity 1	Support at least 1,000 publications focused on basic, translational, and clinical research to combat antibiotic resistance by 2021.	Support at least 1,000 publications focused on basic, translational, and clinical research to combat antibiotic resistance annually through 2025. *ASPR/BARDA added to this target*.	Date changed because this is an ongoing activity.
Goal 4 Activity 2	Provide support to at least 60 new or early-career investigators by 2021	Provide support to at least 60 new or early-career investigators annually through 2025.	Date changed because this is an ongoing activity.
Goal 4 Activity 3	Establish at least two new collaborations for human health and one for agriculture by 2021, through interagency agreements, collaborative programs, and interdisciplinary workshops.	Establish at least two new collaborations for human health and one for agriculture by 2023, through interagency agreements, collaborative programs, and/or interdisciplinary workshops.	Implementation delayed due to COVID-19 response.
Target 4.1.1.1	Report success stories to disseminate new knowledge about antibiotic resistance and inform mitigation strategies in human health (at least two stories) and agriculture (at least one story) by 2021.	Report success stories to disseminate new knowledge about antibiotic resistance and inform mitigation strategies in human health (at least two stories) and agriculture (at least one story) annually through 2025.	Date changed because this is an ongoing activity.

Item	Original	Update	Rationale
Target 4.2.1.4	Report success stories about additional therapeutic options for human health at least five stories) and agriculture (at least one story) by 2021.	Report success stories about additional therapeutic options for human health (≥5 stories) and agriculture (≥1 story) annually through 2025.	Date changed because this is an ongoing activity.
Target 4.3.1.3	Report success stories about improved preventive strategies for human health (≥2 stories) and agriculture (≥1 story) by 2021.	Report success stories about improved preventive strategies for human health (≥2 stories) and agriculture (≥1 story) by 2023.	Implementation delayed due to the COVID-19 response.
Target 4.3.2.1	Convene two meetings to discuss developmental pathways and regulatory considerations, including clinical trial designs, by 2023.	Convene two meetings to discuss developmental pathways and regulatory considerations, including clinical trial designs, by 2025.	Implementation delayed due to the COVID-19 response.
Subobjective 4.4.1	Support creation of a network of clinical trial sites to reduce barriers to research and to establish a comprehensive understanding of safety and effectiveness of new antibiotic agents in challenging clinical settings and indications.	Leverage an existing mechanism to reduce barriers to research and establish a comprehensive understanding of safety and effectiveness of new antibiotic agents in challenging clinical settings and indications.	The U.S. government can more effectively support new antibiotic agents through direct partnerships between drug sponsors and federal partners and by focusing on one challenging clinical trial at a time. Implementation delayed due to the COVID-19 response.
Target 4.4.1.1	Provide scientific and technical support for establishing the network, including recommendations on platform trial design and other regulatory considerations.	Provide scientific and technical support, including recommendations on platform trial design and other regulatory considerations.	Edited to align with updated subobjective 4.4.1.
Target 4.4.1.2	Establish the network and begin enrolling patients by 2023.	Support ≥1 special population clinical trial by 2025.	Edited to align with updated subobjective 4.4.1.

Item	Original	Update	Rationale
Target 5.1.2.1	Support international antibiotic-resistance policy efforts to prioritize and coordinate AR efforts within and across international partner organizations (e.g., UN Food and Agricultural Organization, G7 and G20, Asia-Pacific Economic Cooperation Forum, Global Health Security Initiative, and UN One Health Global Leaders Group on AMR) by 2022.	Support international AR policy efforts to prioritize and coordinate antibiotic resistance efforts within and across international partner organizations (e.g., Global Health Security Agenda [GHSA], World Health Organization [WHO], World Organization for Animal Health [WOAH], UN Environmental Programme [UNEP], UN Food and Agricultural Organization [FAO], G7 and G20, Asia-Pacific Economic Cooperation Forum, Association of Southeast Asian Nations, Pan American Health Organization) by 2022.	Updated relevant partner organizations.
Target 5.1.2.3	Complete and implement the Work Plan of the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) for 2021-2025 and develop a new scope of work for TATFAR by 2021.	Complete the Work Plan of the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) for 2016-2020 and develop and begin implementation of a new scope of work for TATFAR by 2022.	Due to the COVID-19 pandemic, a number of TATFAR priorities in the 2016-2020 workplan and the development and implementation of the 2021-2025 workplan were paused or stopped because of the relocation of staffing priorities and resources towards the COVID-19 response.
Subobjective 5.2.1	Improve capacity in partner countries to implement effective practices to prevent and control infection, including through the availability and proper use of water, sanitation, and hygiene (WASH).	Improve capacity in partner countries to implement effective practices to combat AMR, including preventing and controlling infection through the availability and proper use of water, sanitation, and hygiene (WASH).	Edited to incorporate additional relevant activities.

Item	Original	Update	Rationale
Target 5.2.1.1	Assist governments, civil society, and private sector in a total of 10-15 low- or middle-income countries to develop national plans or capacity for preventing and controlling infections in both animals and humans by 2022.	Assist governments, civil society, and the private sector in a total of 10-15 low- or middle-income countries to develop and implement national plans consistent with the Global Action Plan, establish and implement antibiotic resistance-focused collaborations and activities, and/or build capacity for preventing and controlling infections in both animals and humans annually.	Edited to incorporate additional relevant activities.
Subobjective 5.3.4	Improve the standardization of laboratory methodologies and data collection to improve the quality, reliability, and utility of data to facilitate global comparisons of antibiotic resistance.	Improve laboratory capacity for antibiotic-resistance surveillance, including standardization of laboratory methodologies and data collection to improve the quality, reliability, and utility of data to facilitate global comparisons of antibiotic resistance.	Edited to incorporate additional relevant activities.
Target 5.3.4.1	Implement standardized or harmonized laboratory methods and data collection in AR Lab Network facilities to facilitate comparison of antibiotic-resistance trends when appropriate. Initiate data-reporting efforts with trusted partner nations by 2021.	Implement standardized or harmonized laboratory methods and data collection in AR Lab Network facilities and, with partner countries, strengthen laboratory capacity for antibiotic-resistance surveillance and comparison of antibiotic-resistance trends when appropriate. Initiate data-reporting efforts with trusted partner nations by 2021. Support operations through training and funding annually.	Edited to incorporate additional relevant activities.

Item	Original	Update	Rationale
Subobjective 5.4.1	Collaborate with international scientists and organizations to better understand the development, spread, and health risks of antibiotic resistance and resistance sources present in animals, the environment, the community, and healthcare settings.	Collaborate with international scientists and organizations to better understand and address the development, spread, and health risks of antibiotic resistance and resistance sources present in animals, the environment, the community, and healthcare settings.	Edited to incorporate additional relevant activities.
Target 5.4.1.1	Conduct research and/or surveillance projects to evaluate sources of antibiotic resistance and mechanisms of persistence, with a focus on animal and environmental systems by 2023.	Conduct research and/or surveillance projects to evaluate sources of antibiotic resistance, mechanisms of persistence, and impact of sociological factors, with a focus on animal and environmental systems by 2023.	Edited to incorporate additional relevant activities.
Subobjective 5.4.2	Promote the alignment of U.S. and international translational and clinical research activities to facilitate the development of new products to better diagnose, prevent, and treat infections or to provide data on the best use of existing products.	Promote and enhance the alignment of U.S. and international translational and clinical research activities to facilitate development of new products to better diagnose, prevent, and treat infections or to provide data on best use of existing products.	Edited to incorporate additional relevant activities.
Target 5.4.2.1	Report one success story about products or regimens undergoing preclinical or clinical testing by 2021.	Report at least one new success story annually through 2025 about products or regimens undergoing preclinical or clinical testing.	Date changed because this is an ongoing activity.

Common Challenges and Barriers

The primary challenge to implementing the 2020 plan has been the pandemic of SARS-CoV-2 infection and COVID-19 illness. The pandemic created a perfect storm for HAIs, leading to increased numbers of patients, increased lengths of stay and severity of illness for many patients, staffing shortages, changes in antibiotic use, and departures from standard IPC practices. In July 2022, CDC released *COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022*, the most comprehensive analysis to date of the effects of the COVID-19 pandemic on AR infections in the United States. This analysis found significant surges in antibiotic use and AR infections in U.S. hospitals during the first year of the pandemic, including an alarming 15 percent increase in both resistant hospital-onset infections and deaths.

IPC practices changed in many healthcare settings during the pandemic to accommodate overwhelming numbers of patients and shortages of personal protective equipment, supplies, and staff. The pandemic also disrupted the services provided in acute care hospitals, outpatient settings, and assisted living facilities. Furthermore, efforts to establish new and maintain existing collaborations between federal agencies and partners were delayed or altered due to healthcare facilities' focus on pandemic mitigation efforts with limited staff resources.

To address these challenges domestically, federal agencies tailored COVID-19 IPC guidelines to address the needs and challenges unique to healthcare facilities, such as nursing homes, as well as external factors, such as shortages of personal protective equipment. CDC and CMS also worked together closely to translate evolving COVID-19 guidance into corresponding focused IPC regulatory and oversight requirements. For example, CMS enhanced its enforcement of nursing home infection control policies to by imposing directed plans of correction to improve infection control practices when noncompliance is identified. Federal agencies have also sought to enhance knowledge and implementation of IPC practices among frontline healthcare workers through technical assistance and training. For example, CDC's Project Firstline is a collaborative of diverse healthcare and public health partners that provides engaging, innovative, and effective infection control training for millions of frontline U.S. healthcare workers and members of the public-health workforce. As previously mentioned, CMS has directed the Quality Innovation Networks–Quality Improvement Organizations to provide training and technical assistance for infection prevention in nursing homes. In FY 2021, more than 1,900 nursing homes received technical assistance, including working directly with facility administrators to review infection control procedures and conducting infection prevention training for staff. More than 2,000 nursing homes have used CMS's scenario-based infection prevention training to train 80 percent or more of their staff members.

Over the course of the COVID-19 public health emergency response, U.S. state agencies have also had to pivot or redirect their priorities, activities, and resources in ways that might have affected domestic AS and resistance efforts. In an effort to control the spread of COVID-19 in the early days of the public health emergency, CMS developed a COVID-19-focused infection control survey and directed state agencies to focus their efforts on IPC. CMS also limited onsite surveys and activities to highest-priority complaints and surveys. Unfortunately, this temporary suspension and reprioritization of survey activity nationwide resulted in a backlog of complaint and recertification surveys to be investigated. For a time, requirements for ASPs at participating hospitals, critical access hospitals, and nursing homes were most likely not included as part of their focused infection control surveys. Therefore, monitoring ongoing facility

compliance with the established ASP requirements has presented a significant challenge for state agencies and CMS during the public health emergency.

Similarly, health departments and public health laboratories in the United States and globally prioritized detecting COVID-19 outbreaks, thereby diverting pathogen surveillance resources away from detecting outbreaks of AR infections. U.S. foodborne pathogen and animal health surveillance saw a decreased number of submitted and sequenced isolates and increased difficulty with source attribution due to inconsistent, incomplete, or missing metadata. Reduced staffing at the federal, state, and local levels—along with severe shortages of relevant supplies—decreased the use of WGS on enteric pathogen isolates. The pandemic also saw a drastic decrease in nationally reported cases of sexually transmitted diseases (STDs) due to reduced screenings at clinics, facility closures, and limited testing and laboratory resources. In addition, COVID-19 presented challenges to the AMR research enterprise as resources shifted to support the pandemic response. COVID-19 was an impediment to enrolling in AMR clinical trials, and many research laboratories were closed during various times in the pandemic, delaying AMR research efforts.

The CARB Task Force continues to monitor, evaluate, and adapt to the impact of the COVID-19 pandemic on AR and ongoing efforts to address its threat. To accommodate pandemic-related delays or other resource constraints, several targets in the CARB National Action Plan have been updated to reflect new timelines or scope.

Progress in Fiscal Year 2021

Goal 1: Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

Objective 1.1

Expand national, regional, and state capacity for detecting, containing, and preventing antibiotic-resistant infections.

Subobjective 1.1.1

Reduce the number of infections and deaths from pathogens identified as antibiotic-resistant threats by CDC.

Target 1.1.1.1

Decrease healthcare-associated antibiotic-resistant infections by 20 percent by 2025 and community-acquired antibiotic-resistant infections by 10 percent by 2025.

CDC used NHSN and other electronic health records data from a large number of U.S. hospitals to assess the impact of COVID-19 on AR infections among hospitalized patients. CDC also continues to support the Emerging Infections Program (EIP)—a collaboration between CDC and 10 state health departments working with academic partners to conduct active, population-based surveillance and special studies for several emerging infectious diseases, particularly pathogens that pose an AR threat, and to assess changes in incidence over time. These analyses found substantial increases in some healthcare-associated infections among hospitalized patients diagnosed with COVID-19 vs. hospitalized patients diagnosed with influenza-like illness in 2019. CDC's 2020 *National and State HAI Progress Report* also showed that MRSA increased by 15 percent and *C. difficile* decreased by 11 percent in acute care hospitals during this same period. These findings align with CDC's recently released analysis of the impact of COVID-19 on AR in the United States, *COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022*, which concludes that antibiotic use and AR infections surged significantly in U.S. hospitals during the first year of the pandemic, including a 15 percent increase in both resistant hospital-onset infections and deaths. CDC is also providing support and guidance about screening and infection control to prevent the spread of healthcare-associated fungal infections, including onsite support for outbreaks of *C. auris* and mucormycosis. However, due to the burden of COVID-19 response activities on health departments, EIP collection and submission of data and isolates have been delayed.

CMS continues to enforce regulations that require hospitals and nursing homes to establish and maintain ASPs as set forth at 42 CFR §482.42(b) and §483.80(a)(3), respectively. As a condition of participating in the Medicare and Medicaid programs, hospitals and nursing homes are expected to develop programs that demonstrate adherence to nationally recognized infection prevention and control guidelines, as well as to best practices for improving antibiotic use where applicable.

Subobjective 1.1.2

Support investments in U.S. health departments (including in all states and select tribes, territories, and large cities) to detect, contain, and prevent antibiotic-resistant infections.

Target 1.1.2.1

Award an average of $2.5 million to Epidemiology and Laboratory Capacity Cooperative Agreement-funded health departments by 2025.

CDC awarded $85.8 million in FY 2021 to state health departments (an average of more than $1.34 million per jurisdiction) through the Epidemiology and Laboratory Capacity for Prevention and Control of Emerging Infectious Diseases (ELC) cooperative agreement for support of detection, containment, and response to AR threats. CDC also increased funding and programmatic support for state and local public health laboratories (all regional laboratories and seven additional health departments) to implement WGS for improved detection of rapid and emerging AR threats, including for HAIs, fungi, and *Neisseria gonorrhoeae* (gonorrhea). In FY 2021, CDC also awarded funding for epidemiology and laboratory WGS support for enteric pathogens. Finally, in 2021 CDC announced funding of $1.25 billion over the next five years to 64 state, local, and territorial health departments through the American Rescue Plan Act (ARP) to strengthen and equip state, local, and territorial public health departments and other partner organizations with the resources needed to better prevent and fight infections in U.S. healthcare facilities, including COVID-19 and other known and emerging infectious diseases.

Subobjective 1.1.3

Support responses to identify, prevent, and contain antibiotic-resistant pathogens.

Target 1.1.3.1

Increase capacity nationwide to contain antibiotic-resistant infections and control outbreaks.

DoD/MRSN expanded real-time surveillance of AR bacteria and fungi, from five to 16 MTFs and at one VA medical center (Baltimore, MD). An MRSN employee has been stationed in the clinical microbiology laboratory at each facility to ensure submission compliance. Participating medical facilities submit on average 900 multidrug-resistant (MDR) bacteria every month for WGS and outbreak analysis. In the past year, the MRSN has sequenced 9,168 bacteria, responded to 88 outbreak requests from 18 facilities, and issued 39 "Flash" reports notifying facilities of unrecognized potential nosocomial transmission.

In 2021, as part of the ARP funds mentioned above, **CDC** announced $385 million over five years for significant IPC assistance to public health departments to work with healthcare facilities to improve the quality of healthcare; strengthen interventions for the prevention and containment of infectious diseases to minimize the spread of infection in a variety of healthcare settings; identify, address, and monitor healthcare-related disparities and health equity; and increase capacity to investigate outbreaks of HAIs. Funds provided will also increase state and regional laboratory capacity to strengthen surveillance for emerging pathogens by identifying patients infected with or carrying infectious disease threats, such as resistant pathogens. In addition, CDC's National Tuberculosis Molecular Surveillance Center (NTMSC) at the Michigan Public Health Laboratory, part of CDC's AR Lab Network, performs WGS for more than 8,000 *Mycobacterium tuberculosis* isolates each year. Enhancements to the national system are being developed, including database and analytic improvements to aid outbreak detection. Furthermore, the second five-year cycle of CDC's Strengthening the U.S. Response to Resistant Gonorrhea (SURRG) program began in 2021, funding eight jurisdictions to enhance local capacity for rapid detection of and response to drug-resistant gonorrhea. During the last year, CDC developed materials for veterinarians and pet owners to address animal CRE, designed to help prevent transmission of disease. CDC has also responded to three CRE reports from veterinary medical settings to provide

infection prevention recommendations and prevent outbreaks, including providing onsite technical assistance to state partners.

Subobjective 1.1.4

Conduct consultations or assessments related to antibiotic-resistant cases, outbreaks, and transmission in healthcare and the community for prevention and containment.

Target 1.1.4.1

Increase collaborative efforts at national, regional, and/or state levels to assist with antibiotic resistance response and prevention efforts in the general and military populations.

DoD/MRSN collaborated with the Doctors Hospital at Renaissance network in south Texas to mitigate a large outbreak of *Acinetobacter baumannii* among patients being treated for COVID-19 at the facility.

CDC allocated nearly $56 million to HAI/AR programs in all 50 states and several local health departments and territories for detection and prevention activities, including more than 18,300 responses or consultations to address confirmed or possible outbreaks involving AR threats, COVID-19, other HAI/AR infections, or serious infection control breaches in healthcare settings. Among these responses or consultations, HAI/AR programs provided more than 3,800 reports of emerging resistance, including 423 AR containment responses that involved onsite infection control assessment and/or screening, nearly 14,000 reports of possible COVID-19 outbreaks in healthcare settings, and 454 reports involving other types of HAI/AR outbreaks or infection control breaches. In addition, HAI/AR programs engaged more than 2,300 clinical laboratories to improve testing of targeted organisms to detect AR rapidly.

Under its hospital quality improvement contractor program, **CMS** has prioritized efforts to ensure that hospitals implement robust plans that address strengthening their ASPs dedicated to preventing *C. difficile*, including specific linkages to established evidence-based practices such as the Core Elements of Hospital Antibiotic Stewardship Programs. The hospital quality improvement contractors (HQICs) are aligning their efforts with the national action plan for CARB and leveraging the targeted assessment for prevention strategy provided by CDC, in addition to aligning with state hospital associations, health departments, professional organizations, and patient advocacy groups.

Similarly, through its American Indian/Alaska Native Healthcare Quality Initiative (AIANHQI), **CMS** is helping the IHS enact evidence-based resources to support hospital requests for assistance in implementing enhanced ASPs, including CDC's Core Elements of Hospital Antibiotic Stewardship Programs and AHRQ's AS toolkits. The AIANHQI also provides robust technical support to IHS regarding training on identifying and reporting MRSA and *C. difficile* infections through NHSN, helping to improve timeliness and accuracy of reporting.

Subobjective 1.1.5

Monitor and report on antibiotic resistance among selected animal pathogens to detect new resistance patterns.

Target 1.1.5.1

Publish one report on an animal pathogen describing emerging antibiotic resistance by 2021.

USDA/APHIS published the National Animal Health Laboratory Network AMR Pilot Project: 2020 publication report and Tableau Dashboard, as well as three articles in academic journals: "Evidence for Continental-Scale Dispersal of Antimicrobial Resistant Bacteria by Landfill-Foraging Gulls," "Gulls as Sources of Environmental Contamination by Colistin-resistant Bacteria," and "The Role of European Starlings (*Sturnus vulgaris*) in the Dissemination of Multidrug-Resistant *Escherichia coli* among Concentrated Animal Feeding Operations."

Objective 1.2

Engage the public and other stakeholders to develop, expand, and increase national and State education, training, and communication campaigns focused on using antibiotics responsibly, stopping the spread of antibiotic resistance, and preventing infections and life-threatening conditions like sepsis.

Subobjective 1.2.1:

Expand the scope and reach of CDC's awareness campaigns, including Be Antibiotics Aware and Get Ahead of Sepsis.

Target 1.2.1.1:

Each year, increase clicks, impressions, and earned or paid media.

As of September 30, 2021, **CDC's** Be Antibiotics Aware campaign increased paid/earned media impressions by 173 percent vs. the prior year, generating a total of 39.6 million impressions; clicks increased 337 percent vs. the prior year, with a total of 263,000 clicks during the same period. The Get Ahead of Sepsis campaign increased paid/earned media impressions by 352 percent vs. the prior year, generating a total of 32.9 million impressions; clicks increased 1,513 percent, with a total of 553,700 clicks.

Subobjective 1.2.2:

Develop new or expanded educational training guidelines, outreach, and awareness activities to educate stakeholders, such as consumers, healthcare providers, and industries, on best practices for using antibiotics responsibly, stopping the spread of antibiotic resistance, and preventing infections.

Target 1.2.2.1:

Increase and expand outreach activities each year.

CDC's SURRG provided education to healthcare providers and the public on drug-resistant gonorrhea prevention and control strategies, while the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) continued educational outreach to major stakeholders. During 2020-2021, CDC collaborated to conduct formative research (in-depth interviews) with companion animal owners and dog breeders to learn about antibiotic use practices and barriers to implementing stewardship activities. The results of this work will be used in 2022 to inform development of communication materials to expand outreach to companion animal owners to prevent antibiotic misuse. In addition, updates to healthcare professional continuing education modules on AS are underway for the CDC Antibiotic Stewardship Training Course. CDC's Office of Antibiotic Stewardship released healthcare professional training materials to improve antibiotic prescribing at hospital discharge and expanded pharmacist-specific educational materials to long-term care settings. CDC hosted a clinician outreach and communication activity call to educate about appropriate antibiotic use during the COVID-19 pandemic.

CMS continues to incentivize and support quality improvement activities across a wide range of providers and healthcare settings. Under the Quality Payment Program, CMS offers Merit-Based Incentive Payment System–eligible providers two improvement activity options that focus on AS, including completion of CDC's training on AS and implementation of an ASP. In 2021, more than 11,000 providers participating in the merit-based incentive payment system reported implementing an ASP, and nearly 4,000 reported completing CDC's AS training. Through its quality improvement networks and initiatives, CMS also provided IPC and AS technical assistance to 1,970 hospitals and 1,973 nursing homes in FY 2021.

USDA participated in World Antibiotics Awareness Week 2020 and in multiple virtual meetings and conferences with stakeholders. USDA/APHIS/NAHMS published the Swine Antimicrobial Use and Stewardship Dashboard. **USDA/APHIS/APHIS/National Veterinary Services Laboratories** presented two studies: Characterization of *Salmonella* Dublin Isolates from Cattle in the United States in the 2021 American Society for Microbiology Microbe virtual

meeting, and Antimicrobial Resistance and Genomic Characterization of *Salmonella typhimurium* and *Salmonella* I 4,[5],12:i- isolates from animals in the United States in the 2021 European Congress of Clinical Microbiology and Infectious Diseases virtual meeting.

Subobjective 1.2.3:

Expand the promotion and utility of training guidelines and other communication materials.

Target 1.2.3.1:

Each year, increase the number of individuals trained, continuing education units earned, and reach of efforts.

As of June 2021, users registered for participation in 132,420 modules in **CDC**'s AS training course, and 24,431 unique users have registered for one or more modules since the course was launched in December 2017. In addition, CDC's Gonococcal Isolate Surveillance Project (GISP) hosted a welcome webinar to provide surveillance project information and education to new and returning collaborators, while SURRG hosted a virtual grantee meeting with funded jurisdictions to share data and best practices and identify ongoing challenges. CDC has worked with the Minnesota Food Safety Center of Excellence to develop, refine and evaluate the [Antimicrobial Resistance Learning Site](#) targeted to veterinary students and professionals. CDC also developed online self-guided [training modules](#) about *Candida auris* and infection control for Latin American audiences, which are available in English and Spanish. The Food Safety Center of Excellence projects are also limited as they are funded on a yearly basis, so projects that require more than one year of support cannot be considered.

USDA/APHIS/National Veterinary Accreditation Program saw increased participation in Module 23 ([Use of Antibiotics in Animals](#)) and decreased participation in Module 29 ([Veterinary Feed Directive](#)); this was expected since implementation of the relevant Veterinary Feed Directive rules went into effect in 2017.

Objective 1.3

Develop and implement policies and practices to promote the responsible use of antibiotics.

Subobjective 1.3.1

Improve national outpatient antibiotic use.

Target 1.3.1.1

Lower the annual rate of outpatient antibiotic dispensing per 1,000 U.S. population, overall and among specified subpopulations.

DoD is measuring the annual rate of antibiotic prescribing across all facilities and has just completed the 2020 outpatient antibiotic usage report. Rates for 2020 may be artificially low because of the COVID-19 pandemic.

CDC found that in 2020, the annual rate of outpatient antibiotic dispensing was 613 per 1,000 persons, compared to 765 per 1,000 in 2019. This decrease in prescribing was greater than expected, likely because of decreased utilization of outpatient services during the COVID-19 pandemic. It is not yet clear whether this decrease will be sustained in future years.

Target 1.3.1.2

Lower the annual proportion and rate of antibiotic prescriptions for outpatient visits where antibiotics are not needed (according to evidence-based guidelines) and provide descriptive statistics for trends in unnecessary prescribing patterns.

DoD is currently creating dashboards to assess rates of inappropriate prescribing for specific conditions and will report on these rates when available.

CDC found that in 2018—the most recent year for which appropriateness data are available due to delays in the availability of data that describe the antibiotic prescribing indication—15.5 percent of visits for which antibiotics are never appropriate nevertheless resulted in an antibiotic prescription. Unnecessary antibiotic prescribing occurred in 60.1 percent of bronchitis visits and in 23.6 percent of viral upper respiratory infection visits. Children received fewer unnecessary antibiotics than adults: overall, 10.3 percent vs. 18 percent; for bronchitis, 41.1 percent vs. 65.6 percent; and for viral upper respiratory infections, 10.4 percent vs. 33.1 percent.

CMS's Medicaid and Children's Health Insurance Program (CHIP) Child and Adult Core Sets are measures which, taken together, can be used to estimate the overall national quality of healthcare for Medicaid and CHIP beneficiaries. CMS added a measure of AS, Avoidance of Antibiotic Treatment for Acute Bronchitis/Bronchiolitis, to the 2022 Adult Core Set and the 2023 Child Core Set. These decisions were the result of a rigorous stakeholder engagement process undertaken in FY 2021 and FY 2022 to ensure that only measures that are both appropriate for use at the state level and that states are likely to report to CMS are added to the Core Sets. In recommending this measure, members of the Child and Adult Core Set Annual Review Stakeholder Workgroup indicated the importance of having a measure that encourages avoidance of unnecessary antibiotic use and that states have used this measure to promote appropriate antibiotic dispensing and found significant room for improvement. Reporting on Core Set measures is voluntary for states until 2024, when reporting will become mandatory for the Child Core Set and for behavioral health measures on the Adult Core Set. CMS has collaborated with CDC to host a Quality Technical Advisory Group meeting on this measure to highlight opportunities for state public health departments and Medicaid programs to work together.

Subobjective 1.3.2

Help healthcare providers adopt recommended antibiotic use practices.

Target 1.3.2.1

Each year, increase the number of facilities and providers that implement CDC's best practices.

All **DoD** inpatient MTFs assess compliance with CDC's Core Elements of Hospital Antibiotic Stewardship on a yearly basis. Outpatient MTF implementation of core elements, however, is not assessed at this time.

CDC found that, in 2020, 91 percent of acute care hospitals reported that they had an ASP in place that incorporates all seven of CDC's Core Elements of Antibiotic Stewardship. Health departments engaged a total of 3,704 facilities nationwide in AS work and mailed audit and feedback letters to more than 2,000 high-volume outpatient antibiotic prescribers as of December 2020. With high uptake in hospitals for having a stewardship program, CDC will now begin to build on this base to better understand how to improve the quality of these programs so that they can support the most appropriate prescribing.

Subobjective 1.3.3

Support national and state policies that improve the use of antibiotics across healthcare settings and communities.

Target 1.3.3.1

Develop and optimize interpretive guidance for the antibiotic stewardship requirements within the conditions of participation for Medicare and Medicaid programs.

CMS worked closely with CDC and other federal partners in FY 2021 to develop interpretive guidance for AS requirements for hospitals to participate in Medicare and Medicaid programs (released on July 6, 2022 [QSO-22-20]).

CDC has continued to collaborate with CMS to increase voluntary antimicrobial use and resistance (AUR) reporting through the Promoting Interoperability Program (AUR reporting component planned for 2024). Hospitals will be required to report AUR data through NHSN under the Public Health and Clinical Data Exchange objective. State and local health departments have immediate access to NHSN data reported by healthcare facilities in their jurisdictions. CDC is continuing discussions with CMS and external partners, such as the Joint Commission, to spur additional AUR reporting.

Subobjective 1.3.4

Partner with clinical societies to consider options for improving the development, speed, and harmonization of antibiotic use and diagnostic guidelines that reflect clinical and public health needs for major syndromes.

Target 1.3.4.1

Initiate at least one coordinated effort to improve antibiotic or diagnostic guidelines by 2021.

CDC initiated a project with the Infectious Diseases Society of America to incorporate stewardship principles into clinical guidelines and the guideline development process. In addition, CDC led an international collaboration through the Clinical and Laboratory Standards Institute (CLSI) with the Instituto Nacional de Salud (INS) in Colombia and JMI Laboratories in Iowa to coordinate the media comparison study for antimicrobial susceptibility testing (AST) of *Haemophilus influenzae*, due to issues in the current broth media used to grow microbial assays. Together with CLSI, CDC developed the study design, coordinated testing, and participated as a testing partner. CDC selected and shipped the collection of 100 clinical isolates and provided lab supplies to INS. Testing at all three institutions was completed in August 2021. CDC will collect and collate the AST data from all three institutions and present the data at the CLSI working group meeting in 2022.

Subobjective 1.3.5

Support research to improve the responsible use of antibiotics across settings and translate important findings into practice.

Target 1.3.5.1

Increase research on the responsible use of antibiotics and translate significant findings into practice.

AHRQ committed an additional $7.5 million to research on improving antibiotic use, including for future years of projects initially funded in FY 2021. In addition, AHRQ reissued both CARB NOFOs to invite research applications: 1) the NOFO for large research projects for CARB and 2) the NOFO for large health services research demonstration and dissemination projects for CARB. Both NOFOs emphasize research focused on improving antibiotic use through AS. The AHRQ Safety Program for Improving Antibiotic Use has adapted the Comprehensive Unit-based Safety Program (CUSP) to promote ASPs in acute care hospitals and long-term and ambulatory-care facilities across the country. The project has created the Four Moments of Antibiotic Decision-Making, a significant AS advance that provides step-by-step guidance to empower clinicians to serve as stewards of their own antibiotic prescribing, published in *JAMA*. In February 2021, results of the acute care cohort, published in *JAMA*, described a significant reduction in antibiotic therapy days and *C. difficile* infections in more than 400 acute care hospitals. In June 2021, the project launched a

toolkit for public use on the AHRQ website, focusing on improving antibiotic prescribing in long-term care settings, based on the experiences of more than 400 facilities that participated in the project.

CDC published the results of a project to develop and test an intervention to help nursing staff implement AS practices in nursing homes. CDC's work on implementing electronic assessment of antibiotic appropriateness for inpatient and community-acquired pneumonia treatment and outpatient pharyngitis is ongoing.

Subobjective 1.3.6
Evaluate data on antibiotic use and stewardship practices in production animal species, including cattle, swine, poultry, goats, and sheep.

Target 1.3.6.1
Publish information on relevant practices by 2021.

USDA/APHIS/NAHMS published results from the 2017 cow/calf study and the 2019 goat study.

Subobjective 1.3.7
Engage the animal health community, crop protection community, and other relevant stakeholders to advance strategies intended to foster responsible use of medically important antibiotics in plants and animals.

Target 1.3.7.1
Develop and implement strategies by 2025.

EPA continues to engage with federal partners and consider input during its pesticide regulatory processes. To further these discussions, EPA has committed to evaluate existing published data sources to provide a solid scientific foundation for risk assessment and management decisions on the potential for development of, and subsequent human exposure to, resistant pathogens from the use of pesticides on crops.

To promote judicious use of antibiotic drugs in animals, **FDA/CVM** published a concept paper to obtain early input from the public on a potential framework for how animal drug sponsors could voluntarily make changes to the approved conditions of use for certain medically important antimicrobial drugs in order to establish a defined duration of use for indications that currently lack one. In addition, CVM finalized GFI #263 to outline the process for animal drug sponsors to voluntarily change the approved marketing status of certain medically important antimicrobial drugs from over-the-counter to prescription.

CDC has developed epidemiology and laboratory infrastructure and expertise to investigate resistant infections that are defined as reoccurring, emerging, or persisting strains (e.g., MDR *Salmonella* Newport) to understand the origin, sources, and possible prevention strategies. During 2020-2021, CDC also collaborated with The Ohio State University to develop communication materials to enhance outreach to livestock producers about implementation of AS. In addition, CDC funded the Colorado Food Safety Center of Excellence, the New York Food Safety Center of Excellence, and the Tennessee Food Safety Center of Excellence to explore knowledge, attitudes, and practices regarding usage and prescribing of antibiotics in animals; judicious use of such agents; and how resistant pathogens emerge and spread. This work helps inform educational interventions and materials for veterinarians, pet store and feedstore workers, and pet owners to stop the transmission of resistant pathogens among humans, animals, and the environment.

Objective 1.4

Develop and implement evidence-based policies and practices to prevent infections and stop the spread of antibiotic resistance across One Health.

Subobjective 1.4.1

Support further prevention of healthcare-associated infections prioritized in the National HAI Action Plan.

Target 1.4.1.1
Meet the targets identified in the National HAI Action Plan.

CDC is working with other agencies to develop the next iteration of the HAI National Action Plan. In addition, CDC released the 2020 National and State HAI Progress Report showing significant increases between 2019 and 2020 in some HAIs in the standardized infection ratio (SIR) for some facility types, including: a 35 percent increase for ventilator-associated events, 24 percent increase in central line-associated bloodstream infections (CLABSIs), and a 15 percent increase in hospital-onset MRSA for acute care hospitals. Prior to the COVID-19 pandemic, a widespread decrease in HAI incidence had been observed across U.S. hospitals. Although some infections increased between 2019 and 2020, all 2020 national SIRs except ventilator-associated events remain below the 2015 baseline SIR of one—i.e., a reference point for measuring progress—in acute care hospitals. Other HAIs were unchanged between 2019 and 2020 or showed a significant decrease. This progress in preventing infections is a testament to the dedication of healthcare providers across the country to protect patients from harm despite unprecedented challenges in 2020. The analysis includes data reported to NHSN across four healthcare settings: acute care hospitals, critical access hospitals, inpatient rehabilitation facilities, and long-term acute care hospitals. CDC also released a report, "The Impact of COVID-19 on HAIs in 2020" that includes an in-depth assessment of the impact of the COVID-19 pandemic on HAI incidence, using data reported to NHSN.

CMS has also observed deterioration in multiple patient-safety metrics since the beginning of the pandemic, and CDC and CMS have called for a renewed focus on patient safety—one that fosters greater assessment, transparency, inclusion, resilience, and learning within and across the healthcare system. Increasing health system resilience to (re)emerging infections and AR are central to a broader patient safety effort, and CMS continues to leverage multiple programs and authorities to advance HAI prevention. For example, in the FY 2022 and FY 2023 Inpatient Prospective Payment System/Long-Term Care Hospital (LTCH) Prospective Payment System final rules, CMS implemented measure suppression policy in response to the COVID-19 public health emergency (PHE) that would allow CMS to suppress the use of measure data if the agency determines that circumstances caused by the COVID-19 PHE have significantly affected those measures and the resulting quality scores (86 FR 44774, 87 FR 48780). This policy is intended to ensure that quality programs neither reward nor penalize hospitals based on circumstances caused by the COVID-19 PHE that the measures were not designed to accommodate. Examples of the types of external factors that the PHE has caused that may affect quality measurement include changes to clinical practices to accommodate safety protocols for medical personnel and patients, as well as unpredicted changes in the number of stays and facility-level cases. Although this policy paused some quality measures for payment purposes, the agency remains committed to transparency and patient safety. To that end, CMS continued to collect and publicly report quality data on the Care Compare website, where feasible and appropriately caveated. In addition, CMS continued to provide confidential feedback reports to hospitals as part of program activities to ensure that they are made aware of the changes in performance rates that we observe to inform their quality improvement activities.

DoD/ASPWG/EDC/PVC's HAI targets (i.e., CLABSI, catheter-associated urinary tract infection, and *C. difficile* infection) are tracked by DHA Patient Safety and the Navy EpiData Center and reported on a routine basis.

Subobjective 1.4.2

Support national and State policies to help prevent HAIs and stop the spread of antibiotic resistance within and between settings and communities.

Target 1.4.2.1

Develop and optimize guidance for improving infection control standards across healthcare settings.

CMS continues to work closely with CDC in the development of its IPC and ASP requirements as well as the interpretive guidelines that support these regulations. Through its published rules and guidance, CMS has strongly encouraged healthcare facilities to use CDC's Core Elements of Antibiotic Stewardship as a basis for establishing ASPs in Medicare-participating facilities. Throughout 2021 and 2022, CMS worked closely with CDC to develop and implement aligned IPC recommendations and requirements for multiple types of healthcare facilities to respond to healthcare-associated infections, AR infections, and the spread of SARS-CoV-2/COVID-19 in healthcare settings. These include, but are not limited to, the following 2021 and 2022 guidance releases:

- Revised Long-Term Care Surveyor Guidance: Revisions to Surveyor Guidance for Phases 2 & 3, Arbitration Agreement Requirements, Investigating Complaints & Facility Reported Incidents, and the Psychosocial Outcome Severity Guide (QSO-22-19-NH)
- Infection Prevention and Control and Antibiotic Stewardship Program Interpretive Guidance Update (QSO-22-20-Hospitals)
- COVID-19 Focused Infection Control Survey Tool for Acute and Continuing Care Providers and Suppliers (REVISED) (QSO-21-08-NLTC REVISED)
- Revised Guidance for the Interim Final Rule - Medicare and Medicaid Programs; Omnibus COVID-19 Healthcare Staff Vaccination (QSO-22-07-ALL-Revised 4/05/22)

In 2021, **CDC** updated IPC guidelines for multiple types of healthcare facilities to respond to HAIs, antibiotic-resistant infections, and the spread of SARS-CoV-2/COVID-19 in healthcare settings. This work builds on existing core IPC recommendations issued by the Healthcare Infection Control Practices Advisory Committee. CDC developed and updated its new Infection Control Guidance for Healthcare Professionals about Coronavirus (COVID-19) multiple times throughout the pandemic to adapt to the latest science and respond to the different phases of the pandemic. In addition, CDC tailored these guidelines to address the unique needs and challenges faced by specific healthcare facilities, such as nursing homes, and to address external factors, such as shortages of personal protective equipment. CDC also sought to enhance knowledge and implementation of IPC practices among frontline healthcare workers through Project Firstline, a collaborative of diverse healthcare and public health partners that aims to provide engaging, innovative, and effective infection control training for millions of frontline U.S. healthcare workers as well as members of the public health workforce. Finally, CDC announced a multiyear $2.1 billion investment to improve IPC activities across the U.S. public health and healthcare sectors through American Rescue Plan Act funding. This investment will help strengthen and equip public health departments, healthcare facilities, and other partners with resources to better detect, prevent, and respond to emerging and enduring threats to the healthcare system.

NEW Target 1.4.2.2

Promote equity across public health by incorporating efforts to understand and address health disparities in antimicrobial resistance, including through CDC's CORE Initiative, an agency-wide strategy that includes tailored prevention efforts and materials.

In 2021, **CDC** continued to work to address AR and health equity as a part of its CORE Initiative by working across key agency programs such as: Project Firstline to address training gaps for healthcare workers from diverse educational and training backgrounds; the AR Lab Network to include and analyze patient demographic data alongside laboratory test results to provide a more comprehensive picture of AR in certain populations; and the National Healthcare Safety

Network to enhance patient demographic data for future analysis and drive improvement in healthcare quality. CDC also continues to look closely at lessons learned during the COVID-19 pandemic to improve and innovate to address disparities related to AR.

Subobjective 1.4.3

Promote biosecurity practices on farms and other animal care facilities to reduce the risk from antibiotic-resistant pathogens.

Target 1.4.3.1

Develop updated biosecurity educational materials by 2022.

USDA/APHIS is currently updating existing biosecurity educational materials and developing new ones.

Subobjective 1.4.4

Collect information about biosecurity practices on farms to optimize educational materials about biosecurity for different industries.

Target 1.4.4.1

Report results of biosecurity data from National Animal Health Monitoring System from 2019 (Goats) and 2021 (Feedlot, Swine) by 2022.

USDA/APHIS/NAHMS reported that the results from the 2019 goat study are currently going through clearance and that data collection is ongoing for the 2021 feedlot and swine studies.

Subobjective 1.4.5

Increase research on infection prevention and the emergence and spread of antibiotic resistance and use this research to prevent infections and the spread of antibiotic resistance.

Target 1.4.5.1

Increase research in this area and translate significant findings into practice.

DoD ASPWG/EDC/PVC reported that different DoD entities are working on research in this area. Several projects have been initiated to look at predictors for MDROs.

In 2021, **CDC** funded 11 academic centers through the Prevention Epicenters Program to conduct collaborative research that leads to the prevention of HAIs and AR and selected 25 organizations to participate in the Safety and Healthcare Epidemiology Prevention Research Development (SHEPheRD) Program to develop and conduct research and innovative prevention projects related to HAIs and AR across the healthcare spectrum. In addition, CDC's SURRG program presented project findings at national and international conferences and published 20 articles in scientific journals to disseminate findings and lessons learned. Using an extensive archived collection of tuberculosis (TB) isolates, CDC is also investigating the molecular mechanisms of resistance in TB, such as an analysis that combines DNA sequencing and determination of minimum inhibitory concentrations for different drugs, including new and repurposed anti-TB drugs. New bioinformatic pipelines and a broth microdilution assay have been developed as resources to aid these evaluations. Findings inform interpretations for mutations identified through the molecular detection of drug resistance clinical testing service, and CDC intends to share these interpretations with partner organizations such as public health laboratories in the near future. CDC has also partnered with The Ohio State University to conduct sampling of animal feed and pet food to isolate bacteria and assess resistance, looking for the presence of resistance genes and potential mechanisms of transmission of bacteria containing resistance genes from feed to animals. In addition, CDC is working to strengthen monitoring and surveillance for enteric pathogens, including *Salmonella Infantis* samples from humans in the United States and internationally. This work helps identify sources of resistance and inform prevention activities to reduce the spread of AR.

AHRQ significantly increased its support for research to develop improved methods for preventing HAIs, committing additional funding of $10.7 million, including future years of projects initially funded in FY 2021. AHRQ also reissued both NOFOs to invite research applications for prevention of HAIs: 1) for large research projects for HAI prevention and 2) for large health services research demonstration and dissemination projects for HAI prevention. AHRQ's support for HAI prevention research is ongoing. AHRQ has collaborated with NIH to translate the results of clinical trials into practical materials for clinical use. In September 2021, the agency completed the two-year development of a toolkit based on the NIH-sponsored Active Bathing to Eliminate (ABATE) Infection Trial, which indicated that targeted decolonization to remove bacteria from the bodies of adult non-ICU patients who have indwelling medical devices produced a significant reduction in bloodstream infections. The project included a usability assessment of draft toolkit materials, which informed revisions of the toolkit materials. The final toolkit was published on the AHRQ website in the spring of 2022.
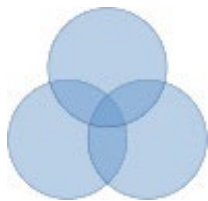
Goal 2: Strengthen National One Health Surveillance Efforts to Combat Resistance

Objective 2.1

Strengthen testing and training capacities and capabilities, enhance integration and harmonization of testing data, and expand the reach of Federal antibiotic resistance laboratory networks across One Health.

Subobjective 2.1.1

Expand surveillance through existing systems to monitor antibiotic resistance from multiple sources across One Health.

Target 2.1.1.1

Increase the amount of laboratory testing for antibiotic resistance, the number of isolates accompanied by test results and available data, and the number of different specimen sources and specimen types collected.

USDA/APHIS/NAHMS conducted antimicrobial susceptibility testing of enteric microbes from the 2019 goat study. Sample collection, culture, and isolation occurred in previous years.

USDA/APHIS/NAHLN received 555,361 antimicrobial susceptibility test results from 30 participating laboratories in 2021, exceeding the target of 5,000 isolates tested. NAHLN also expanded WGS by two to include *Streptococcus zooepidemicus* in swine and *Campylobacter* in all animal species.

USDA/Wildlife Services (WS) is studying the prevalence of bacteria resistant to colistin and other antibiotics in feral pigs that frequent landfills. This year, the number of samples collected more than doubled over previous years, and analysis is ongoing for all samples.

USDA/FSIS is working to better understand AMR in bacteria from food animal species by expanding NARMS sampling to include additional animal sources and by retrieving isolates from additional NARMS projects for microbial AMR diversity testing and direct detection of CRE.

FDA/Center for Devices and Radiological Health received several applications for review and regulatory decision of new devices and cleared more than 18 devices that will have direct impact on AMR when implemented for use in clinical laboratories.

CDC continues to support and expand national surveillance of *N. gonorrhoeae* and its AR mechanisms through the GISP, enhanced GISP (eGISP), and SURRG programs, collecting specimens from genital and extragenital sites of men and women, across more than 30 jurisdictions.

In addition, improvements to the NARMS-CDC WGS analysis workflow increased **CDC'**s AR detection output from approximately 20,000 to more than 65,000 clinical isolates per year, including 10,000 food animal isolates this year. These improvements also increased the timeliness of CDC's detection of AR from near real time (two weeks) to real time (24 hours). During 2021, CDC has also worked with state and federal partners to facilitate testing of animal-origin *Salmonella* isolates upon request and to compare genetic determinants of resistance against information in national databases. CDC also funded the Minnesota Food Safety Center of Excellence to characterize MDROs, identify changing trends in susceptibility, and develop preliminary definitions of healthcare-associated infections in the veterinary clinical setting. The site established draft reporting protocols to the Minnesota Department of Health for carbapenem-resistant organism cases among companion animals, which can be shared with other sites.

In addition, CDC is providing support and guidance about screening and infection control to prevent the spread of *C. auris*. CDC's AR Lab Network offers antifungal susceptibility testing for resistant fungal infections and testing to screen for *Aspergillus fumigatus* through two pilot sites. Preliminary 2020 data demonstrate that the prevalence of elevated minimum inhibitory concentrations (MICs) for ceftriaxone and cefixime have remained stable at 0.1 percent and the prevalence of elevated MICs for azithromycin has continued its previous increasing trend. CDC is also in the process of launching FungiNet, a network for molecular surveillance and genomic epidemiology of fungal disease. Finally, CDC's eGISP Part B was added to the overall GISP project to improve antimicrobial susceptibility surveillance by using polymerase chain reaction (PCR) testing. In addition to collecting samples for culture, this component of eGISP collects remnant nucleic acid amplification test samples for determination of resistance by identifying known resistance-associated mutations. CDC also submitted gonorrhea and enteric pathogen data to the World Health Organization's (WHO) Global Antimicrobial Resistance and Use Surveillance System (GLASS) for the 2019 data call. The country assessment was completed for 2019 and for 2020. However, only CDC's *N. gonorrhoeae* 2020 data were submitted. Additional data are not yet available during the WHO timeframe because of delays due to the COVID-19 pandemic. Teams continue to collect data as available, but delays continue.

Target 2.1.1.2

Submit all identified multidrug-resistant bacterial and fungal isolates of concern (e.g., antibiotic-resistant pathogens identified in the CDC 2019 AR Threats Report) from DoD Defense Health Agency Medical Centers for centralized and standardized genetic characterization at the Multidrug-Resistant Organism Repository and Surveillance Network (MRSN) by 2023.

DoD/MRSN received and processed 9,694 isolates from 7,371 patients across 44 locations in 2021. The genomes of >9,000 isolates were sequenced. GEIS continues to provide the MRSN with regular fiscal support.

NEW Target 2.1.1.3

Increase laboratory capacity for colonization screening to at least 25 CDC Antimicrobial Resistance Laboratory Network laboratories to detect and respond to existing and emerging pathogens, such as CRE and *C. auris*, that can be exacerbated by COVID-19, and other novel threats by 2025.

CDC's AR Lab Network currently identifies CRE and carbapenem-resistant *Acinetobacter* in every state and is expanding colonization screening from seven regional laboratories to 26 laboratories across the United States for asymptomatic carriage of carbapenem-resistant organisms in 2022. CDC is also rapidly expanding for support 27 laboratories to detect *C. auris* infections and colonization at the local level to target interventions and to slow spread. Since 2016, the AR Lab Network has performed more than 500,000 different tests, including more than 125,000 colonization screenings.

Subobjective 2.1.2

Increase whole-genome sequencing and antibiotic resistance phenotypic and genotypic testing in laboratory networks for antibiotic-resistant pathogens listed in CDC's 2019 AR Threats Report and upload sequenced data to the National Institutes of Health (NIH) National Center for Biotechnology Information at the National Library of Medicine or to other approved, secure, and widely accessible databases.

Target 2.1.2.1

Increase numbers of isolates with test results and uploaded sequence data.

DoD/MRSN generated test results for 100 percent of submitted isolates. Discussions are ongoing with other federal agencies to identify a suitable platform for securely storing genome data. Lack of necessary security at current public-facing genome databases has resulted in limited options for data deposition.

USDA/APHIS/NAHLN received 5,411 AST results and 872 WGS results in 2020, and 5,361 AST results and 1,132 WGS results in 2021. **USDA/FSIS** conducted AST analysis on 1,967 isolates (*Salmonella*, *Campylobacter*, *Enterococcus*, *E.*

coli), and of these 1,102 isolates (all *Salmonella*, all *Campylobacter,* and the rest *Enterococcus* and *E. coli*) were subject to WGS analyses. All the sequences from FSIS WGS analysis were uploaded into the National Library of Medicine's (NLM's) Sequence Read Archive in real time.

CDC increased funding to support screening activities to detect AR pathogens and contain their spread. In August 2021, CDC's seven regional laboratories were funded to support WGS of *C. auris*. Additional sites were funded to perform AST for gonorrhea in cases of suspected treatment failure. Between October 2020 and October 2021, CDC supported the AR Lab Network to complete ASTs on >6,800 gonorrhea isolates and WGS of >3,500 isolates from national surveillance and rapid response programs (GISP, eGISP, and SURRG). More than 3,300 of those sequences are available in the NLM Sequence Read Archive. Select gonorrhea genome sequences are uploaded to public global genomic surveillance databases (e.g., PathogenWatch).

Subobjective 2.1.3

Establish an accelerator program to advance implementation of whole-genome sequencing, metagenomics, and other molecular testing for antibiotic-resistant pathogens in humans, animals, plants, and the environment and to coordinate training guidance across agencies and among public and private organizations.

Target 2.1.3.1

Establish at least one collaboration through this program to enhance whole-genome sequencing or metagenomics techniques by 2022.

DoD held preliminary discussions with CDC on establishing a collaboration to enhance WGS techniques.

CDC developed an initial fit-for-purpose framework for extramural capacity building, tool and resource development, and improved integration of sequence data (e.g., from public repositories such as those managed by NLM's National Center for Biotechnology Information [NCBI]) and results into complementary epidemiologic and microbiologic data streams and sources to enhance the value of sequence data in patient safety and public health. CDC has drafted a NOFO to foster technical capacity and innovation in pathogen genomics across One Health and is collaborating internally on mechanisms for supporting an accelerator program if/where appropriate for healthcare and AR. CDC also expanded activities of the Association of Public Health Laboratories/CDC/state public health laboratories HAI/AR sequencing workgroup to further support and advance method development and harmonization for HAI/AR pathogens nationwide. Due to the COVID-19 pandemic response, testing and sequencing capacities and expanded activity at state public health laboratories for HAI/AR are limited. CDC experts also began to develop a long-read sequencing-based assay to detect multiple bacterial STD pathogens (including *N. gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma genitalium*, and *Treponema pallidum*) and to characterize the AR point in selected samples, without the requirement of bacterial culture.

Objective 2.2

Continue expanding and improving access to specimen and data repositories for research and innovation.

Subobjective 2.2.1

Expand the contents of current repositories across One Health of bacterial and fungal strains and their associated genotypic, phenotypic, and descriptive data and, where possible, improve and increase the accessibility, transparency, interoperability, security, storage, and utility of these data.

Target 2.2.1.1

Increase the number of isolates, panels, and data available and relevant publications in the scientific literature.

USDA/APHIS/NAHMS engaged in ongoing cooperative agreements that support research on AMR in cattle, swine, and poultry pathogens.

USDA/FSIS published aggregate AMR tables for FSIS commodities (product and cecal-content samples) on the FSIS website. The most current quarterly aggregate AMR table starting from 2016 is available on the FSIS website. Also, NARMS partners published two scientific papers—in the journals *Genes* and *Frontiers in Microbiology*—with collaborating authors from FSIS.

DoD/MRSN staff members authored or coauthored nine peer-reviewed publications in 2021. The MRSN deposited a diversity panel for *Klebsiella pneumoniae* at NIAID-supported BEI Resources for distribution to the research community at no additional cost. The COVID-19 pandemic has seen an approximately 25 percent decrease in isolate submissions across all DoD healthcare facilities, reflecting the reduced number of patients seeking non-COVID-related treatments.

FDA and CDC continue their collaboration with a new interagency agreement to enhance the number of isolates in the CDC and FDA AR Isolate Bank, as well as the information available on the isolates. The AR bank isolates continue to be distributed to researchers who request the isolates for verification, validation testing, and research and development, while conducting studies for regulatory submissions to FDA. Since 2016, the AR Isolate Bank has filled nearly 3,500 orders, shipping nearly 6,000 isolates as of August 2021. Currently, the AR Isolate Bank contains >1,000 isolates placed into 32 different panel categories (e.g., aminoglycoside-tetracycline resistance panel, gram-negative carbapenemase detection, *Candida* species, *C. auris* panel, *N. gonorrhoeae* panels). Since 2021, **CDC** has added several isolates to the AR Isolates Bank: extended-spectrum beta-lactamase (ESBL) bacterial isolates drawn from Multi-Site Gram-Negative Surveillance Initiative (MuGSI); one blaSIM (a gene conferring resistance to carbapenems); a positive *Pseudomonas aeruginosa* isolate; and cefiderocol susceptibility data for 38 AR Isolate Bank isolates. In addition, the AR Isolate Bank website now contains a dedicated section listing publications that reference AR Isolate Bank isolates. During 2021, CDC began adding to a set of *Shigella* isolates from the NARMS for enteric bacteria, with a target goal of 30 isolates in 2022, that represent different mechanisms of resistance to fluoroquinolones and a range of susceptibility to fluoroquinolones and azithromycin.

In 2020, **FDA's** NARMS Now: Integrated Data dashboard began reporting antimicrobial sensitivity profiles based on genomic sequencing using the AMRFinder tool developed in collaboration with NLM's NCBI. In December 2020, an expanded version of the Resistome Tracker AMR data tool was released that allowed analysis of AMR in additional bacterial genera. Similar to NARMS Now, the Resistome Tracker tool is updated weekly, providing timely resistance monitoring data for global access. Lack of appropriated funding continues to be one of the largest barriers to accomplishing this goal. Many laboratories still need updated equipment and funds for supplies in order to perform standardized susceptibility testing for a large monitoring program.

NIH's National Database of Antibiotic Resistant Organisms (NDARO) is a centralized hub for researchers to access AMR data to facilitate real-time surveillance of pathogenic organisms. The project aims to make AMR-related data more widely available by collecting genetic and antibiotic susceptibility data in a centralized website hosted by the NLM's NCBI. To increase standardization, NIH/NLM/NCBI has developed and maintains a curated reference database of AMR, virulence, and stress response genes. **NIH/NLM/NCBI** has developed the AMRFinderPlus algorithm to identify these genes in bacterial genomes using the reference database. NIH/NLM/NCBI has also developed the Isolates Browser that provides information on clonality of isolates and allows researchers to identify bacterial genomes with AMR, virulence, and stress response genes, along with associated metadata. As of September 30, 2021, there were >950,000 bacterial and fungal genomes available in the isolates browser. In addition, the NIH/NIAID-supported Bacterial and Viral Bioinformatics Resource Center (BV-BRC) is a public knowledge base that provides open-source bioinformatics tools and a platform to analyze integrated data for bacteria and viruses. It houses >600,000 bacterial genomes and >36 million annotated AMR genes. BV-BRC continued the development of machine learning and artificial intelligence models to predict AMR directly from genomic sequences. The BV-BRC provided bioinformatics services to the CDC, FDA, and other researchers via BV-BRC annotation services and the Rapid Annotations using Subsystems Technology to predict potential AMR-related outbreaks with accuracies of 88 to 99 percent for carbapenem resistance in *A. baumannii*, MRSA*,* and beta-lactam and cotrimoxazole resistance in *Streptococcus pneumoniae.*

Subobjective 2.2.2

Support and expand efforts to provide rapid, accurate, and comprehensive access to antibiotic-resistant isolates, integrated data sources (including genomic, phenotypic, and functional data), and up-to-date computational analysis tools, and improve adherence to the "FAIR" (findability, accessibility, interoperability, and reusability) principles for scientific data management and stewardship.

Target 2.2.2.1
Award new grants that support access to data and computational tools focused on antibiotic resistance.

NIH's AMRFinderPlus is a tool developed to identify AMR genes and point mutations, virulence, and stress response genes in bacterial genomes. The reference set of genes and point mutations is curated and includes allele submissions (NIH/NLM/NCBI is the authority for naming alleles for most beta-lactamases and *mcr* and *qnr* genes). Curation includes collaborative efforts with other AMR databases and occurs directly from the literature when new genes and point mutations are discovered. There is an ongoing collaboration with the Public Health Alliance for Genomic Epidemiology (PHA4GE) to standardize results from different bioinformatics tools. The software has been downloaded >49,000 times, and the publications about the tool have been cited >300 times in journals such as *Antimicrobial Agents and Chemotherapy* and *Scientific Reports*.

In addition, the NIH/NIAID-funded Strain Genome Explorer (StrainGE) is a toolkit that analyzes same-species, strain-level diversity in metagenomic sample mixtures (e.g., microbiome analyses and other complex community samples). Distinguishing at the strain level is important because organisms of the same species, such as *E. coli*, can cause distinct diseases, including diarrhea and urinary tract infections, or be benign. The tool uses short-read metagenomic sequencing, is more sensitive, and has a higher resolution than other available tools.

Target 2.2.2.2
Offer training opportunities and outreach for FAIR principles.

As part of the NDARO, **NIH/NLM/NCBI** is submitting annotated microbial genomes to GenBank in standard formats to make the data easily findable, accessible, interoperable, and reusable. In addition, a new interface, the Microbial Browser for Genetic and Genomic Elements (MicroBIGG-E), contains the detailed sequence information, including location, of the AMR genes and point mutations, stress response, and virulence genes identified using AMRFinderPlus for pathogen genomes in the NDARO that have been submitted to GenBank. As of September 30, 2022, >757,000 genomes have been submitted to GenBank as part of the analysis pipeline and are available in the MicroBIGG-E. The total number of genetic elements in the MicroBIGG-E is >17 million, including point mutations, acquired resistance genes, virulence, and stress response genes. NIH/NLM/NCBI also has made the databases used by AMRFinderPlus more accessible to the scientific community through the release of three interactive browsers, the Reference Gene Catalog, the Reference Gene Hierarchy, and the Reference HMM [hidden Markov models] Catalog. Training was held in conjunction with FDA at the International Association of Food Protection annual meeting, and again with FDA for the NARMS annual meeting for the various resources for NDARO.

In addition, the **NIH/NIAID**-supported BV-BRC offers multiple training opportunities, ranging from webinars, online tutorials, onsite workshops, workshops at conferences, and a Massively Open Online Course (MOOC). The BV-BRC implemented hybrid outreach activities to accommodate the exponentially increased demand for online training and resources used during the COVID-19 pandemic while rebooting the in-person BV-BRC training, which was paused and has been critical for developing the bioinformatics workforce.

Subobjective 2.2.3

Through the National Antimicrobial Resistance Monitoring System (NARMS) and the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), contribute antibiotic-resistant isolates from food and animals to the existing CDC and FDA AR Isolate Bank.

Target 2.2.3.1

Establish mechanisms for sharing food and animal isolates by 2021.

The **USDA/FSIS** cecal content sampling and AMR testing programs operate under the FDA-FSIS NARMS Interagency Agreement, which includes a formal mechanism to routinely share bacterial AMR isolates with the FDA. Under this agreement, from February/March 2020 to October 8, 2021, FSIS shared 17 isolates with the FDA for conducting in-depth genomic sequencing, also known as long-read sequencing.

FDA's Vet-LIRN AMR isolates are being archived in isolate repositories located at Vet-LIRN Source and WGS laboratories. NARMS AMR isolates are archived onsite at the FDA. Both Vet-LIRN and NARMS isolates are provided to AR repositories upon request. With the growing number of isolates being collected and archived, isolate repositories will need to be expanded, requiring continuous investment in infrastructure (e.g., for isolate storage equipment and to expand laboratory space for isolate archiving).

Subobjective 2.2.4

Migrate DoD's bacterial and fungal genome sequencing data and associated phenotypic data to a secure, cloud-based or equivalent environment to allow authorized Federal users to access pathogen data.

Target 2.2.4.1

Identify suitable storage solutions that will satisfy access requirements by 2022.

DoD/GEIS's Digital Biobank rollout is pending connectivity to MHS medical record systems. GEIS and the MRSN are working to prioritize infectious disease surveillance focus on the platform.

Objective 2.3

Strengthen the national infrastructure for antibiotic resistance surveillance data across One Health, by improving capacity, utility, timeliness, and the use of harmonized terminology.

Subobjective 2.3.1

Expand the number of sources for and quantity of antibiotic resistance surveillance data collected from inpatient healthcare facilities.

Target 2.3.1.1

Explore interagency collaborations to examine options for increased reporting to the CDC National Healthcare Safety Network (NHSN) Antibiotic Resistance Option.

During FY 2021 and FY 2022, **CDC** and **CMS** worked together to implement a new AUR surveillance measure for eligible hospitals and Critical Access Hospitals (CAHs) under the Medicare Promoting Interoperability Program's Public Health and Clinical Data Exchange Objective. In the CMS FY 2023 Inpatient Prospective Payment System Prospective Payment System Final Rule, released in August 2022, CMS finalized a policy to require these eligible hospitals and CAHs to report the AUR surveillance measure beginning in with the CY 2024 electronic health record (EHR) reporting period.

CMS utilizes NHSN data to collect, examine, and evaluate HAIs. CMS is in the early stage of working with CDC to see if there is a way to use AMU/AR measures through its hospital quality reporting and value-based payment programs.

VA's ongoing conversion to an updated EHR system will contribute to future efforts to submit to the NHSN Antibiotic Resistance Option.

Target 2.3.1.2

75 percent of acute care hospitals, 100 percent of DoD hospitals, 100 percent of applicable VA hospitals that have transitioned to the VA's updated electronic health record, and 25 percent of critical access hospitals reporting to the NHSN Antibiotic Resistance Option.

As of October 1, 2021, **CDC** reported that 22 percent of general acute care hospitals and 6 percent of CAHs had submitted data to the NHSN AR Option. Compared to large hospitals, CAHs usually have relative limited recourses to implement AR Option reporting. CDC remains steadfast in coordinating with multiples states and public health partners to develop AR reporting requirements, despite slower rates of expansion due to setbacks from the COVID-19 pandemic. In addition, CDC has been coordinating with CMS on the Promoting Interoperability Programs requirements for AUR module reporting to NHSN, which is expected to lead to increased reporting among hospitals.

DoD MTFs are currently transitioning to a new electronic health record. All the facilities that completed this transition as of October 1, 2021, were reporting to the NHSN AR Option.

VA's ongoing conversion to an updated EHR system will contribute to future efforts to submit to the NHSN Antimicrobial Resistance Option.

Target 2.3.1.3

Expand DoD and VA collaborations to increase the number of VA medical centers submitting multidrug resistance data or isolates from multidrug-resistant pathogens to the MRSN.

In July 2021, the **DoD/MRSN** placed an employee at the Baltimore VA center, and they have been submitting MDR pathogens from their clinical laboratory regularly. Expansion into other VA centers is ongoing, and sporadic shipments have been arriving from the San Antonio VA center in Texas. Differences between DoD and VA computer systems, hiring requirements, and privacy regulations have complicated these collaborations.

VA's ongoing conversion to an updated EHR will contribute to future efforts to submit to the NHSN AR Option.

Subobjective 2.3.2

Expand the number of sources for and quantity of community-transmitted antibiotic resistance surveillance data from humans, including sexually-transmitted infections, enteric diseases, respiratory illnesses, and other diseases caused by antibiotic-resistant pathogens.

Target 2.3.2.1

Each year, increase the number of human isolates collected and analyzed.

DoD/GEIS placed multiple projects and protocols on hold during FY2021 due to COVID-19-related disruption. Supply chain issues and movement restrictions further limited remaining active projects.

CDC continues to support population-based surveillance for AR pathogens through EIP, including collecting and submitting specimens and isolates for further characterization (e.g., CRE, carbapenem-resistant *A. baumannii*, ESBL-producing bacteria; MRSA; nontuberculous mycobacteria). CDC's SURRG continues to collect and analyze isolates across community-associated pathogens (such as gonorrhea), perform AR testing across specimen sources, and respond to emerging resistance. However, isolate numbers were lower than prior years due to the COVID-19 pandemic. The EIP Foodborne Disease Active Surveillance Network (FoodNet)—the principle foodborne disease component of EIP—continues surveillance of enteric pathogens, including *Campylobacter*, *Salmonella*, shiga toxin-

producing *E. coli*, and *Shigella,* from 10 sites comprising 15 percent of the U.S. population. In 2020, there was a 26 percent overall decrease in enteric infections vs. the previous three years.

Subobjective 2.3.3

Expand the number of sources for and quantity of antibiotic resistance surveillance data from animals, farms, and production facilities.

Target 2.3.3.1

Increase the number of animal, feed, or food isolates collected, analyzed, and used for prevention and response efforts.

USDA/APHIS/NAHMS engaged in cooperative agreements that support studies involving sampling, isolation, and resistance testing of cattle and swine pathogens to support informed decision-making for veterinarians and researchers. **USDA/APHIS/NAHLN** sequenced 309 isolates in 2019, 872 isolates in 2020, and 1,132 isolates in 2021. The last group are still being submitted to the National Veterinary Services Laboratories for sequencing. AST data are updated monthly on a Tableau® dashboard. **USDA/WS** reported that studies ongoing in 2020-2021 in which bacteria are being tested for AMR and isolates stored included prevalence of bacteria resistant to colistin and other antibiotics in feral pigs frequenting landfills.

In February/March 2020, **USDA/FSIS** expanded the NARMS program to include sampling from additional animal sources, including cecal-content samples from minor species (sheep, goat, lamb) and veal, and mesenteric lymph nodes from cattle. The samples analyzed under NARMS expansion included 545 minor species (sheep, goat, lamb), 726 veal, and 503 cattle mesenteric lymph nodes. In case of *Siluriformes* fish, a subset of 544 out of 2,260 samples that were taken for *Salmonella* testing were also analyzed for NARMS indicator bacteria.

NIH reported that, during FY 2021, >40,000 pathogen genomes of a food, environmental, animal, or feed isolate have been submitted and made available in the NDARO, the vast majority from U.S. surveillance efforts.

To improve the timely identification of zoonotic and animal health pathogens, **FDA/CVM** has established and expanded the AMR monitoring program through Vet-LIRN laboratories, including building and expanding capacity for WGS. To date, through the Vet-LIRN AMR monitoring program, FDA/CVM collected susceptibility testing data from >15,000 animal pathogens routinely isolated by veterinary diagnostic laboratories across the United States and Canada, and WGS data from >4,000 of those isolates. WGS data are available in public repositories housed by NIH.

In connection with NARMS, in 2021 **FSIS** conducted AMR testing in veal, goat, sheep, and lamb gut contents and in *Siluriformes* fish samples. Two pilot projects have been completed: 1) to examine microbial AMR diversity in NARMS samples and whether *E. coli* can be represented by this diversity and 2) to screen cattle and swine isolates for the presence of CRE.

Sub-objective 2.3.4

Establish new capacities for collecting antibiotic resistance data from the environment, including water and soil.

Target 2.3.4.1

Establish at least two projects to expand antibiotic resistance data collection from the environment, including national-scale testing of surface waters as part of NARMS by 2022.

USDA/ARS is involved in the Antimicrobial Resistance in Surface Waters: Pilot Environmental Monitoring Effort, which includes method development to standardize analytical approaches and culture methods for analyzing *Salmonella* and *E. coli* with AR in environmental surface water samples and conducting a field assessment to test the developed methods and help finalize the design of the watershed-scale study.

FDA reported that, as part the NARMS Environmental Surface Water Pilot, NARMS established an interagency agreement with USDA's Agriculture Research Service to conduct initial development for detection of bacterial and AR gene targets.

CDC did not have the capacity for surface water testing projects for 2021, and staff leads for environmental AR work were diverted to COVID-19 response activities.

NEW Target 2.3.4.2
Pilot collection of antimicrobial resistance data from wastewater surveillance by 2023.

In 2020, **CDC** established the National Wastewater Surveillance System (NWSS) to provide community-level data on COVID-19 infection trends by looking for markers in wastewater that tell scientists when SARS-CoV-2 is present. The framework for NWSS was built on an AR Solutions Initiative investment made in 2018 to the University of South Carolina to study resistant pathogens in wastewater treatment plants. As of August 2022, CDC has provided support to 46 states, five cities, seven tribes, and two territories for COVID-19 wastewater surveillance. Through this program, NWSS implementing partners have collected >91,000 samples from municipal wastewater systems serving approximately two in five people in the United States (>130 million people). CDC continues to invest in these capabilities by exploring the possibilities for adding AR wastewater surveillance capacity in states, territories, and tribes. In addition, NWSS continues to evolve and expand wastewater surveillance globally through CDC's Global AR Lab & Response Network.

Sub-objective 2.3.5
Establish a platform for more comprehensive understanding of the carriage of antibiotic resistance genes (also known as the resistome) present across One Health.

Target 2.3.5.1
Establish a pilot sampling strategy to collect healthy human, animal, plant, and environmental specimens and epidemiological data by 2023.

CDC has no update due to challenges encountered resulting from the public health response to the COVID-19 pandemic.

Objective 2.4
Strengthen the national infrastructure for antibiotic use surveillance data across One Health, by improving capacity, utility, timeliness, and the use of harmonized terminology.

Sub-objective 2.4.1
Expand the number of sources for and quantity of surveillance data on the use of antibiotics from inpatient and outpatient healthcare facilities to improve understanding and implementation of the optimal use of antibiotics.

Target 2.4.1.1
Explore interagency collaborations to examine options for increased reporting to the CDC National Healthcare Safety Network (NHSN) Antibiotic Use Option.

CMS utilizes NHSN data to collect, examine, and evaluate HAIs. CMS is collaborating with CDC on strategies to use AU/AR measures through CMS's Health Information technology program. **CDC** and CMS continue to collaborate to require hospital antimicrobial use/antimicrobial resistance reporting under the Promoting Interoperability Program 2023 reporting period. This AUR reporting component will be required in 2024.

DOD/ASPWG/EDC/PVC has no update.

VA's ongoing conversion to an updated EHR will contribute to future efforts to submit to the NHSN Antibiotic Resistance Option.

Target 2.4.1.2
100 percent of acute care and 50 percent of critical access hospitals reporting to the CDC NHSN Antibiotic Use Option.

All **DoD** hospitals are enrolled in the NHSN antibiotic use option, and most are reporting to it. MTFs that have transitioned to the new EHR are not able to report to the Antibiotic Use Option.

As of October 1, 2021, **CDC** reported that 49 percent of general acute care and 16 percent of CAHs reported data to the NHSN Antimicrobial Use Option. CDC remains steadfast in coordinating with multiples states and public health partners to develop AR reporting requirements, despite slower rates of expansion due to setbacks from the COVID-19 pandemic. In addition, CDC has been coordinating with CMS on the Promoting Interoperability Programs requirements for AUR module reporting to NHSN, which is expected to lead to increased reporting among hospitals.

Target 2.4.1.3
Improve timelines of annual outpatient antibiotic use tracking and reporting by 2021.

CDC's Office of Antibiotic Stewardship has gained access to several data sources for more timely tracking of outpatient antibiotic use and appropriateness, including CMS Virtual Research Data Center Medicare data, IQVIA National Prescription Audit and Total Patient Tracker (TPT) data, IQVIA Longitudinal Prescription Data and Medical Claims Data.

Target 2.4.1.4
Implement tracking of antibiotic use in all DoD Military Health System facilities, using the Standardized Antimicrobial Administration Ratio (SAAR) (based on observed inpatient antimicrobial days of therapy), by 2021.

All **DoD** hospitals are enrolled in the NHSN AU option, and most are tracking SAAR. MTFs that have transitioned to the new EHR are not able to track SAAR.

CDC's NHSN continues to provide analytic tools, technical assistance, user support, and education materials to assist NHSN users, including all DoD facilities, using the SAAR.

Target 2.4.1.5
Increase the percentage of optimal antibiotic prescriptions in the DoD Military Health System.

DoD/ASPWG/EDC/PVC is creating dashboards to assess inappropriate prescribing for specific conditions.

Subobjective 2.4.2
Develop new or expand the number of sources for and quantity of surveillance data on the use of antibiotics collected from animals, farms, and production facilities to improve understanding and implementation of responsible use of antibiotics.

Target 2.4.2.1
Increase published reports and dashboards on antibiotic use in animals.

USDA/APHIS/NAHMS published the 2017 cow/calf study and the swine antimicrobial use and stewardship dashboard.

FDA/CVM has funded four cooperative agreements in an effort to develop methods for collecting antimicrobial use data in veterinary sectors. This effort includes FDA funding since August 2016 for two pilot projects to develop approaches for collecting data on AMU in four major food-producing animal groups (cattle, swine, and chickens and turkeys). Initial data from the food animal cooperative agreements were published in November 2020 in the journal *Zoonoses and Public Health*. Due to COVID-19-related delays throughout 2020 and early 2021, preparation of final reports for both food animal cooperative agreements were delayed. CVM has also funded two pilot projects in August 2020 to collect AMU data in the companion animal sector (dogs and cats).

In addition, CVM published a report in 2022 that integrates and analyzes available information (2016-2019) about antimicrobial sales, use, and resistance in U.S. animal agriculture and the related food chain to assess the progress of efforts to foster AS and reduce AR development.

CVM began a collaboration with the Reagan-Udall Foundation for the FDA in 2021 to facilitate listening sessions with a variety of affected stakeholders to determine the benefits, costs, and challenges facing the veterinary, agricultural, and public health communities associated with collection of AMU data in food-producing animals. The project is considering strategies for collaboration through public-private partnerships to leverage existing data systems and minimize burdens. Existing antimicrobial sales data are not representative of the volume of antimicrobials used or indications for use. Furthermore, collecting AMU information has presented numerous challenges, including the number and diversity of settings in which antimicrobials are used in animals, the lack of existing infrastructure for capturing such data, the limited resources available to develop such an infrastructure, and concerns about protecting privacy and confidential commercial information.

Goal 3: Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria

Objective 3.1

Develop and validate new diagnostics.

Subobjective 3.1.1

Develop new or enhance existing diagnostics that use isolates and primary samples to determine the presence, severity, or antimicrobial susceptibility or resistance of bacterial or fungal infections and to identify appropriate treatment.

Target 3.1.1.1

Support 10 new antibiotic resistance-related diagnostics projects across the U.S. Government annually through 2025, through funding or scientific or technical support.

DoD/MIDRP/Detrick has three DOD/Medical Research and Development Command–funded small business innovation research projects that have successfully completed Phase 1 and moved into Phase 2 development.

USDA published research articles on *Streptococcus suis* isolates, natural horizontal gene transfer of AMR genes in *Campylobacter* species in turkeys and swine, and chromosomal *mcr*-3/7 in *Aeromonas* samples from U.S. animals.

ASPR/BARDA awarded two new contracts for AR-related diagnostic projects, and its current portfolio includes six companies supporting diagnostic projects for bacterial identification and phenotypic AST results, detection of bacterial vs. viral infections, sequencing, and identification of molecular markers of resistance. BARDA is evaluating white papers and full proposals through its broad agency announcement (BAA). This announcement seeks proposals to develop tests to differentiate bacterial vs. viral infections, sequencing technologies, and phenotypic AST platforms. Due to the COVID-19 pandemic, some focus was shifted from supporting AMR diagnostics to COVID-19 diagnostics during FY 2021. However, in FY 2022 BARDA plans to review BAA submissions for AMR diagnostics.

CDC expanded antimicrobial susceptibility surveillance for *N. gonorrhoeae.* eGISP Part A detects antimicrobial susceptibility patterns in infections in the pharynx and rectum and in women. eGISP Part B utilizes remnant nucleic acid amplification test samples to identify known resistance-associated genetic mutations in settings without culture capacity. For TB, a targeted next-generation sequencing assay—with testing across 18 genetic loci for detection of mutations associated with drug resistance for 11 first- and second-line anti-TB drugs, including the newer drug bedaquiline—has been finalized. In addition, CDC is participating in a global postmarketing surveillance project to determine MIC for pretomanid (approved as part of a BPaL [bedaquiline/pretomanid/linezolid] regimen) in MDR TB isolates.

FDA/Center for Devices and Radiological Health received several applications for new devices in 2021 for review and regulatory decision. More than 18 devices were cleared that will have direct impact when implemented for use in clinical laboratories.

NIH/NIAID supported more than 10 new projects on AR-related diagnostics to inform treatment options for bacterial infections and improve AS. With NIH/NIAID support, Visby Medical, Inc. developed a point-of-care diagnostic to detect chlamydia, gonorrhea, and trichomonas that delivers results within 30 minutes. Visby Medical's PCR sexual health test

received FDA clearance and a Clinical Laboratory Improvement Amendments waiver in August 2021. NIH/NIAID also supported a clinical study to evaluate this diagnostic test, which was an important step toward licensure. NIH/NIAID's support is a positive example of how public-private partnerships can transform patient care and reduce the epidemic spread of infectious diseases (NCT03852316; *Lancet Infectious Diseases*).

Objective 3.2

Support research to determine the appropriate use of diagnostics.

Subobjective 3.2.1

Stimulate research to better understand the appropriate use of diagnostics to determine the presence, severity, or antimicrobial susceptibility or resistance of bacterial or fungal infections in human and veterinary care.

Target 3.2.1.1

Invite research applications and support research on the appropriate use of CARB-related diagnostics in human clinical and veterinary care.

CDC is collaborating with the CDC Foundation and academic institutions to learn about the presence of *C. auris* in different body sites to guide screening practices.

AHRQ reissued both CARB NOFOs to invite research applications: 1) for large research projects for CARB and 2) for large health services research demonstration and dissemination projects for CARB. In both NOFOs, the following revised statement now appears in the section describing AHRQ's research objectives: "The role of new and existing diagnostics, including rapid diagnostics, in improving antibiotic use, including how diagnostics should be integrated into clinicians' decision making about antibiotic use." The reissued NOFOs thus address this objective to invite research applications on the appropriate use of CARB-related diagnostics.

The **NIH/NIAID**-supported Antibacterial Resistance Leadership Group (ARLG) is preparing to conduct the Fast Antibiotic Susceptibility Testing for Gram-Negative Bacteremia trial, a prospective, randomized trial to evaluate clinical outcomes among patients with gram-negative bacteremia who have blood culture evaluation using standard methods vs. rapid AST.

Objective 3.3

Stimulate the appropriate adoption and use of diagnostics.

Subobjective 3.3.1

Develop evidence-based guidance to promote the appropriate use of new diagnostics and to improve the use of existing diagnostics that determine the presence, severity, or antimicrobial susceptibility or resistance of bacterial or fungal infections in human clinical care.

Target 3.3.1.1

Support the development of evidence-based guidelines for the use of new and existing antibiotic and antifungal resistance-related diagnostics.

FDA's Center for Devices and Radiological Health (CDRH) initiated several scientific studies that aim to provide better understanding of the relationships between genotypic determinants of AMR in bacteria and yeast pathogens and the expressed phenotype by the organism against an antimicrobial drug. The findings from these studies will inform regulatory decision-making and evaluation of new diagnostics for detection of AMR.

CDC used GISP and SURRG data to guide updates to the [2020 gonorrhea treatment recommendations](#) published in the *Morbidity and Mortality Weekly Report*. These data were used in determining recommended treatment regimens and for test-of-cure testing recommendations.

Goal 4: Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines

Objective 4.1

Expand basic and applied interdisciplinary research to better understand the emergence, spread, and persistence of antibiotic resistance, and develop mitigation strategies for antibiotic resistance in human, animal, agricultural, and environmental settings.

Subobjective 4.1.1

Advance our understanding of the emergence, spread, and persistence of antibiotic resistance.

Target 4.1.1.1

Report success stories to disseminate new knowledge about antibiotic resistance and inform mitigation strategies in human health (at least two stories) and agriculture (at least one story) annually through 2025.

CDC worked with multiple domestic and international partners to highlight the important role medical tourism can have in introducing resistant organisms into the United States. In one instance, CDC identified the introduction of a carbapenem-resistant organism from patients returning after undergoing bariatric surgery in Mexico. That outbreak was halted, and the investigation called attention to a new CDC recommendation for screening these patients when they return to the country. CDC also identified the spread of AR pathogens, including *C. auris*, on clinical units caring for patients with COVID-19. For drug-resistant gonorrhea, the SURRG program published 20 scientific journal articles in 2021 to disseminate findings and lessons learned about drug-resistant gonorrhea rapid detection and response, including through utilizing eGISP Part A AST data. Both the STD Surveillance Report and the GISP profiles were published, providing overall and site-specific AST and epidemiological findings for all participating GISP sites. CDC released two partnership stories highlighting the collaboration between CDC and the University of Utah to estimate the annual healthcare costs of six MDR pathogens, and the first AMR Exchange webinar focused on actions to combat AR after the COVID-19 pandemic. In addition, CDC has produced eight fact sheets on AR, highlighting COVID-19 funding, the scope and impact of CDC's AR innovations portfolio, AR Solutions Initiative activities by setting, and the impact of the AR Lab Network.

From 2020 to 2021, CDC also hosted eight webinars with >27,000 registrants and >10,000 attendees. In addition, CDC's NARMS established and communicated CLSI clinical breakpoints for azithromycin for *Shigella* that were a result of years of research and surveillance by CDC NARMS laboratory scientists and epidemiologists in collaboration with the University of Virginia and the California Department of Public Health. CDC also collaborated with The Ohio State University to develop communication materials to enhance outreach to livestock producers about implementation of AS. An additional success story has been detailing a One Health response to a MDR *Salmonella* Heidelberg outbreak.

USDA ARS scientists in Peoria, Illinois, and their collaborators found success in testing a compound that could bolster the potency of beta-lactam antibiotics, potentially reducing the dosages required and helping stave off the development of resistance in the germs they are meant to kill.

USDA NIFA funded research that identified natural resistance to horn fly infestation in Holstein cattle, which could potentially be leveraged through breeding to reduce the need for antibiotics in these animals.

NIH is committed to advancing microbiome science, which holds significant promise for addressing public health challenges like antibiotic resistance. As part of this work, CDC and NIH/NIAID coedited a unique supplement issue for

the *Journal of Infectious Diseases* that highlighted the state of microbiome science and its relevance to AR. In addition, intramural researchers at the NIH/National Human Genome Research Institute (NHGRI) collaborated with CDC to investigate the effects of routine chlorhexidine gluconate bathing on the skin microbiome of residents in nursing homes with endemic *C. auris*. These studies were published in [*Nature Medicine*](#) and [*mSphere*](#).

NIH/NIAID also established a collaborative research program to address key research gaps in the field of antibacterial resistance. The CARBIRUs bring together investigators from diverse disciplines to address key research gaps in the field of antibacterial resistance and support fundamental, collaborative research ranging from discovery to early development, with a focus on combating CDC-designated AR threats such as carbapenem-resistant *Acinetobacter* and *Enterobacteriaceae*, *C. difficile*, and MRSA.

Objective 4.2

Intensify basic, translational, and clinical research to support the discovery and development of new treatments, including antibiotics, nontraditional therapeutics, and optimized treatment regimens.

Subobjective 4.2.1

Support the discovery and preclinical development of new therapeutics.

Target 4.2.1.1

Award 100 new projects (e.g., grants, contracts, CARB-X awards) aimed at therapeutic discovery or development by 2024.

In September 2021, **ASPR/BARDA** added Genentech's GDC-0892 candidate, a novel preclinical *lepB* gene inhibitor to the advanced research and development portfolio. From October 2020 through September 2021, the BARDA- and NIH/NIAID-supported CARB-X program awarded funding for four new therapeutic projects and seven new nontraditional projects.

NIH/NIAID supported >100 new projects through grants, contracts, and preclinical services aimed at therapeutic discovery or preclinical development. The projects included research covering a range of products and strategies to treat AR infections, including small molecules, peptides, monoclonal antibodies, and phage therapies. NIH/NIAID also provides [preclinical service support](#) to fill gaps in the product development pathway, including evaluating *in vitro* and *in vivo* activity, pharmacokinetics, and toxicology of new candidate therapeutics for MDR bacteria. [The NIH/NIAID Structural Genomics Centers](#) determine 3D structures of proteins from priority human pathogens to address key research gaps using state-of-the-art structural biology methods and respond to emerging infectious disease threats and NIH/NIAID priorities. They have solved the structures of >650 pathogens from different target proteins related to antimicrobial organisms or antimicrobial resistance and include ESKAPE pathogens (*Enterococcus faecium*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *Enterobacter* species) as well as *C. difficile, Chlamydia, and Neisseria*. The 3-D structure information and reagents are made publicly available.

Target 4.2.1.2

Identify one candidate therapeutic for bacterial infections in human medicine for further research and development by 2022.

DoD supported preclinical development of Debio-1452-Az-NH3, a first-in-class, broad-spectrum antibiotic intended to treat MDR bacterial infections and sepsis associated with combat wounds.

Target 4.2.1.3

Identify one candidate therapeutic for bacterial infections in agriculture for further research and development by 2021.

USDA/ARS scientists in Peoria, Illinois, and their collaborators continue garnering success in their [tests](#) of a compound that could bolster the potency of beta-lactam antibiotics, potentially reducing the dosages required and helping stave off resistance in the pathogens they target.

Target 4.2.1.4

Report success stories about additional therapeutic options for human health (at least 5 stories) and agriculture (at least 1 story) annually through 2025.

USDA/ARS and US Biologic, Inc., have developed an [oral solution](#) as an antibiotic alternative to fight poultry coccidiosis, which costs the global poultry industry $3.5 billion in annual losses.

USDAUSDA/NIFA supported research into the [relationship](#) between high-fat diet, antibiotic use, and risk of inflammatory bowel disease.

DoD/WRAIR contributed in vitro data to Entasis Therapeutics as part of their new drug application filing with the FDA for sulbactam-durlobactam targeting *A. baumannii* infections. DoD/WRAIR also conducted preclinical studies with Paratek Pharmaceuticals for omadacycline, a fourth-generation tetracycline, to evaluate the potential for expanding its clinical use for preventing or treating combat wound infections. DoD/WRAIR is collaborating with the University of Illinois on investigational new drug (IND) studies for Debio-1452-Az-NH3, a novel broad-spectrum inhibitor of the bacterial target FabI, noting promising results against gram-negative pathogens, including *A. baumannii* and *K. pneumoniae.* DoD is also looking to expand efforts to evaluate dual-acting lipoxygenase inhibitors to combat gram-negative pathogens using artificial intelligence developed by SRI International.

NIH/NIAID-supported researchers have developed an effective discovery program based on exploiting unculturable bacteria to resolve the bottleneck of antimicrobial drug discovery. Investigators have discovered several new compounds from this source. One compound, [darobactin](#), has a novel mode of action that makes it particularly effective against gram-negative bacteria. NIH/NIAID also awarded a contract to establish the [Chemistry Center for Combating Antibiotic Resistant Bacteria](#) (CC4CARB), an initiative that oversees the design, synthesis, and management of external investigator-submitted libraries of chemical compounds specifically targeting gram-negative bacteria.

NIH/NIAID supports a robust fungal research portfolio covering topics of basic fungal biology; mechanisms of resistance and virulence; and the development of diagnostics, therapeutics, and vaccines. Discoveries from this work may help identify promising candidates active against MDR *C. auris*. Finally, NIH/NIAID scientists have used two different bacteriophage viruses individually or in combination to successfully treat mice infected with MDR *K. pneumoniae* sequence type 258 (ST258). [This study](#) represents a first step in evaluating the use of phage therapy for treatment of severe *K. pneumoniae* ST258 infection in humans.

Subobjective 4.2.2

Support clinical research into and development of new treatments, including antibiotics, nontraditional therapeutics, and optimized treatment regimens.

Target 4.2.2.1

Facilitate development of 10 novel potential therapeutics for bacterial infections in humans by 2022.

In March 2021, **ASPR/BARDA** awarded a contract to ContraFect Corporation to develop exebacase for treatment of *S. aureus* bacteremia, including MRSA. From October 2020 through September 2021, the BARDA-funded CARB-X portfolio supported the progression of four candidates into Phase 1 clinical trials.

NIH/NIAID supported more than 10 clinical trials at various stages of development for several novel potential therapeutics for CARB pathogens in FY 2021. Select trials include the ARLG's "DOTS: Dalbavancin as an Option for Treatment of *S. aureus* Bacteremia*"* trial and an interventional study that will evaluate bacteriophage therapy among cystic fibrosis patients chronically colonized with *P. aeruginosa*. NIH/NIAID is also supporting the development of a proof-of-concept Phase 1/2 clinical trial to determine the safety and efficacy of ShigActive,™ a bacteriophage cocktail that targets all four serogroups of *Shigella*.

Target 4.2.2.2

Provide guidance on regulatory requirements, including clinical trial designs and other relevant topics.

FDA developed a guidance document Nontuberculous Mycobacterial Pulmonary Disease Caused by *Mycobacterium avium* Complex: Development Drugs for Treatment, and completed the guidance report Development of Anti-Infective Drug Products for the Pediatric Population. Also, FDA/CBER and **NIH/NIAID** hosted a public workshop on phage therapy that featured speakers from government, academia, and industry and covered topics such as single-patient investigational new drugs, NIH/NIAID funding mechanisms, and clinical trials.

Target 4.2.2.3

Support New Drug Application (NDA) filings for three new therapeutics to treat bacterial infections in humans by 2025.

ASPR/BARDA supported an NDA filing that was submitted to FDA in October 2021.

Subobjective 4.2.3

Provide specimens, testing, data, and evaluations to collaborations aimed at developing new agents or older agents for new uses and to support establishment or revision of antibiotic-susceptibility testing standards.

Target 4.2.3.1

Establish at least two projects supporting the development of new agents and standards by 2021.

CDC's Modeling Infectious Diseases in Healthcare Program (MInD-Healthcare) created a mathematical model demonstrating that antibiotics that decolonize carriers of drug-resistant organisms can be highly cost-effective when considering indirect benefits in populations vulnerable to outbreaks. This work demonstrates that public health could benefit from finding ways to incentivize development of decolonizing pharmaceutical agents in the United States. CDC also expanded the antifungals included in antifungal susceptibility testing performed by the AR Lab Network to include two newly developed drugs. CDC's GISP and SURRG routinely provide isolates to the AR Isolate Bank that collaborators (internal and external to CDC) can request for research purposes. In addition, CDC established a project to evaluate novel host-directed therapies and new drug combinations for treatment of susceptible and drug-resistant TB

infections. CDC has also developed a novel 3D tuberculoma bioplatform (i.e., cell culture model) to screen potential host-directed therapy compounds and identify new therapy targets.

Objective 4.3

Intensify basic, translational, and clinical research to support the discovery and development of new preventative products or strategies.

Subobjective 4.3.1

Support the discovery and development of new preventative strategies.

Target 4.3.1.1

Award 25 new projects aimed at discovering or developing new preventative products for use in human medicine by 2022.

From October 2020 through September 2021, the **ASPR/BARDA**- and **NIH/NIAID**-supported CARB-X program awarded six new preventive projects, doubling the existing CARB-X portfolio of vaccines and covering a range of pathogens and approaches considered attractive for product development, including novel monoclonal antibody programs.

NIH/NIAID awarded >20 new projects through grants and contracts aimed at discovering or developing new preventive products, including studies of novel vaccines utilizing a variety of platforms.

Target 4.3.1.2
Support two candidate preventative agents for agricultural uses by 2021.

USDA/ARS published two articles focused on candidate preventive agents for agricultural uses: "Antibacterial Activities of Nepetalactones Against Public Health-Related Pathogens" and "The Biological Effects of Microencapsulated Organic Acids and Botanicals Induces Tissue-Specific and Dose-Dependent Changes to the *Gallus gallus* Microbiota*. "

USDA/NIFA supported two projects focused on candidate preventive agents for agricultural uses: "UConn Researcher to Lead New Sustainable Poultry Production Project" and "Grant to Help Fill Gaps in How Livestock Manure Management Affects Antibiotic Resistance."

Target 4.3.1.3
Report success stories about improved preventive strategies for human health (at least two stories) and agriculture (at least one story) by 2023.

CDC's Antimicrobial Resistance Coordination and Strategy Unit (ARX) published two partnership stories, highlighting the collaboration between CDC and the University of Utah to estimate the annual healthcare costs of six MDR pathogens. In 2021, CDC also held its first AMR Exchange focused on ways forward and actions needed to combat AR after the COVID-19 pandemic. In addition, ARX has produced eight fact sheets on AR, highlighting COVID-19 funding, the scope and impact of CDC's AR innovations portfolio, AR solutions initiative activities by setting, and the impact of the AR lab network. CDC has also hosted eight webinars with >27,000 registrants and >10,000 attendees. CDC also worked to develop and is now supporting the AHRQ Safety Program for MRSA Prevention, which aims to reduce MRSA invasive infections in ICUs, non-ICUs, high-risk surgical services, and long-term care facilities. CDC has worked to develop and test, through mathematical modeling, strategies to address the spread of targeted AR pathogens in healthcare across the United States.

USDA/ARS and collaborators at the University of California-Riverside designed a model for an economical filter system that can remove antibiotics from wastewater.

USDA/NIFA cofunded, with Genome Canada, academic researchers to establish a consortium with swine breeding companies to establish a natural disease challenge to better understand the genetic basis of disease resilience and how to select for this trait.

NIH/NIAID is supporting a project to develop a novel probiotic yeast-based platform to deliver antibodies for prevention of the infections and diseases associated with norovirus and *C. difficile*. These pathogens are the leading causes of acute gastroenteritis with significant morbidity and mortality, and to date there is still no vaccine for either infection available on the market. NIH/NIAID continued to contribute to an international effort led by WHO to provide a guideline for gonococcal vaccine development. In 2019 and 2020, NIAID staff provided subject matter expertise in consultation meetings and draft reviews for the technical document "WHO Preferred Product Characteristics for Gonococcal Vaccines" that was released in November 2021.

Subobjective 4.3.2

Clarify pathways for new pharmaceutical preventatives by defining appropriate clinical trial designs, including endpoints.

Target 4.3.2.1

Convene two meetings to discuss developmental pathways and regulatory considerations, including clinical trial designs, by 2025.

NIH/NIAID, FDA, and CDC cosponsored a public workshop, Development Considerations of Antimicrobial Drugs for the Treatment of Gonorrhea, to discuss the nonclinical and clinical pharmacology data and clinical trial design considerations regarding developing antimicrobial drugs for the treatment of gonorrhea.

FDA/CBER and **NIH/NIAID** also hosted a workshop on phage therapy, featuring speakers from government, academia, and industry and covered topics such as single-patient INDs, NIH/NIAID funding mechanisms, and clinical trials.

During FY 2021, **CDC** and **FDA** coplanned and cosponsored a 2022 public workshop, Drug Development Considerations for the Prevention of Healthcare-Associated Infections, to consider developmental and regulatory approval pathways for novel pharmaceutical agents that can prevent AR infections. In 2021, CDC convened two meetings with FDA to discuss regulatory considerations for self-testing technologies for gonorrhea.

Subobjective 4.3.3

Facilitate development of vaccines that prevent bacterial and fungal infections with known rates of resistance and augment existing post-licensure evaluation systems to evaluate vaccination rates and antibiotic or antifungal use and resistant infections over time.

Target 4.3.3.1

Establish at least two antibiotic-resistant pathogen-related projects to further vaccine development or uptake by 2022.

CDC continues to support EIP sites to conduct population-based surveillance for AR pathogens and invasive infections due to these pathogens. Data gathered through these surveillance activities can be used to inform development of or evaluate the effect of new AR prevention interventions, such as vaccines. CDC is currently in the process of sharing 300 gonorrhea isolates obtained from GISP sites with a pharmaceutical company to produce a vaccine.

Target 4.3.3.2

Further support existing active, laboratory, population-based bacterial and fungal monitoring activities to provide vital serotype distribution and resistance data to inform development of vaccine candidates for bacteria or fungi with known resistance.

CDC continues to support EIP sites to conduct population-based surveillance for AR pathogens and invasive infections due to these pathogens. Data gathered through these surveillance activities can be used to inform development of or evaluate the effect of new AR prevention interventions, such as vaccines.

Objective 4.4

Enhance efforts to promote sustainability of the commercial market for new antibiotic products.

Subobjective 4.4.1

Leverage an existing mechanism to reduce barriers to research and establish a comprehensive understanding of safety and effectiveness of new antibiotic agents in challenging clinical settings and indications.

Target 4.4.1.1

Provide scientific and technical support, including recommendations on platform trial design and other regulatory considerations.

This target is being updated to reflect a new strategy, which FDA will support as appropriate.

Target 4.4.1.2

Support at least one special population clinical trial by 2025.

Since March 2021, **ASPR/BARDA** has met with federal partners that have existing clinical trial networks (CTNs) to evaluate whether these existing networks could be leveraged to support the evaluation of new antibacterials in challenging clinical trials for special populations. The analysis showed that the demand for these special-population studies is not high enough to efficiently sustain a CTN and that not all sponsors would be open to using a CTN. As a result, BARDA determined that the federal resource and financial requirements to establish a CTN to evaluate this need would outweigh the benefit of creating a CTN.

Subobjective 4.4.2

Examine changes in new technology add-on payments under the CMS Inpatient Prospective Payment System (IPPS) Final Rules, starting with the FY2020 IPPS/long-term care hospital prospective payment system final rule, to inform potential additional actions.

Target 4.4.2.1

Report the number of applications, approvals, and renewals for new technology add-on payments and the estimated amount of those payments.

CMS continues to support new antibiotics with the payment policy. Per CMS regulation, novel antibiotics designated under certain approval pathways by the FDA are considered new and not substantially similar to an existing technology and do not need to meet the substantial clinical improvement criterion. Medicare pays 75 percent of the cost of the antimicrobial (or the portion of the cost exceeding the Medicare severity diagnosis-related group payment, whichever is lower). In comparison, other new technology add-on payment (NTAP) products receive payment of 65 percent of the cost of the product.

CMS has approved eight antimicrobials for NTAP in recent years, six of which are currently receiving NTAP payments. One antimicrobial, meropenem plus vaborbactam (VABOMERE®), was approved for NTAP in FY 2019 and has since exceeded the two-to-three-year newness period based on its date of FDA approval. Two antimicrobials, omadacycline (NUZYRA®) and plazomicin (ZEMDRI®), received an extension through the end of FY 2022. Cefiderocol (FETROJA®) and imipenem/cilastatin/relebactam (RECARBRIO®) were both approved for NTAP for two consecutive years for two different indications, for urinary tract infections in FY 2021 and for pneumonia in FY 2022. NTAP for the urinary tract infection indication is expected to end after FY 2022, whereas NTAP for the pneumonia indication is expected to continue through the end of FY 2023. Fosfomycin (CONTEMPO®) was granted conditional NTAP approval in both the FY 2021 and FY 2022 final rules but has not received FDA approval. Approximately $5 to 6 million in add-on payments were given to these antimicrobials in 2020.

Subobjective 4.4.3

Strengthen commercial markets for antibiotic products through direct Public Health and National Security purchases.

Target 4.4.3.1

Acquire antibiotics to ensure national security and to provide revenue to encourage commercialization.

In July 2021, **ASPR/BARDA** purchased and accepted its first delivery of the antibiotic omadacycline (NUZYRA®) from Paratek Pharmaceuticals as a potential medical countermeasure for postexposure prophylaxis and treatment of anthrax following emergency-use authorizations.

Subobjective 4.4.4

Support efforts to secure U.S.-based manufacturing infrastructure.

Target 4.4.4.1

Work with innovator companies to generate domestic production of critically needed products and expand U.S.-based manufacturing capabilities.

ASPR/BARDA's funding to Paratek Pharmaceuticals through Project Bioshield enabled onshoring efforts for the production of omadacycline (NUZYRA®), thereby creating a stable U.S. supply of a key drug for public health emergencies. In FY 2021, BARDA also worked toward the release of a solicitation in FY 2022 to support up to two products through Project Bioshield with potential onshoring of manufacturing.

Objective 4.5

[Activity 1] Enhance basic research on antibiotic resistance mechanisms, as well as translational and clinical research on therapeutics, vaccines, and diagnostics.

Subobjective 4.5.1

[Activity 1 Target] Support ≥1,000 publications focused on basic, translational, and clinical research to combat antibiotic resistance annually through 2025.

USDA/ARS scientists published 78 articles related to AR. NIFA supported 322 publications, approximately half of which were peer-reviewed manuscripts, and approximately half of which were conference abstracts and posters.

NIH/NIAID supported ≥1,000 peer-reviewed publications spanning a range of basic, translational, and clinical research topics concerning combating AR.

Objective 4.6

[Activity 2] Support the training of new investigators and new entrants in the field to improve research capacity on antibiotic resistance.

Subobjective 4.6.1

[Activity 2 Target] Provide support to at least 60 new or early-career investigators annually through 2025.

USDA/ARS has supported eight new/early-career investigators. NIFA supported seven new investigators.

NIH/NIAID supported >60 new or early-career investigators in CARB-related pathogen research through several different grant mechanisms. In addition, the ARLG has supported two early-stage investigator seed grants, two fellows, and four trialists in training in FY 2021.

CDC began supporting two additional Oak Ridge Institute for Science and Education fellowships, with an additional six Oak Ridge Institute for Science and Education (ORISE), Association of Public Health Laboratories, and Laboratory Leadership and Service fellows serving during this time to support STD laboratory research.

Objective 4.7

[Activity 3] Enhance interagency collaborations to accelerate basic and applied research for developing new antibiotics, therapeutics, and vaccines.

Subobjective 4.7.1

[Activity 3 Target] Establish at least two new collaborations for human health and one for agriculture by 2023, through interagency agreements, collaborative programs, and interdisciplinary workshops.

USDA/ARS is collaborating with **FDA** on the Antimicrobial Resistance in Surface Waters: Pilot Environmental Monitoring Effort, which includes method development to standardize analytical approaches and culture methods for analyzing AR *Salmonella* and *E. coli* in environmental surface water samples and is conducting a field assessment to test the developed methods and help finalize the design of the watershed-scale study.

USDA/NIFA established the United States–Ireland Research and Development Partnership with the Irish Department of Agriculture, Food and the Marine, which will fund researchers to advance knowledge in agriculture/food-related areas, including beneficial and pest species in agricultural production systems, animal health and welfare, animal nutrition, AR across the food chain, and animal breeding and genomics.

In March 2021, **ASPR/BARDA** held a workshop with industry, academia, and other government partners (**DoD, NIH, FDA, CDC**) to identify urgent AMR threats that could be candidates for vaccine development. In May 2021, BARDA facilitated an interagency joint anti-infective annual meeting with NIH and DoD.

CDC is in the process of sharing 300 gonorrhea isolates obtained from GISP sites with a vaccine producer.

FDA cites TATFAR as a continued forum for collaboration on AMR throughout completion of its most recent work period (2016 to 2020). A report summarizing TATFAR progress was published in 2021. During 2020, TATFAR partners began work on developing a new work plan for 2021 to 2026, which has now been finalized.

NIH/NIAID collaborated with FDA to host a virtual workshop, Science and Regulation of Bacteriophage Therapy, featuring nearly 40 speakers and >1,100 registrants from academia, government, and industry. In April 2021, **FDA, CDC, and NIH/NIAID** sponsored a workshop, Development Considerations of Antimicrobial Drugs for the Treatment of Gonorrhea, to discuss nonclinical and clinical pharmacology data considerations regarding developing antimicrobial drugs for treatment of gonorrhea as well as clinical trial design.

Goal 5: Improve International Collaboration and Capacities for Antibiotic-resistance Prevention, Surveillance, Control, and Antibiotic Research and Prevention

Objective 5.1

Enhance U.S. leadership in the global fight against antibiotic resistance.

Subobjective 5.1.1

Examine mechanisms for appointing a U.S. Federal Champion for international CARB, who would support the Secretaries of HHS, USDA, DoS, and the Administrator of USAID by advocating for U.S. policy positions on antibiotic resistance at international fora and organizations using a One Health approach and who would report to the CARB Task Force to inform international engagements.

Target 5.1.1.1

Convene a working group of the CARB Task Force to define interagency needs and develop options for appointing a Federal Champion for International CARB by 2021.

OGA convened the Federal Champion Working Group on March 30, 2021, with participants discussing initial questions concerning the feasibility and logistics of a federal champion. Participants were challenged to identify unique needs and benefits of a federal champion that were not adequately addressed by agency-specific efforts. The COVID-19 pandemic has taken priority of agencies' time, resulting in only one meeting of the working group. Dedicated funding to support the position with salary and travel has not been identified.

Subobjective 5.1.2

Enhance engagements with multilateral organizations to support progress on U.S. priorities to combat antibiotic resistance.

Target 5.1.2.1

Support international antibiotic resistance policy efforts to prioritize and coordinate antibiotic resistance efforts within and across international partner organizations (e.g., Global Health Security Agenda [GHSA], World Health Organization [WHO], World Organization for Animal Health [WOAH], the United Nations Environmental Program [UNEP], Food and Agricultural Organization [FAO], G7 and G20, Asia-Pacific Economic Cooperation Forum, Association of Southeast Asian Nations, Pan American Health Organization) by 2022.

USDA/ARS participated in a United Nations (UN) Environment Assembly working group tasked with preparing, by the fifth session of the UN Environment Assembly, a report on the environmental impacts of antimicrobial resistance and the causes for the development and spread of resistance in the environment, including the gaps in understanding of those impacts and causes.

OGA supported U.S. participation in the UN High Level Dialogue on AMR on April 29, 2021. The United States supported and signed on to the Call to Action outcome document that resulted from the meeting. The United States participated in the Global AMR R&D Hub as a board member. OGA will continue efforts to promote high-level coordination and alignment of efforts to leverage much-needed investments in AMR research and development and look for new opportunities to engage with and highlight the value of the R&D Hub. OGA advocated and negotiated for

the United States on AMR equities in the G7 leaders, health, finance, and environmental tracks, resulting in AMR being included in all declarations. OGA and the Department of the Treasury coled negotiations for the joint health and finance ministers' declaration on AMR economic incentives, resulting in agreed-upon valuation principles and a statement in support of postmarket incentives. There has been ongoing engagement with the G20 for AMR inclusion in the priorities for 2021 and for the coming year, 2022. OGA serves as cochair of the TATFAR on behalf of the United States. Together with partners from **CDC, NIH, FDA, ASPR/BARDA, and USDA**, they share best practices to strengthen domestic and global efforts for stewardship, surveillance, prevention, and research and development.

In October 2021, **CDC** and the Association of Southeast Asian Nations (ASEAN) established the U.S.-ASEAN IPC/AMR Task Force, a joint initiative to collaboratively advance detection and prevention of AMR and health threats in healthcare settings. This task force will strengthen regional and national approaches to promoting laboratory detection and IPC to protect patients and healthcare workers.

Target 5.1.2.2

Chair the Global Health Security Agenda AMR Action Package by 2022.

The United States successfully chaired the GHSA AMR Action Package from November 2020 to December 2021. During that year, the United States led monthly meetings at which global AMR leaders were invited to present their work. The United States also drafted AMR Action Package workplan and developed a new AMR Antibiotic Resistance in Communities and Hospitals webpage for the GHSA website.

Target 5.1.2.3

Complete the Work Plan of the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) for 2016-2020 and develop and begin implementation of a new Scope of Work for TATFAR by 2022.

TATFAR continued to serve as a forum for collaboration on AMR for its partners throughout completion of its most recent work period (2016 to 2020). Activities spanned three key areas: 1) appropriate therapeutic use of antimicrobials in human and veterinary medicine, 2) prevention of drug-resistant infections, and 3) strategies for improving the pipeline of new antimicrobial drugs. Working together during the past five years, TATFAR member agencies continued valuable technical work and engagement on several actions in each of these three areas and across human, animal, and environmental/plant health sectors. A report summarizing TATFAR progress was published in 2021. During 2020, TATFAR partners—including **CDC, FDA, ASPR/BARDA, OGA, FDA, USDA, DoD, and NIH/NIAID**— began work on developing a new work plan for 2021 to 2026. Revisions of the plan have continued through early 2021, and a final work plan is now available and was adopted February 2022.

Target 5.1.2.4

Work with international partners through the Codex Alimentarius Commission's Task Force on Antimicrobial Resistance to develop global science- and risk-based guidance on managing foodborne antimicrobial resistance and surveillance, including revising the Codex Code of Practice to Minimize and Contain Foodborne Antibiotic Resistance and developing new Guidelines for Integrated Surveillance of Antimicrobial Resistance.

FDA and **USDA** led the U.S. delegation to the five-year Codex ad hoc Intergovernmental Task Force on Antimicrobial Resistance (2017-2022), which revised and updated the Code of Practice to Minimize and Contain Foodborne Antimicrobial Resistance and drafted Guidelines for Integrated Monitoring and Surveillance for Foodborne Antimicrobial Resistance. The United States chaired the electronic working group on revising the Code of Practice to Minimize and Contain Foodborne Antimicrobial Resistance. Both documents were adopted for final publication at the 44th session of the Codex Alimentarius Commission in November 2021.

Target 5.1.2.5

Continue to support member governments' sharing of antibiotic-resistant pathogen information to the relevant collaborating centers, including the WHO Global Antimicrobial Resistance Surveillance System (GLASS).

USAID implementing partners worked with partner governments to enhance reporting through the Global Antimicrobial Resistance and Use Surveillance System. In Liberia, USAID, in partnership with UN Food and Agriculture Organization (FAO), supported monthly meetings of the AMR Technical Working Group under the National One Health Platform to harmonize AMR activities in the country, specifically on how to generate data and share through GLASS. In Kenya and Cameroon, the Infectious Disease Detection and Surveillance (IDDS) program provided technical and logistical assistance to Ministry of Health and National Coordination Center groups to generate and report national AMR surveillance data to GLASS.

From 2020 to 2021, **CDC** worked with partners to help expand national and global AR surveillance networks to improve detection and response to infectious disease threats. CDC and partners supported work in Thailand, Brazil, Kenya, Vietnam, and India to develop regional and national surveillance networks to enhance the ability of laboratories in these countries to detect and report AR. These efforts include collaborating with the Thailand Ministry of Health to develop a network of 21 hospitals and four regional laboratories and with the Bangkok Metropolitan Administration to build a network of nine hospitals to improve AR detection and response in Thailand. Additionally, CDC is working to expand Ethiopia's AR surveillance network to nine participating sites and is collaborating with Brazil's Foundation for Scientific and Technological Development in Health (FIOTEC) to enhance laboratory capacity for detection of AMR pathogens across 15 sentinel hospitals and state public health laboratories to increase the representativeness of clinical laboratories in the national AMR surveillance program. CDC has also worked in coordination with CDC India, supporting partners at the national and state levels to support and expand surveillance, detect and report AMR pathogens, respond to outbreaks in healthcare settings, develop hospital IPC programs, and initiate ASPs.

In 2021, the **NIH** Common Fund's Harnessing Data Science for Health Discovery and Innovation in Africa (DS-I Africa) Program was launched to spur new health discoveries and catalyze innovation in healthcare, public health, and health research on the continent through application of data science. The DS-I Africa consortium is awarded to seven research hubs, seven research training programs, four ethical, legal, and social implications research projects, and one open data science platform and coordinating center, a gateway for data and data analysis tools. One of the research hubs, Combatting Antimicrobial Resistance in Africa Using Data Science (CAMRA), is studying the clinical and molecular epidemiology of AMR and MDROs in Nigeria and Rwanda.

Subobjective 5.1.3

Provide additional financial or technical support to public and private organizations to further U.S. priorities to combat antibiotic resistance.

Target 5.1.3.1

Support international policy efforts to reduce antibiotic resistance beyond the current mandates of U.S. Government Departments and Agencies by 2022.

In April 2021, **USAID** launched Transformational Strategies for Farm Output Risk Mitigation (TRANSFORM), a project that will harness private sector-led innovation to address emerging infectious diseases and antimicrobial resistance in animal production in Asia and Africa. In one effort, TRANSFORM will develop and implement globally harmonized, evidence-based antimicrobial stewardship policies across the animal production industry.

OGA has met with a number of public and private organizations in 2021 to discuss potential engagements, including groups that focus on research and development. Discussions concerned progress with their missions and clarification

regarding what is and is not necessary to accomplish their goals. OGA met with the AMR Coalition—a community of AMR stakeholders that works on solutions to strengthen the antibiotic pipeline and invest in stewardship, surveillance, and prevention—to discuss the need for action to build an innovative antimicrobial ecosystem and share the U.S. government's framing of AMR in global health engagements and pandemic preparedness. OGA met with the Clinton Health Access Initiative (CHAI), a global health organization committed to saving lives and reducing the burden of disease in low- and middle-income countries, to discuss their interest in looking at antibiotic access and AMR. OGA described the U.S. government's role and explained the different federal stakeholders with which CHAI could also engage. In addition, OGA discussed with U.S. Pharmacopeia—a nonprofit focused on building trust in the supply of safe, quality medicines—their desire to work on antibiotic supply chains and to apply their medicine supply map to identify drivers and predict shortages of antibiotic drugs. The goals of these meetings were to increase awareness of the international activities and initiatives to combat AMR and to identify potential areas for collaboration.

CDC and **OGA** met with the Joint Programming Initiative on Antimicrobial Resistance about potential engagement.

Subobjective 5.1.4

Increase the U.S. Government's presence in international organizations and other multilateral efforts to combat antibiotic resistance.

Target 5.1.4.1

Provide at least one AMR expert either by secondment or appointment to a multilateral organization to enhance the U.S. Government's programmatic collaborations and provide high-level technical and policy guidance by 2022.

DoD AMR experts from the MRSN and GEIS currently serve on the TATFAR advisory panel.

OGA is working with CDC to explore technical support to WHO to increase capacity building in surveillance.

USDA/APHIS/Center for Veterinary Biologics has continued to be an active participant in both the Institute for International Cooperation in Animal Biologics and the Veterinary International Conference on Harmonization regarding international harmonization on veterinary biologics.

Subobjective 5.1.5

Enhance domestic and international communications about the U.S. Government's activities to combat antibiotic resistance and increase the coordination of Federal Departments and Agencies on the CARB Task Force around large-scale efforts and announcements.

Target 5.1.5.1

Increase coordination among the CARB Task Force on communication strategies by instituting regular calls by 2021.

CARB Task Force agencies participated in the communications subcommittee to support the rollout of the 2020-2025 CARB National Action Plan and coordinate communications-related activities for World Antibiotic Awareness Week (WAAW) 2020.

CDC is the secretariat for TATFAR and the TATFAR communications working group and helps coordinate quarterly calls with working group members—including OGA, NIH, USDA, and FDA—to discuss ways to best communicate AR materials across healthcare settings, community, and environmental audiences in the United States and abroad. In September 2021, CDC hosted the first communications working group call with TATFAR members, focusing on best practices and lessons learned from communicating with healthcare providers about AR and antibiotic use. CDC also holds monthly calls with OGA to discuss international activities, resources, funding opportunities, priorities, and ways to promote these topics to relevant U.S. and international policy-makers and partners.

Target 5.1.5.2

Increase high-level social-media promotion of antibiotic-resistance activities among the Departments and Agencies on the CARB Task Force.

CARB task force agencies participated in WAAW 2021 by sharing and amplifying each other's social media posts.

OGA shared key messages and visuals on AMR through OGA's Twitter account for Global Handwashing Day and One Health Day. For WAAW 2021, OGA shared a video message from the Assistant Secretary for Global Affairs to kick off WAAW, a link to OGA's Pandemics and Emerging Threats Director's video for the AMR Industry Alliance, and a graphic and message from the Director's message during the AMR Youth Summit. OGA also amplified posts from other HHS agencies and U.S. government departments that shared WAAW content.

From October 2020 to July 2021, **CDC** promoted new resources, activities, and publications through the National Center for Emerging and Zoonotic Infectious Diseases social media accounts, resulting in >60,000 engagements (i.e., total number of retweets, likes, mentions, replies, and comments). In July 2021, CDC launched a new Twitter handle, @CDC_AR, to promote new and existing AR resources, activities, and publications to policy-makers, partners, and the public. Between July 2021 and October 2021, ARX published 156 tweets, resulting in 3,765 engagements.

USDA agencies blogged, tweeted, and shared social media posts regarding AR activities and research during WAAW 2021.

DoD/GEIS has continued intermittent news media releases covering GEIS network surveillance in AR surveillance activities.

To mark WAAW 2021, **NIH/NIAID** amplified CDC's social media messaging and published a short question-and-answer video blog tied to WAAW on the NIAID Now blog. The video focuses on the INSPIRE-ASP Trial (INtelligent Stewardship Prompts to Improve Real-time Empiric Antibiotic Selection for Patients) for intra-abdominal, skin, and soft-tissue infections. The study aims to improve AS and physicians' choice of antibiotics for hospitalized patients by reducing the unnecessary use of broad-spectrum antibiotics.

Objective 5.2

Promote increased awareness and capacity in countries to address the emergence and slow the spread of antibiotic resistance.

Subobjective 5.2.1

Improve capacity in partner countries to implement effective practices to combat antimicrobial resistance, including preventing and controlling infection through the availability and proper use of water, sanitation, and hygiene (WASH).

Target 5.2.1.1

Assist governments, civil society, and the private sector in a total of 10-15 low- or middle-income countries to develop and implement national plans consistent with the Global Action Plan, establish and implement antimicrobial resistance-focused activities, and/or build capacity for preventing and controlling infections in both animals and humans.

USAID partners supported diverse efforts to directly strengthen local and national infectious disease prevention and control capacities in human and animal health in at least seven low- or middle-income countries. With the support of USAID's Medicines, Technologies, and Pharmaceuticals Services (MTaPS) program, 39 healthcare facilities in five countries performed either baseline or repeat IPC assessments using the WHO's Infection Prevention and Control Assessment Framework tool. For example, in Senegal, use of the updated IPC supervision checklist resulted in

increased capacity in core components, such as hand hygiene, biomedical waste management, and biocleaning. In animal health settings, appraisals of IPC measures in poultry, dairy, and swine value chains were used to inform strategic FAO interventions. MTaPS supported the formation and operation of 39 IPC committees in Cameroon, Côte d'Ivoire, Mali, and Senegal. USAID implementing partners contributed to the training of >273 committee members and healthcare workers on various aspects of IPC program implementation. USAID partners MTaPS and FAO continue to support the ongoing development of IPC action plans at both state and national levels in four low- or middle- income countries.

USAID in partnership with FAO supported the Democratic Republic of the Congo (DRC), Ethiopia, India, Indonesia, Niger, and Sierra Leone, and in partnership with MTaPS supported Bangladesh, Côte d'Ivoire, and Burkina Faso, in developing, updating, and/or endorsing national AMR action plans. MTaPS Côte d'Ivoire helped identify major risks for AMR development, which informed Côte d'Ivoire's new NAP-AMR 2021-2025. To support implementation of the Zanzibar Action Plan for AMR (ZAP) 2019-2024, USAID in partnership with FAO supported a government workshop, which included experts from each of the Zanzibar Multisectoral AMR Coordinating Committee (ZMCC) technical working groups (TWGs), to review, prioritize, and identify funding for AMR activities to be implemented in the next three years of ZAP (2022-2024). USAID helped support country participation in the annual Tripartite AMR Country Self-Assessment Survey (TrACSS) for 2021, which is used to monitor country progress on implementing AMR action plans. In DRC, the MTaPS-supported TrACSS 2021 results revealed significant improvement from 2020.

USAID-funded partners in ≥12 countries supported the establishment, strengthening, and/or operationalization of multisectoral coordination (MSC) bodies and technical groups at the national, subnational, and/or district level. For example, in Tanzania, USAID in partnership with FAO supported the One Health Coordination Desk (OHCD) to establish AMR One Health MSC committees in three districts to encourage best practices among the public; policy-makers; and health, environment, community development and agriculture professionals, and political and religious leaders to limit further emergence and spread of antimicrobial resistance at subnational levels. USAID also supported the occurrence of and/or participation by diverse stakeholders in MSC bodies and/or TWGs in ≥14 countries that resulted in outcomes and products that helped advance action on AMR in the respective countries. For example, in Kenya, in partnership with FAO, USAID implementing partners MTaPS and Infection Disease Detection and Surveillance (IDDS) programs supported workshops organized in collaboration with the National Antimicrobial Stewardship Interagency Committee (NASIC), which brought together multisectoral participants from the human health, livestock health, wildlife, and environment sectors and enabled the County Antimicrobial Stewardship Interagency Committee (CASIC) for Murang'a and Bungoma counties to develop two-year costed work plans, based on the Kenya National Action Plan (NAP) on Prevention and Containment of Antimicrobial Resistance (2017-2022).

To raise awareness and promote action on AMR, USAID partners supported broad efforts in nine countries during the 2020 WAAW. Notably, in Bangladesh, USAID partner FAO supported the Bangladesh AMR Response Alliance (BARA) to organize a Facebook live discussion that engaged >1,000 human and animal health professionals in a discussion of appropriate AMU. In collaboration with FAO and USAID's One Health Workforce-Next Generation (OHW-NG), 10 countries across Africa have made significant contributions to public outreach and education on AMR issues. The OHW-NG team helped to develop a complete two-year master's program on AMR in Cameroon while also assisting with the organization of AMR training modules in Kenya, a hackathon focused on promoting AMR awareness at the African One Health University Network in Uganda, and AMR sensitization education in Rwanda that reached >6,000 schoolchildren and 130 teachers. Partner countries (Uganda, Kenya, Ethiopia, and Tanzania), supported by FAO and IDDS, produced and distributed AMR newsletters, guidelines, curricula, and general education materials, including leaflets, street banners, and digital media, which helped to educate the general public, farmers, sectoral experts, and policy-makers on AMR and AMU. Printing and distribution of a Veterinary Pharmaceuticals Management Manual to 500 animal healthcare providers in Ethiopia served to further responsible stewardship efforts.

USAID implementing partners FAO and IDDS support key stakeholders in Bangladesh, Vietnam, Burkina Faso, Tanzania, Mali, Uganda, and Kenya as they build capacity to address AMR through a range of training opportunities. For

example, the Facility Management and Leadership Programme (FMLP) is a joint effort between FAO and the United Nations Population Fund that uses a One Health approach to build competencies in both IPC and prudent use of antimicrobials for improving COVID-19 case management. Through FMLP, FAO facilitated more than a dozen trainings of clinicians and nurses in Bangladesh, and in-service training has covered 662 participants since its inception in September 2020. In the animal health sector, FAO organized several forums on farm biosecurity in Vietnam and held several webinars on AMR activities and AMU in livestock in Mali and Uganda.

USAID partners have contributed to continuous efforts in seven countries to educate broad audiences, ranging from government officials, healthcare workers, and university officials, to private sector veterinarians, farmers, and the public, on all aspects of AMR. In Burkina Faso, seven awareness-raising sessions on taking a One Health approach to addressing AMR were able to reach nearly 250 participants. Furthermore, in Cameroon, Côte d'Ivoire, Ethiopia, Kenya, and Senegal, FAO supported a variety of sensitization workshops aimed at educating hundreds of participants from across sectors on AMR, AMU, and IPC issues.

USDA/Foreign Agricultural Service's Faculty Exchange Program (FEP) on African Veterinary Science pairs instructors from African veterinary colleges with mentors at host U.S. universities to build the African fellows' capacities to improve curricula and instruction at their respective schools. FY 2021 FEP activities were postponed due to the COVID-19 pandemic international travel restrictions but will be implemented by USDA as soon as such international exchange programs resume. USDA/FAS is also funding two ongoing projects at the InterAmerican Institute for Cooperation on Agriculture to help participating Western Hemisphere countries build their capacities for CARB. The institute is developing a swine biosafety and husbandry best practices manual to help farmers in the region optimize their animals' health and minimize their need for antimicrobials.

In late 2021, **CDC** launched the Global AR Lab & Response Network, funding >20 organizations to work across nearly 50 countries to identify risk factors driving the emergence and spread of AR across One Health sectors, including in healthcare, communities, food, animals, and the environment (e.g., water and soil). CDC also responded on the ground to AR threats emerging across healthcare regarding sexually transmitted, fungal, enteric, and invasive bacterial and respiratory pathogens. CDC also invested in short-term global AR innovation research projects, working with investigators to identify new public health solutions to prevent resistant infections and their spread. Findings from the global AR innovation projects may later be integrated into the Global AR Lab & Response Network to transform the way the world responds to AR across the One Health spectrum.

From 2020 to 2021, CDC has also worked with >30 countries at national or facility levels to improve IPC capacity in humans through training and other support. These trainings are pivotal to protect healthcare workers, patients, and communities while helping stop the spread of HAIs, including AMR infections and COVID-19.

In addition, CDC has been working since 2020 with WHO's Regional Office for Africa to establish and strengthen national IPC programs based on the minimum requirements for IPC programs in the following countries: Madagascar, South Sudan, Rwanda, Guinea, Senegal, and Côte d'Ivoire. From 2020 to 2021, CDC supported Amref and implementing partner Tanzania to provide IPC training and mentorship to >600 frontline healthcare workers across the country to improve IPC activities. CDC also supported the Jhipiego to develop a bloodstream infection Targeted Assessment for Prevention (TAP) for neonatal intensive care unit (NICU) patients, with pilot testing of the tool in Brazil, Colombia, and Paraguay. A bloodstream infection prevention network implemented in four NICUs in Brazil now identifies gaps in IPC (using TAP for NICU) and has trained almost 200 healthcare workers to help address those gaps.

In Central America, CDC is funding an IPC specialist to support Secretaría Ejecutiva del Consejo de Ministros de Salud de Centroamérica y República Dominicana on Extension for Communication Healthcare Outcome IPC sessions and virtual IPC courses in multiple countries in the region. Beyond this, CDC is supporting IPC capacity building in hospitals in Guatemala, El Salvador, and Belize with activities that include assessments, action plan development, national workshops/trainings, and virtual communities of practice. In India, CDC has worked with the Society for Health Allied Research Education (SHARE) to assist the state of Andhra Pradesh to participate in an IPC capacity-building initiative.

Assessments of 21 hospitals in Andhra Pradesh were completed and were used to develop action plans to improve IPC programs to prevent the transmission of COVID-19 and other HAIs. These assessments were used to make recommendations to the Andhra Pradesh Ministry of Health, the Indian Council of Medical Research, and the National Centre for Disease Control concerning what they could do to improve IPC programs. This work helps prevent and stop the spread of infectious disease threats, such as AR.

Target 5.2.1.2

Assist governments, civil society, and the private sector in 10 to 15 low- or middle-income countries to improve the monitoring of WASH in healthcare facilities or to create and/or implement standards for environmental health in healthcare settings.

USAID's MTaPS program strengthened WASH capacities in healthcare facilities, including assessments in ≥13 facilities (three in Nigeria and 10 in Côte d'Ivoire). In Cameroon, nearly all MTaPS-supported facilities have improved their WASH and waste management infrastructures. USAID works to maintain essential WASH and health services for crisis-affected populations, primarily targeting vulnerable and population-dense settings such as urban areas or internally displaced person camps, and focusing on supporting the health response—e.g., providing soap for hand washing and ensuring continuity of WASH services in humanitarian settings. To mitigate a potential water and sanitation crisis, USAID is leveraging existing water programs and networks to help partner countries throughout the world to keep water flowing during the COVID-19 pandemic and beyond, while also promoting hygiene. USAID published a technical brief of the details of WASH in healthcare facilities.

As a part of the work happening across >30 countries, **CDC** supported the development of guidance and best practices, healthcare worker capacity building and mentorship, and support for response to the COVID-19 pandemic. Through this work, CDC began in 2019 to collaborate with global IPC experts and the African Infection Control Network to develop a toolkit to help implement Best Practices for Environmental Cleaning in Resource-Limited Settings to provide guidance for healthcare facility cleaning procedures and programs. To help countries implement the best practices, CDC has collaborated with IPC experts globally on the development and piloting of a toolkit. CDC also supported the Sierra Leone Ministry of Health and Sanitation in development of the Advanced IPC Certification Course, a six-month IPC specialist training program. As of September 30, 2021, two cohorts comprising 43 IPC specialists had completed the course.

In East Africa and Central America, from 2020 to 2021, CDC supported basic WASH capacity for healthcare facilities by establishing local networks of production of key hand hygiene materials and instituting low-cost, sustainable monitoring of hand hygiene supplies in smaller healthcare facilities. These projects are being scaled to regional levels to support hand hygiene materials in outbreak response through ties to regional emergency operation centers in Uganda and other countries.

Subobjective 5.2.2

Optimize the use of antibiotics in humans, animals, and agriculture outside of the U.S.

Target 5.2.2.1

Assist governments, civil society, and the private sector in at least four low- or middle-income countries with capacity building for antibiotic stewardship and regulation to address the appropriate use and availability of quality-assured antibiotics in humans and animals by 2022.

In ≥12 countries, **USAID**, in partnership with FAO, MTaPS, and host governments, supported assessments to strengthen AMU and antimicrobial stewardship (AMS) capacities. USAID also worked in partnership with FAO to support the development of tools to facilitate AMS practices. For example, in Bangladesh, a simple AMU monitoring tool was developed to gather and receive feedback from AMS leaders through the AMS teams and AMS committee. In

Uganda, the AMU tool AMUSE was pretested at the district level. USAID partners also supported countries in developing AMU/AMS action plans in livestock and in human health. For example, MTaPS, in partnership with the Democratic Republic of the Congo, supported the Direction de la Pharmacie et du Médicament and the National Commission on AMR to develop a three-year antimicrobial stewardship work plan using the findings from two rapid assessments (AMS policies and regulations and antimicrobial consumption).

USAID partners supported countries in developing, adopting, and reviewing/updating/validating standard treatment and other guidelines in human and/or animal health (terrestrial, aquatic, and companion animals) in ≥10 countries to include the integration of AWaRe categorization in essential medicines lists and standard treatment guidelines. The USAID Momentum Country and Global Leadership (MCGL) project partnered with UN International Children's Emergency Fund under the umbrella of the global integrated community case management task team to support countries to conduct a gap analysis for community health systems, particularly integrated community case management. USAID in partnership with MTaPS and the Promoting the Quality of Medicines Plus (PQM+) program are working with partner countries to improve the availability, quality, and safe use of antimicrobials. USAID, in collaboration with a wide range of partners in seven countries, has facilitated a variety of sensitizations, trainings, and workshops on antimicrobial use and stewardship across animal and human healthcare sectors.

In late 2020, **CDC**, in collaboration with Jhpiego and Health Security Partners, launched a project in 12 hospitals across five countries in South America and Southeast Asia to assess the pandemic's impact on rates of AU and AR. Preliminary analyses show that intravenously administered antibiotics commonly used to treat respiratory infections increased during the COVID-19 pandemic by 6.7 to 35.1 percent in a majority of the hospitals in South America, and half of the hospitals had increases in use of broad-spectrum antibiotics. Data collection in Southeast Asia is in final stages.

Subobjective 5.2.3

Promote the use of existing and new vaccines, including pneumococcal and typhoid-conjugate vaccines, to reduce the unnecessary use of antibiotics.

Target 5.2.3.1

Promote prevention and vaccine use in low- and middle-income countries, including through the U.S. Government's partnership with Gavi, the Vaccine Alliance, supported by funding and technical assistance from USAID and CDC worldwide.

In 2020, partner countries immunized an additional 64 million children with multiple vaccines with support from Gavi and **USAID**. Due to COVID-19-related disruptions, this represents a decrease of 2 million children from the number reached in 2019. USAID's technical assistance also supports countries to introduce and scale new vaccines not yet in their immunization programs. USAID's MOMENTUM Routine Immunization Transformation and Equity (M-RITE) project was awarded in July 2020 and has since supported partner countries to strengthen routine immunization programs and overcome entrenched obstacles contributing to stagnating or declining immunization rates and barriers to reaching zero-dose and underimmunized children. In addition to supporting the maintenance and adaptation of routine immunization services, M-RITE supported COVID-19 vaccine rollout in the Democratic Republic of the Congo, India, Kenya, Mozambique, and Niger. Although the M-RITE in-country project team has deep experience in vaccine introduction, the multiple novel aspects and speed of this introduction and the rapidly changing context pose additional obstacles. In 2021 and 2022, coverage of routine vaccinations and new vaccine introductions are expected to be further impacted, as country immunization systems will be increasingly utilized and stressed by the scale-up in global COVID-19 vaccination.

The COVID-19 response has delayed **CDC's** progress on this target.

Subobjective 5.2.4

Conduct surveillance that identifies the presence and movement of antibiotic resistance genes of concern within partner nations as part of DoD/GEIS-funded surveillance to protect military force health.

Target 5.2.4.1

Submit isolates of multidrug-resistant pathogens to the MRSN for advanced characterization and provide reports to the labs that can also inform surveillance of antibiotic resistance, by 2021.

DoD/MRSN reported that five of the seven overseas laboratories regularly submit MDR pathogens to the MRSN for WGS. Between October 2020 and September 2021, the MRSN provided the laboratories with 14 reports for use in AR surveillance. GEIS's support of this target was delayed in FY 2021 due to the prioritization of COVID-19 sequencing initiatives. Isolate submission from GEIS-funded surveillance activities is pending standardization. Challenges for this target include many countries' implementation of strict shipping quarantines during the COVID-19 pandemic. Two of the seven overseas laboratories were unable to ship any samples during this time. DoD/MRSN expects to complete this target by the end of FY 2022 after COVID-19 restrictions have been lifted.

Objective 5.3

Generate consistent and actionable global data on antibiotic resistance, including by extending CDC's AR Lab Network to global sites to address the identification, emergence, spread, and effects of antibiotic resistance.

Subobjective 5.3.1

Expand the AR Lab Network and other networks (e.g., PulseNet International) internationally to implement networks for detection and containment that can rapidly test and respond to high-threat antibiotic-resistant pathogens in key regions.

Target 5.3.1.1

Launch at least one international AR Lab Network project and make operational at least one international AR Lab Network laboratory by 2022. Incorporate five additional laboratories by 2026.

In late 2021, **CDC** launched the Global AR Lab & Response Network, a comprehensive, One Health network that spans nearly 50 countries and works with >20 organizations worldwide to build laboratory capacity to detect AR organisms, prevent infections in healthcare settings and the community through proven infection control practices, and apply new and innovative ways to respond to AR threats. The Global AR Lab & Response Network tackles AR threats such as: resistant pathogens in healthcare the Antimicrobial Resistance in Communities and Hospitals (including the ARCH) study consortium which evaluates AR colonization among people to better understand resistance across the shared community-hospital-environment settings, and through CDC's Global Action in Healthcare Network (GAIHN), also launched in 2021, to identify, prevent, and contain resistant pathogens and other emerging threats in healthcare settings; resistant gonorrhea through strengthened international surveillance using the Enhanced Gonococcal Antimicrobial Surveillance Programme to build understanding of spread in geographically diverse areas and to inform clinical treatment guidelines; resistant fungi through enhanced detection, monitoring, and control of drug-resistant *C. auris* and other *Candida* species and strengthened data reporting and sharing through the WHO GLASS; resistant enteric pathogens through improved surveillance using the existing PulseNet International platform to understand the emergence of resistance and spread in humans and respond to these threats in drinking, surface, and wastewater; and resistant invasive bacterial and respiratory pathogens through enhanced laboratory capacity to detect emerging resistance among *S. pneumoniae*, *Neisseria meningitidis*, and *Bordetella pertussis*, and help respond to outbreaks when and where they occur.

Subobjective 5.3.2

Charge the global AR Lab Network with detecting and containing new and critical antibiotic-resistance threats.

Target 5.3.2.1

Establish the capacity of the global AR Lab Network to receive and test isolates and deploy rapid responses to control and contain infections.

DoD/GEIS's Data to Decision initiative (in collaboration with MRSN) provides near-real-time reporting of AMR events of operational significance to stakeholders and key partners in the combat commands and military health system. In FY 2021, GEIS/MRSN reported on four Data to Decision events to facilitate response by DoD and MHS stakeholders. Challenges for this target include the lack of standardization or harmonization among the GEIS network partners.

In 2021, **CDC** initiated capacity assessments of six hospitals in South America to receive, test, and deploy rapid responses through CDC's Global AR Lab & Response Network via Global Action in Healthcare Network (GAIHN). Expansion of additional capacities is being developed for other Global AR Lab & Response Network–funded partners.

Subobjective 5.3.3

Identify innovative and effective strategies for stopping the spread of antibiotic-resistant pathogens in low- and middle-income countries.

Target 5.3.3.1

Establish "learning laboratories" through the AR Lab Network to develop or test innovative, cost-effective solutions for containing critical-threat antibiotic-resistant pathogens by 2021.

CDC has implemented an innovative surveillance method in six countries for gram-negative bacteria, called the Antibiotic Resistance in Communities and Hospitals (ARCH) platform, now part of the Global AR Lab & Response Network. Research partners are tracking the amount and spread of colonization in hospitals and communities and are studying predictors and outcomes of colonization. The data from the ARCH studies will help researchers identify new strains of resistance and understand the source of new resistance threats, how widespread the threats are, and how they can tailor prevention strategies to lessen the impact. The ARCH methodology addresses many of the biases that influence data from WHO's GLASS system and produces complementary data. GLASS relies on reporting AMR in clinical specimens, but clinical specimens are less readily available from low- and middle-income countries because specimens may be unaffordable or healthcare access may be more limited. By using colonization to track AMR, the burden of AMR can be more accurately assessed.

Subobjective 5.3.4

Improve laboratory capacity for antimicrobial-resistance surveillance the standardization of laboratory methodologies and data collection to improve the quality, reliability, and utility of data to facilitate global comparisons of antibiotic resistance.

Target 5.3.4.1

Implement standardized or harmonized laboratory methods and data collection in AR Lab Network facilities, and, with partner countries, strengthen laboratory capacity for antibiotic resistance surveillance and comparison of antibiotic-resistance trends when appropriate. Initiate data-reporting efforts with trusted partner nations by 2021. Support operations through training and funding annually.

DoD/GEIS's program office improved directive approaches in the FY 2021 strategic and operational guidance updates, including work to harmonize data collection to help forward GEIS-collected data to the AR Lab Network. (GEIS is not

currently part of the AR Lab Network.) Challenges include travel restrictions that have limited the ability to conduct site visits and in-person training for wet and dry lab standardization.

In 2021, **CDC** established the Global AR Lab & Response Network, funding >20 recipients across 50 countries to support standardized and harmonized laboratory methods and data collection of AR threats. As a part of this network, GAIHN is assisting laboratories and partners to harmonize detection and prevention of carbapenem-resistant organisms in 12 hospitals in five countries. In addition, FungiNet, a network for molecular surveillance and genomic epidemiology for fungal disease, has been piloted domestically in Utah and New York in the AR Lab Network and is in the process of launching. Internationally, FungiNet is being launched in Colombia and South Africa through the Global AR Lab & Response Network in 2023. Through this network, in 2021, CDC also funded work to support laboratory surveillance of *B. pertussis* and assess resistance to macrolides in nasopharyngeal specimens from patients who test positive for pertussis, focusing on participating sites of the established platform for culture diagnosis and PCR capacity. Target countries for this activity are Brazil and Mexico, with CDC technical support.

USAID in partnership with FAO worked with six countries in Africa to assess AMR surveillance in agriculture sectors using the FAO Assessment Tool for Laboratories and Antimicrobial Resistance Surveillance Systems (FAO-ATLASS). USAID partners FAO and IDDS supported the development and implementation of appropriate protocols, guidelines, and benchmarks in 12 countries, including strengthening capacities in specimen collection, data storage and reporting, supply chain, and inventory management. Training, a key component of strengthening laboratory capacity, prioritizes sustainable capacity gains through empowering individuals to contribute to national and global efforts to address AMR. USAID partners have facilitated a wide variety of training for personnel to appropriately conduct AMR surveillance in Cameroon, Liberia, Nigeria, Tanzania, Kenya, Senegal, and Vietnam. Furthermore, training of individuals from both human and animal health sectors in Cameroon, Nigeria, and Tanzania will help promote a One Health perspective on AMR surveillance. With the support of USAID partners FAO and IDDS, >20 laboratories across seven countries were able to secure critical equipment, reagents, and supplies to conduct ongoing AMR surveillance efforts.

Through partnership with FAO and USAID, Bangladesh and Senegal have improved livestock value chain testing capacities and surveillance to detect prioritized AR pathogens in poultry and livestock in more than two dozen farms. USAID partner IDDS has strengthened AMR surveillance programs at sentinel sites analyzing human samples by facilitating data collection and review activities in Cameroon, Kenya, and Tanzania. Supporting the laboratory and surveillance ecosystem, from sample transportation to data analysis and reporting, has increased these countries' capacity to routinely assess AMR threats through consistent monitoring. FAO Guinea has supported the Central Veterinary Diagnostic Laboratory (LCVD) to implement an antimicrobial surveillance program of milk and eggs produced in 10 localities across the country. In collaboration with the Bangladesh Livestock Research Institute, USAID in partnership with FAO supported the assessment of milk samples from eight companies to identify potential antibiotic contamination, with results being shared with the appropriate authorities to facilitate action.

Subobjective 5.3.5

Expand overseas screening of long-term visitors to the U.S. (e.g., international workers and students) from high-risk countries to prevent the importation of cases of multidrug-resistant tuberculosis.

Target 5.3.5.1

Pilot screening in five countries by 2021. Expand to 45 countries by 2025.

CDC was not able to start the pilot screening for nonimmigrant visa applicants in countries with high rates of TB due to challenges resulting from various ongoing public health responses.

Objective 5.4

Increase international collaborations to facilitate basic, translational, and clinical research into understanding the causes of antibiotic resistance and developing countermeasures.

Subobjective 5.4.1

Collaborate with international scientists and organizations to better understand and address the development, spread, and health risks of antibiotic resistance and resistance sources present in animals, the environment, the community, and healthcare settings.

Target 5.4.1.1

Conduct research and/or surveillance projects to evaluate sources of antibiotic resistance, mechanisms of persistence, and impact of sociological factors, with a focus on animal and environmental systems by 2023.

DoD/GEIS added a new surveillance category called One Health to two focus area roadmaps, which provided guidance to GEIS partner laboratories to evaluate and consider opportunities to conduct AR surveillance with a focus on human and animal systems. The FY 2021 GEIS requests for proposals yielded seven One Health proposals. Final decisions on funded proposals are pending release of the annual budget.

USDA/ARS conducted two research projects to evaluate sources of AR and mechanisms of persistence: "Serotyping of Sub-Saharan Africa *Salmonella* Strains Isolated from Poultry Feces Using Multiplex PCR and Whole Genome Sequencing" and "Coproduction of Tet(X7) Conferring High-Level Tigecycline Resistance, Fosfomycin FosA4 and Colistin Mcr-1.1 in *Escherichia coli* Strains from Chickens in Egypt."

Through the Global AR Lab & Response Network, **CDC** began work in 2021 with external partners to increase enteric WGS capacity through PulseNet International in the Middle East and Asia Pacific regions. CDC has also begun work with an external partner to build environmental laboratory AR surveillance capacity, building on CDC's Global WASH efforts to detect and respond to these threats in drinking, surface, and other environmental waters in East Africa, beginning in Kenya.

USAID is supporting AMR research efforts in both animal and human populations in four countries in Africa and Asia. USAID partner FAO supported an ongoing, large-scale study in Cameroon to map AMR prevalence on poultry and pig farms, as well as an effort to classify prevalence of MDR bacteria in Burkina Faso. In Vietnam, pilot testing of archived bacterial samples aims to assess the historical prevalence of various resistance genes. In addition, OHW-NG supported a research project to identify AMR in wastewater samples in Myanmar. In April 2021 USAID launched TRANSFORM, a project that will harness private sector-led innovation to address emerging infectious diseases and antimicrobial resistance in animal production value chains in Asia and Africa. TRANSFORM will support on-farm research to develop, test, and scale innovative solutions that sustainably improve animal health. USAID also supports applied research on sociological factors that influence sustainable action addressing AMR. For example, in partnership with FAO, Mozambique is conducting studies of knowledge, attitudes and practices when it comes to AMR and antimicrobial use along the poultry, aquaculture, and beef value chains.

Subobjective 5.4.2

Promote and enhance the alignment of U.S. and international translational and clinical research activities to facilitate the development of new products to better diagnose, prevent, and treat infections or to provide data on the best use of existing products.

Target 5.4.2.1

Report one success story about products or regimens undergoing preclinical or clinical testing annually through 2025.

In November 2020 and June 2021, **ASPR/BARDA** produced two ASPR blogs: BARDA's Reflections on Antibiotic Resistance and the Path Forward and BARDA's Antimicrobial Resistance (AMR) Program Looks to the Future. In November 2020, the BARDA-funded CARB-X program highlighted Vedanta Biosciences' VE303 candidate as the first CARB-X-funded therapeutic to receive follow-on BARDA support for late-stage development and the first live biotherapeutic product project in BARDA's antibacterial portfolio.

NIH/NIAID is collaborating with academia, industry, and the DoD Uniformed Services University on an international study to evaluate the efficacy of a widely available, licensed Group B meningococcal vaccine (Bexsero) in preventing gonorrhea. If found to be efficacious, this vaccine could be a helpful gonorrhea prevention tool as there are currently no licensed vaccines against gonorrhea. This study, known as Safety and Efficacy Study of Meningococcal Group B Vaccine rMenB+OMV NZ (Bexsero) to Prevent Gonococcal Infection, began enrollment in December 2020 and includes sites in the United States and Thailand. NIH/NIAID's ARLG supported a prospective study on the clinical outcomes and bacterial characteristics of carbapenem-resistant *K. pneumoniae* (CRKP) among patients from different global regions. The study, called CRACKLE-2, enrolled 991 hospitalized patients with cultures positive for CRKP from 71 hospitals in Argentina, Australia, Chile, China, Colombia, Lebanon, Singapore, and the United States. Researchers found that CRKP epidemics have regional differences in bacterial characteristics and patients' clinical outcomes. These findings may have implications regarding whether the study results on diagnostics, treatments, and clinical prognosis can be applied from one area of the world to another.

Given the potential for vaccines to prevent infections and thereby mitigate the impact and spread of resistance, **USAID** supports the Coalition for Epidemic Preparedness Innovations' (CEPI) mission to stimulate and accelerate the development of vaccines against high-consequence pathogens and emerging infectious diseases and enable access to these vaccines during outbreaks.

Target 5.4.2.2

Convene a meeting with international regulators to seek alignment on clinical trial designs for new products by 2023.

In April 2021, FDA, the European Medicines Agency, and the Japanese Pharmaceuticals and Medical Device Agency participated in a joint workshop on trial designs pertaining to developing drugs for treatment of gonorrhea. FDA and the European Medicines Agency will plan additional meetings.

Appendix A: Acronyms and Abbreviations

AIANHQI	American Indian/Alaska Native Healthcare Quality Initiative
AR/AMR	antimicrobial resistance, antimicrobial-resistant
AMS	antimicrobial stewardship
AMU	antimicrobial use
ARCH	Antibiotic Resistance in Communities and Hospitals
ARLG	Antibacterial Resistance Leadership Group
ASEAN	Association of Southeast Asian Nations
ASP	antibiotic stewardship program
ASPWG	Antimicrobial Stewardship Program Working Group
AST	Antimicrobial Susceptibility Test
AU	antibiotic use
AUR	antibiotic use and resistance
BV-BRC	Bacterial and Viral Bioinformatics Resource Center
CAMRA	Combatting AntiMicrobial Resistance in Africa Using Data Science
CARB	Combating Antibiotic-Resistant Bacteria
CARBIRU	CARB Interdisciplinary Research Units
CARB-X	Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator
CBER	Center for Biologics Evaluation and Research
CC4CARB	Chemistry Center for Combating Antibiotic-Resistant Bacteria
CDRH	Center for Devices and Radiological Health
CHAI	Clinton Health Access Initiative
CLABSI	central line-associated bloodstream infections
CRE	carbapenem-resistant *Enterobacterales*
CRKP	carbapenem-resistant *Klebsiella pneumoniae*
CTN	clinical trial network
CUSP	Comprehensive Unit-based Safety Program
CVM	Center for Veterinary Medicine
ECDC	European Centre for Disease Prevention and Control
eGISP	enhanced Gonococcal Isolate Surveillance Project
EHR	electronic health record
EIP	Emerging Infections Program
ESBL	extended-spectrum beta-lactamase
FAIR	findability, accessibility, interoperability, and reusability
ESKAPE	*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* species
FAO	Food and Agriculture Organization
FY	fiscal year
GAIHN	Global Action in Healthcare Network
GFI	guidance for industry
GHSA	Global Health Security Agenda
GISP	Gonococcal Isolate Surveillance Project
GLASS	Global Antimicrobial Resistance Surveillance System
HAI	healthcare-associated infections
HQIC	hospital quality improvement contractor
IHS	Indian Health Service

IND	investigational new drug
IPC	infection prevention and control
IPPS	Inpatient Prospective Payment System
LTC	long-term care
MDR	multidrug-resistant
MIC	minimum inhibitory concentration
MDRO	multidrug-resistant organism
MHS	military healthcare system
MOU	memorandum of understanding
M-RITE	MOMENTUM Routine Immunization Transformation and Equity
MRSA	methicillin-resistant *Staphylococcus aureus*
MTaPS	Medicines, Technologies, and, and Pharmaceuticals Services
MTF	military treatment facility
NAHLN	National Animal Health Laboratory Network
NAHMS	National Animal Health Monitoring System
NARMS	National Antimicrobial Resistance Monitoring System
NCBI	National Center for Biotechnology Information, National Library of Medicine
NDA	new drug application
NHGRI	National Human Genome Research Institute
NHSN	National Healthcare Safety Network
NIAID	National Institute of Allergy and Infectious Diseases
NICU	neonatal intensive care unit
NLM	National Library of Medicine
NOFO	notice of funding opportunity
NTAP	new technology add-on payment
ORISE	Oak Ridge Institute for Science and Education
SAAR	standardized antimicrobial administration ratio
SIR	standardized infection ratio
STD	sexually transmitted disease
SURRG	Strengthening the United States Response to Resistant Gonorrhea
TAP	Targeted Assessment for Prevention
TATFAR	Transatlantic Taskforce on Antimicrobial Resistance
TB	tuberculosis
UTI	urinary tract infection
VAE	ventilator-associated event
Vet-LIRN	Veterinary Laboratory Investigation and Response Network
WAAW	World Antimicrobial Awareness Week
WASH	water, sanitation, and hygiene
WGS	whole-genome sequencing
WHO	World Health Organization