
NIH Update on National Action Plan Goals 2-5

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PACCARB public meeting
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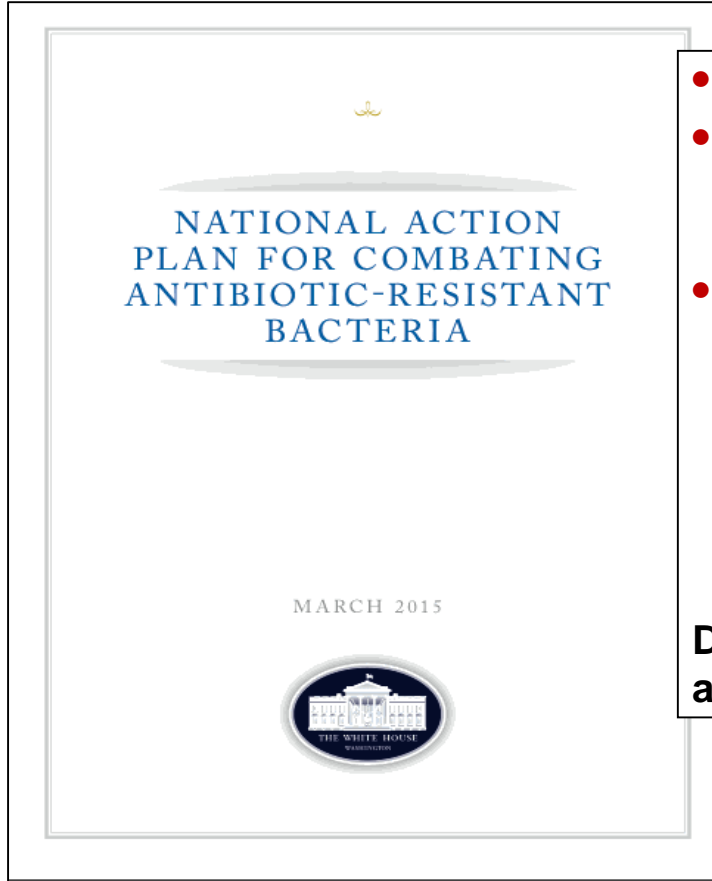
Mission Statements

National Institutes of Health (NIH)

- Seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability.

National Institute of Allergy and Infectious Diseases (NIAID)

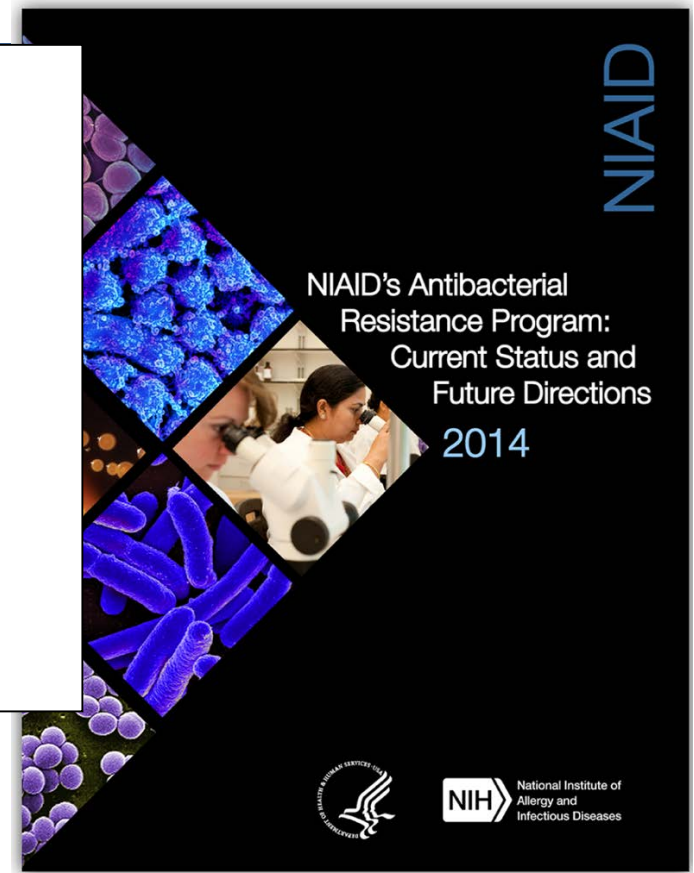
- Conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases.



- **Basic Research**
- **Translational Research/ Product Development**
- **Clinical Research**



Diagnosis, Prevention and Treatment



Web search term: NIAID

AMP RRE

Objective 2.1.4: Develop and maintain a national sequence database of resistant pathogens

- **NIH-CDC-FDA Collaboration**
 - Providing sequencing support for reference bacterial strains identified by CDC and FDA
 - NIH has sequenced 66 genomes; 89 additional genomes in progress
 - Since 2012, NIAID has sequenced 3000+ bacterial genomes
 - All genomic data is rapidly released to the public
- **NIH National Database of Resistant Pathogens**
 - Data on 130,000+ pathogen isolates collected from publicly accessible information
 - Includes genome sequence data and if available, drug susceptibility phenotypic data
 - Web interface to search isolates and explore their genetic relatedness
- **Pathosystems Resource Integration Center (PATRIC)**
 - NIAID-funded Bioinformatics Resource Center
 - Open access to diverse data sets (e.g., genomic sequence, transcriptomics and drug susceptibility data), workspaces and data analytical tools
 - Extensive web-based and hands-on-training in bioinformatics

Objective 3.1: Develop and validate new diagnostics

- NIAID: Targeted funding opportunities since 2015
 - FY15: Partnerships for Diagnostics to Address Antimicrobial Resistance of Select Bacterial Pathogens
 - FY17: Partnerships for Countermeasures Against Select Pathogens
 - FY18: Partnerships for Development of Clinically Useful Diagnostics for Antimicrobial- Resistant Bacteria
- NIH: AMR Diagnostic Challenge Competition (\$20 million) – collaboration with BARDA

Antibacterial Resistance Leadership Group (ARLG)

Diagnostics Activities

- Host-based signature to distinguish viral from bacterial respiratory infections
- Virtual biorepository
- Capability to collect clinical specimens for diagnostics development
- Master protocol for validation of multiple diagnostics simultaneously
- Using procalcitonin levels to identify community-acquired pneumonia patients who will not benefit from antibiotics

CARB Goal 4: NIH Responsibilities

| | |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Objective 4.1 | Conduct research to enhance understanding of environmental factors that facilitate the development of antibiotic-resistance and the spread of resistance genes that are common to animals and humans. |
| Objective 4.2 | Increase research focused on understanding the nature of microbial communities, how antibiotics affect them, and how they can be harnessed to prevent disease. |
| Objective 4.3 | Intensify research and development of new therapeutics and new and improved vaccines, first-in-class drugs, and new combination therapies for treatment of bacterial infections. |
| Objective 4.4 | Develop non-traditional therapeutics, vaccines, and innovative strategies to minimize outbreaks caused by resistant bacteria in human and animal populations. |
| Objective 4.5 | Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates and promising vaccines that can reduce the need to treat bacterial infections. |
| Objective 4.7 | Create a biopharmaceutical incubator—a consortium of academic, biotechnology, and pharmaceutical industry partners—to promote innovation and increase the number of antibiotics in the drug-development pipeline. |

CARB Goal 4: Antibacterial and Vaccine Development at NIAID



- 10 targeted funding opportunities for AMR therapeutics since 2015 (basic, translational and clinical research)
- 3 targeted funding opportunities for AMR vaccines since 2015
- Preclinical Services
- Clinical Trial Networks
- Workshops

NIAID's Support through the Development Enterprise – Synthetic Tetracyclines

Methodological advances permit the stereocontrolled construction of diverse fully synthetic tetracyclines containing an all-carbon quaternary center at position C5a

Peter M. Wright, Andrew G. Myers*

Department of Chemistry & Chemical Biology, Harvard University, Cambridge, MA 02138, United States

Tetrahedron 67 (2011) 9853–9869

TETRAPHASE

PHARMACEUTICALS

Development of
new chemistry to make
unlimited new
tetracyclines




NIAID grant and
contract support

TP-271: Currently in
Phase I

Eravacycline (TP-434)
Phase III

- IGNITE 1 (cIAI)
- IGNITE 2 (cUTI)

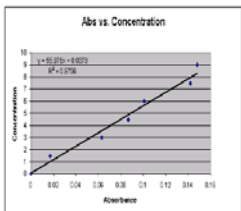
NIAID grant
support*

-  Investigator activity (grant support)
-  NIAID/Company activity
-  BARDA/Company activity

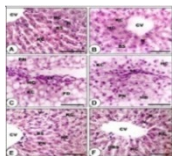
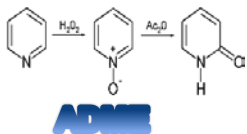
Product Development Services

Therapeutics

In Vitro Assessment of Antimicrobial Activity



Interventional Agent



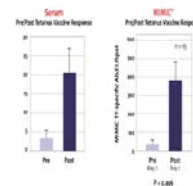
Biopharmaceutical Products



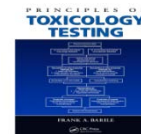
Chemistry, Manufacturing, and Controls (CMC) Documentation for IND

Vaccines

Testing



Manufacturing

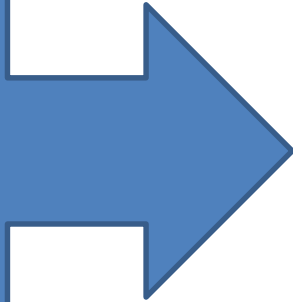


Animal Models



Clinical Research to Address AMR

- Targeted Clinical Trials
- ARLG
- Vaccine and Treatment Evaluation Units
- Phase I Clinical Trial Units for Therapeutics
- Sexually Transmitted Infections Clinical Trials Group



**Optimization
Trials**

**Pharmacokinetics/
Pharmacodynamics
(PK/PD) Studies**

**Testing New
Drugs**

**Diagnostics
Studies**

CARB-X Antibacterial Treatment and Prevention Product Portfolio

| Sponsor | Product | Description |
|----------------------------|----------------------|-------------------------------------|
| Tetraphase Pharmaceuticals | TP-6076 | Next-generation tetracycline |
| Cidara Therapeutics | CD201 | Bifunctional immunotherapy |
| Microbiotix | T3SS Inhibitor | Virulence modifier |
| Spero Therapeutics | SPR741 | Potentiator |
| Entasis Therapeutics | ETX000 | Oral Gram-negative combination |
| Forge Therapeutics | FG-LpxC | Inhibitor of LpxC |
| Oppilotech | LPS | Targets synthesis of LPS |
| ContraFect | Gram-negative lysins | Recombinant lysin protein |
| Redx Pharma | NBTI | Dual-acting topoisomerase inhibitor |
| Visterra | VIS705 | Antibody-drug conjugate |

■ NIH/NIAID provided previous support to 7 of the 10 companies prior to CARB-X

Objective 5.5: Establish/promote international collaboration and PPPs to incentivize development of new products to combat AMR

- Via its membership on the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR), NIH has
 - Aligned clinical trials addressing key questions in antibacterial resistance treatment and product development
 - Co-organized international workshops with European funders
 - Co-presented research opportunities at international meetings with European funders
- The ARLG has initiated collaborations with several countries in S. America, Asia, and Australia