

The National Action Plan for Combating Antibiotic-Resistant Bacteria 2015-2020:

Progress to date

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Acknowledgements

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- Federal agency contacts

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- **VA:** Allison Kelly, Gary Roselle, Katherine Wallace

Overview

- Project charge and scope
- Methods
- Quantitative summary
- Agency-specific highlights
- Primary challenges and barriers
- Key lessons learned
- Antibiotic resistance trends
- Conclusions

Project Charge and Scope

- **Charge:** To examine progress made on the US National Action Plan (NAP) for Combating Antibiotic-Resistant Bacteria.
- **Scope:** This presentation summarizes progress on the goals, objectives, and milestones in the 2015-2020 NAP. Efforts beyond the scope of the first NAP are not addressed.

Goals Outlined in the 2015-2020 CARB NAP

1. Slow the emergence of resistant bacteria and prevent the spread of resistant infections.
2. Strengthen national one-health surveillance efforts to combat resistance.
3. Advance development and use of rapid and innovative diagnostic tests for the identification and characterization of resistant bacteria.
4. Accelerate basic and applied R&D for new antibiotics, other therapeutics, and vaccines.
5. Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, and control, and antibiotic R&D.

Methods

- Created agency-specific tables for all milestones in the NAP.
- Reviewed past progress reports from ASPE, the 2020 GAO Report on Antibiotic Resistance, and conducted online searches to identify relevant information and supporting evidence.
- Sent each table to the appropriate agency for review.
- Held one or more Zoom calls with agency personnel to clarify questions and fill in gaps in the table.
- Sent each completed table back to agency personnel for review and sign off.

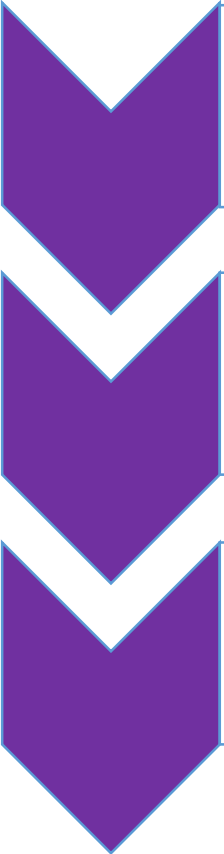
Methods

- Agency tables outline the status of each milestone and identify supporting evidence.
- Agency personnel were also asked about the following:
 - Primary agency accomplishments
 - Challenges and barriers to completing the work
 - Key lessons learned
- Findings are preliminary and may change slightly for the final written report.

Quantitative Summary

Agency	Total Milestones	Completed	Partially Completed	In Progress	Not Achieved
BARDA	13	13	--	--	--
CDC	92	89	1	--	2
CMS	14	11	1	1	1
DOD	32	30	--	1	1
EPA	2	1	--	--	--
FDA	56	54	--	2	--
HHS	28	26	--	1	1
NIH	34	34	--	--	--
USAID	10	10	--	--	--
USDA	57	53	2	2	--
VA	4	4	--	--	--

Quantitative Summary

- 
- 230 milestones in the CARB NAP
 - 215 (93%) fully completed

- Milestones partially completed: 4 (1.6%)
- Milestones in progress: 5 (2.2%)

- Milestones not achieved: 5 (2.2%)

Milestones Not Achieved

Within 5 years:

CDC will expand capacity to prevent the importation of cases of multidrug-resistant tuberculosis (TB) (MDR-TB) by doubling TB screening among migrants from high-incidence countries from 500,000 to 1 million persons per year.

Comment:

Efforts were stalled because of the COVID-19 pandemic.

Milestones Not Achieved

Within 3 years:

. . . CMS will begin the process of proposing new inpatient quality report (IQR) rules [for requiring hospitals to report AU/AR to NHSN as part of the IQR Program].

Comment:

There is no mandate for hospitals to report AU/AR data to NHSN; however, voluntary reporting continues to expand.

Milestones Not Achieved

Within 3 years:

CDC will establish up to 10 additional EIP sites, including sites in the West and Midwest that will monitor drug-resistant pathogens. . .

Comment:

Owing to limited resources, CDC did not expand the number of EIP sites; however, the number of pathogens being reported by existing EIP sites has been increased (GAO 2020 Report).

Milestones Not Achieved

Within 3 years:

HHS will establish a process that allows product developers to provide data to CMS for use in developing Interpretive Guidelines that facilitate the use of tests for patient treatment, hospital infection control, and reporting of cases of disease during outbreaks.

Comment:

HHS determined that CMS does not have the authority to ask for this information in the manner described by this milestone; therefore, this milestone cannot be completed.

Milestones Not Achieved

Within 1 year:

CBDP/DTRA will submit an Investigational New Drug (IND) application to FDA to initiate the clinical investigation of an antibiotic developed with DOD funding.

Comment:

The IND was expected for Emergent BioSolutions compound GC-072. An IND was not filed for GC-072 because it failed toxicology studies in 2019.

Agency Highlights: HHS

HHS Office of the Assistant Secretary for Planning and Evaluation (ASPE) has coordinated the USG CARB Task Force and this coordination role has proved to be very valuable.

Global action plan on antimicrobial resistance



Agency accomplishments:

- BARDA
- CDC
- CMS
- FDA
- NIH

Agency Highlights: BARDA



The screenshot shows the CARB-X website. At the top, there is a navigation bar with 'CONTACT' and social media icons for Twitter and LinkedIn. Below this is a header section with the 'CARB-X' logo, the tagline 'Combating Antibiotic-Resistant Bacteria', a search bar, and the Boston University logo. A menu bar lists: 'ABOUT CARB-X • PORTFOLIO • PARTNERS • APPLY • RESOURCES • NEWS • EVENTS'. The main banner features a background of colorful, textured spheres and the text 'About CARB-X' with a sub-link 'ABOUT CARB-X > OVERVIEW'. Below the banner, a section titled 'Accelerating global antibacterial innovation' describes CARB-X as a global non-profit partnership dedicated to accelerating antibacterial research to tackle the global rising threat of drug-resistant bacteria. It mentions funding of up to US\$480 million to invest in 2016-22, stating that CARB-X funds the best science from around the world.

CARB-X
Combating Antibiotic-Resistant Bacteria

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About CARB-X
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Accelerating global antibacterial innovation

Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) is a global non-profit partnership dedicated to accelerating antibacterial research to tackle the global rising threat of drug-resistant bacteria. With up to US\$480 million to invest in 2016-22, CARB-X funds the best science from around the world.

Approval of 3 antibiotics:



Agency Highlights: CDC

Accessible version: <https://www.cdc.gov/drugresistance/solutions-initiative/ar-lab-networks.html>

Antibiotic Resistance (AR) Solutions Initiative: AR Lab Network

CDC's AR Lab Network closes the gap between local capabilities and the data needed to combat AR in healthcare, food, and the community.



CDC Laboratory Expertise & Coordination

7 Regional Labs

1 National Tuberculosis Molecular Surveillance Center

55 State & Local Labs, building on CDC's existing healthcare, food, and community programs.

CDC & FDA Antibiotic Resistance (AR) Isolate Bank



AR Isolate Bank Logo

The CDC and FDA AR Isolate Bank provides information on resistance to support innovation in diagnostics and drug development. CDC provides isolates (pure samples of a germ) to approved institutions. [Access the AR Isolate Bank.](#)

On This Page

[Advancing the Fight against Antibiotic Resistance](#)

[Why the AR Isolate Bank is Unique](#)

[Order Isolates](#)

[Isolates and AST Data Available from Other Resources](#)

Innovating to Slow the Spread: CDC Combats Antibiotic Resistance (AR)

Each year in the United States, **more than 3 million people** are infected by an antibiotic-resistant germ or *C. difficile* (a bacterium associated with antibiotic use), and **nearly 50,000 people** die. Since 2016, **CDC has invested more than \$160 million** in AR innovation to drive aggressive action and empower the United States and the world to comprehensively respond to AR. CDC continuously works to address threats from CDC's 2019 AR Threats Report through these projects. **More resources are needed to invest in this critical research addressing gaps across healthcare, the community, and the environment.**



Since 2016, CDC has only been able to invest roughly

\$32 MILLION

a year on average in new ways to stop AR threats.



Nearly **80% of these investments**

are cross-cutting to fight not only AR threats but other emerging, infectious disease threats in healthcare, community, and the environment.



CDC has invested in

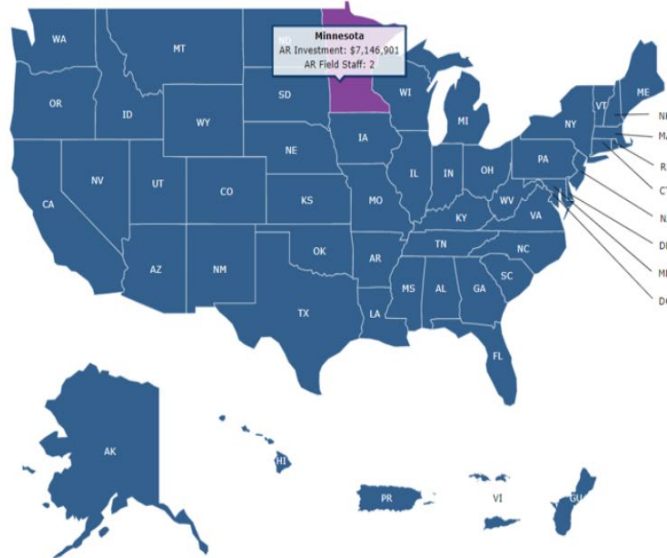
60+ innovative AR projects

in more than 30 countries, since 2016.

Agency Highlights: CDC

[Visit the AR Investment Map](#)

CDC's 2020 AR Investment Map



Antibiotic Prescribing and Use

Be Antibiotics Aware is a national effort to help fight antibiotic resistance and improve antibiotic prescribing and use.



Antibiotics can save lives, but any time antibiotics are used, they can cause side effects and contribute to the development of antibiotic resistance. In U.S. doctors' offices and emergency departments, at least 28% of antibiotic courses prescribed each year are unnecessary, which makes improving antibiotic prescribing and use a national priority.

Agency Highlights: CMS

- In October 2016, CMS published a final rule, “Medicare and Medicaid Programs: Reform of Requirements for Long-Term Care Facilities” (81 FR 68688).
- In September 2019, CMS finalized new regulations that require US hospitals to develop and implement antibiotic stewardship programs.

Agency Highlights: FDA

CDC & FDA Antibiotic Resistance (AR) Isolate Bank



AR Isolate Bank Logo

The CDC and FDA AR Isolate Bank provides information on resistance to support innovation in diagnostics and drug development. CDC provides isolates (pure samples of a germ) to approved institutions. [Access the AR Isolate Bank.](#)

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ADMINISTRATION

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FACT SHEET: Veterinary Feed Directive Final Rule and Next Steps

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Development & Approval Process

Environmental Impact Considerations

Background

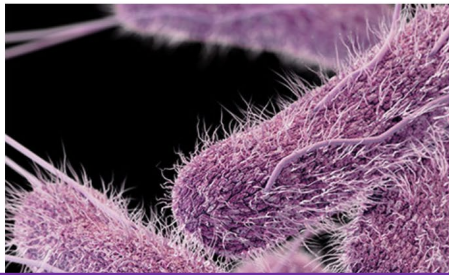
Over the past several years, the FDA has taken important steps toward fundamental change in how medically important antibiotics can be legally used in feed or water for food-producing animals. The agency has moved to

Content current as of:
02/11/2021

Agency Highlights: NIH

National Database of Antibiotic Resistant Organisms (NDARO)

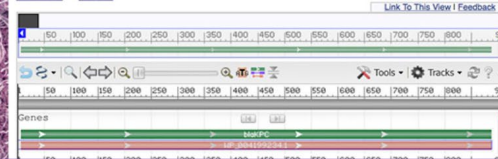
Welcome to the NCBI National Database of Antibiotic Resistant Organisms (NDARO), a collaborative, cross-agency, centralized hub for researchers to access AMR data to facilitate real-time surveillance of pathogenic organisms.



Klebsiella pneumoniae blaKPC gene for carbapenem-hydrolyzing class A beta-lactamase KPC-2, complete CDS

NCBI Reference Sequence: NG_049253.1

[GenBank](#) [FASTA](#)

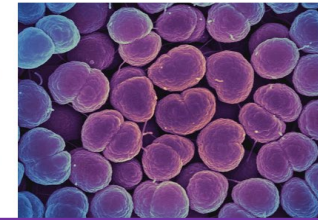


Wednesday, August 5, 2020

Rapid diagnostic for gonorrhea wins \$19 million federal prize competition to combat antibiotic resistance



A diagnostic test capable of accurately and reliably detecting the microorganism that causes gonorrhea and rapidly determining in under 30 minutes if the microorganism is susceptible to a single-dose antibiotic is the winner of the Antimicrobial Resistance (AMR) Diagnostic Challenge. Visby Medical, Inc., will receive \$19 million as a prize for its winning diagnostic.



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Accelerating global antibacterial innovation

Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) is a global non-profit partnership dedicated to accelerating antibacterial research to tackle the global rising threat of drug-resistant bacteria. With up to US\$480 million to invest in 2016-22, CARB-X funds the best science from around the world.

Agency Highlights: NIH

- Clinical trials support:
 - Expanding and strengthening the Antibiotic Resistance Leadership Group (ARGL).
 - Completing several clinical trials to inform optimal use of existing antibiotics.
- NIH has also strongly supported the development of non-traditional therapeutics (e.g., phage therapy, antivirulence inhibitors, monoclonal antibodies, microbiome-based approaches).

Agency Highlights: DOD

Created a centralized laboratory network, which has allowed DOD to identify emerging threats early (e.g., *Candida auris*).

Implemented a web application for clinicians, which ensures that information relevant to antimicrobial stewardship is available to clinicians via the mobile app.

Established the ASP Working Group (ASPWG):

- EpiData Center (EPC)
- Multidrug-Resistant Organism Repository & Surveillance Network (MRSN)
- Pharmacovigilance Center (PVC)

Agency Highlights: EPA

- During the latter part of the 2015-2020 NAP, EPA was working on creating interagency links into existing programs, which was a critical step for building the One Health perspective into surveillance and monitoring.
- EPA has entered into a more formal agreement for working with NARMS (National Antibiotic Resistance Monitoring System), including the formation of an environmental working group within NARMS.

Agency Highlights: USAID

- **Governance**

- Provided support for countries to develop and implement national multi-sectoral AMR strategies or national action plans.

- **Preventing Infections**

- Strengthened infection prevention and control (IPC) measures to help prevent healthcare-associated infections, including development and strengthening of national IPC committees, national IPC action plans, and national IPC standards.
- With USAID support, partners have pioneered the Clean Clinic Approach, a quality improvement strategy to strengthen WASH in health facilities.

Agency Highlights: USAID

- **Surveillance**

- Provided technical assistance, training, and commodities to strengthen laboratory capacity to detect AMR, including in large poultry markets.

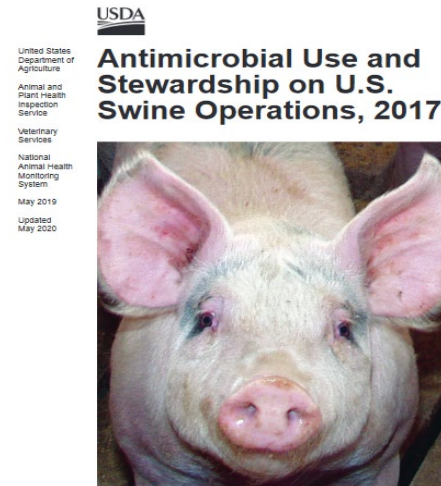
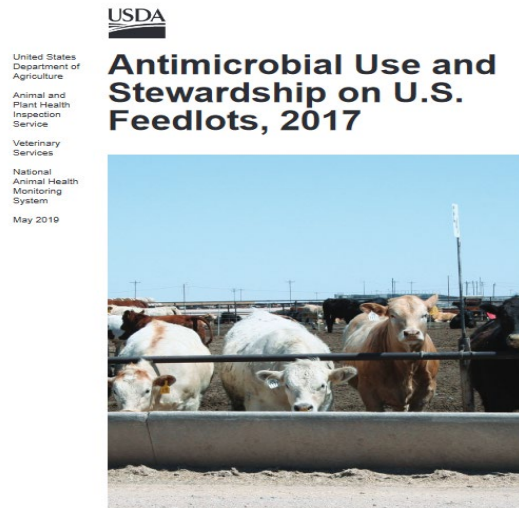
- **Stewardship and Case Management**

- Supported development of antimicrobial stewardship plans and activities that promote appropriate antibiotic use.
- Provided support in 25 countries to strengthen the timely diagnosis and appropriate case management of severe bacterial infections.
- Supported correct diagnosis, assessment, and care by trained health workers according to evidence-based guidelines to promote judicious use of antimicrobials.

Agency Highlights: USDA

NAHMS (National Animal Health Monitoring System) surveys conducted in 2017

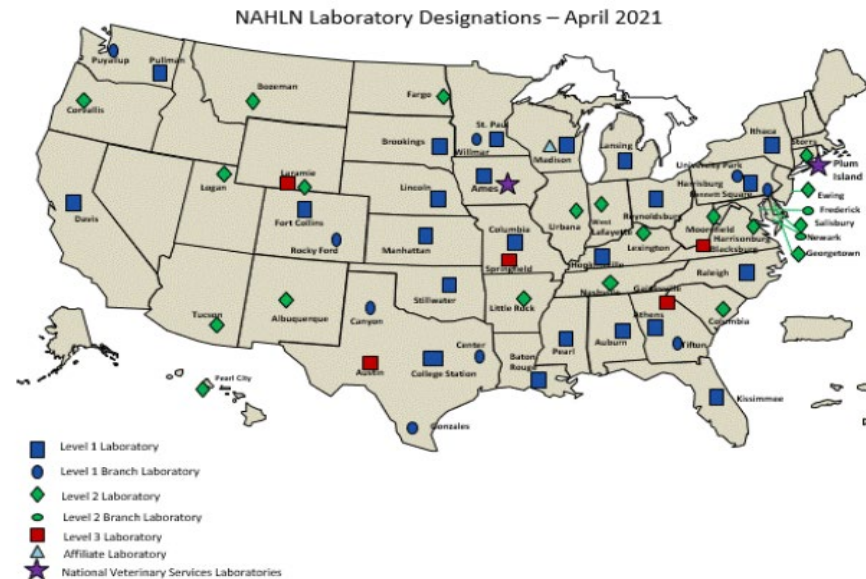
- Provided important information to understand antimicrobial use and practices before the VFD went into effect.



Agency Highlights: USDA

NAHLN (National Animal Health Laboratory Network)

- Provides a better understanding of resistance in animal pathogens—livestock and companion animals.



Please refer to lab list for testing capabilities.

April 8, 2021

Agency Highlights: USDA

Expansion of AMR testing, such as the inclusion of more commodities and initiating the cecum sampling program.

Research funded through ARS and NIFA.

Conducting whole genome sequencing (WGS) for NARMS (National Antibiotic Resistance Monitoring System) and publishing data in NDARO (National Database of Antibiotic Resistant Organisms) in near-real time.



Agency Highlights: VA

The VA has functional stewardship programs at all VA centers, regardless of the type of center.

- This includes identifying champions (pharmacists and providers) to promote stewardship.
- All 140 medical centers have stewardship programs and are in compliance with VHA Directive 1031.
- All VA facilities report data on antibiotic use to CDC.

VA's Antimicrobial Stewardship Program

Monday, April 21, 2014 8:00 am Guest Posts Melinda Neuhauser and Gary Roselle 849 views



Ever since Sir Alexander Fleming discovered penicillin nearly 90 years ago, antibiotics have been a powerful means for treating bacterial infections and saving lives. Unfortunately, prescribing practices around these drugs have resulted in "antibiotic resistance." Whether it's the use of antibiotics without testing to first confirm infection, improper dosing, or poor communication with patients regarding compliance, the end result is the same. Many antibiotics are no longer effective at killing the bacteria they once killed, making it difficult, if not impossible for doctors to treat certain infections.

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Barriers and Challenges

General Challenges

- AMR is highly complex (e.g., 18 different pathogens in the 2019 AR Threats Report).
- Harmonizing a One Health approach across different sectors.
- Limited resources for agencies to fully implement the CARB NAP and funding disparities between agencies.
- The COVID-19 pandemic.
- Data integration and electronic data management.

Barriers and Challenges

Public Health Resources

- The capacity needs at the state/territorial level are much greater than the support that can be offered.
- Funding cycles for states are not always consistent and sustained over time.

Agricultural Outreach

- Much of the work on farms is voluntary.
- Gaining producer trust and developing support of industry groups is key.
- Better risk communication is needed to ensure voluntary participation.

Barriers and Challenges

Drug Discovery and Development

- Lack of adequate funding for drug development.
- The pipeline of AMR drugs is a challenge and there are few companies left in this space.
- There is a need for more “pull” incentives.
- Incentivizing industry to invest in the development of new drugs can be challenging.
- The regulatory pathway for non-traditional therapeutics is not clearly defined.

Barriers and Challenges

International Challenges

- Adequate surveillance to define the problem.
- Resources to implement national action plans globally.
- Data reconciliation: systems are based on different standards.
- Differences in terminology, disease conditions, methodologies, regulatory structures, antimicrobial resistance patterns, antimicrobial access, priorities, approaches to basic translational research cultures, and resources in different countries.

Key Lessons Learned

- Political will has been essential to success.
- The NAP is a model for successful collaboration across the US Government.
- AR prevention through public health action is possible.
- The One Health approach of the NAP has been validated, including the importance of the environment.
- The capabilities built during NAP implementation can be dual use (such as in pandemic response).

Key Lessons Learned

- It is important to de-risk R&D and provide companies the needed support to advance products.
- For drug R&D, it's important to stimulate and support early stages of discovery—this seems to be a critical bottleneck.
- On the international level: measurable targets, tools to assess capacity, and guidance are needed.

Progress Toward Targets

CDC's 2019 AR Threats Report: **PREVENTION WORKS.**

↓ 18% fewer deaths from
antibiotic resistance
overall since 2013 report

↓ 28% fewer deaths from
antibiotic resistance
in hospitals since 2013 report

AND DECREASES IN INFECTIONS CAUSED BY:

↓ 41% Vancomycin-resistant
Enterococcus

↓ 33% Carbapenem-resistant
Acinetobacter

↓ 29% Multidrug-resistant
Pseudomonas aeruginosa

↓ 25% Drug-resistant
Candida

↓ 21% Methicillin-resistant
Staphylococcus aureus
(MRSA)

STABLE Carbapenem-resistant
Enterobacteriaceae (CRE) &
drug-resistant tuberculosis
(TB disease cases)

Conclusions

- Implementation of the 2015-2020 CARB NAP was highly successful, as evidenced by milestone completion and given that the plan was intended to be “aspirational.”
- USG agencies are committed to this work with highly dedicated staff.
- The 2015-2020 NAP fundamentally changed the way various stakeholders think of AR and elevated the topic to an issue of national and international concern.
- Implementation of the NAP has built important infrastructure that will have long-range benefits.
- Continued and sustained funding is essential for ongoing progress over the next 5 years.

Questions

