NIH/NIAID

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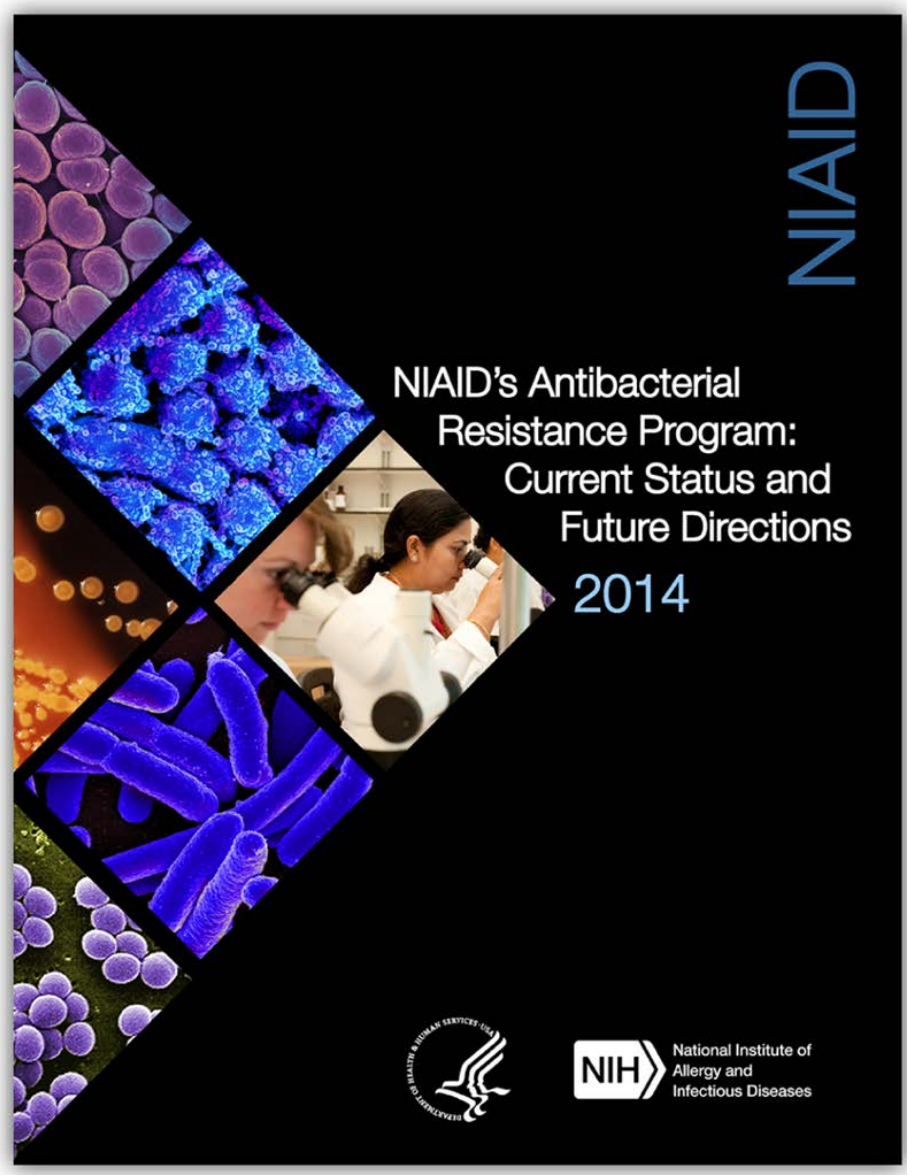
November, 2019
FDA Meeting at White Oak
Silver Spring, Maryland

National Institute of Allergy and Infectious Diseases

NIAID Antibacterial Resistance Program



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

Diagnosis, Prevention and Treatment

Web Search Term: **NIAID AR pdf**

Preclinical Services-Suite of Contracts

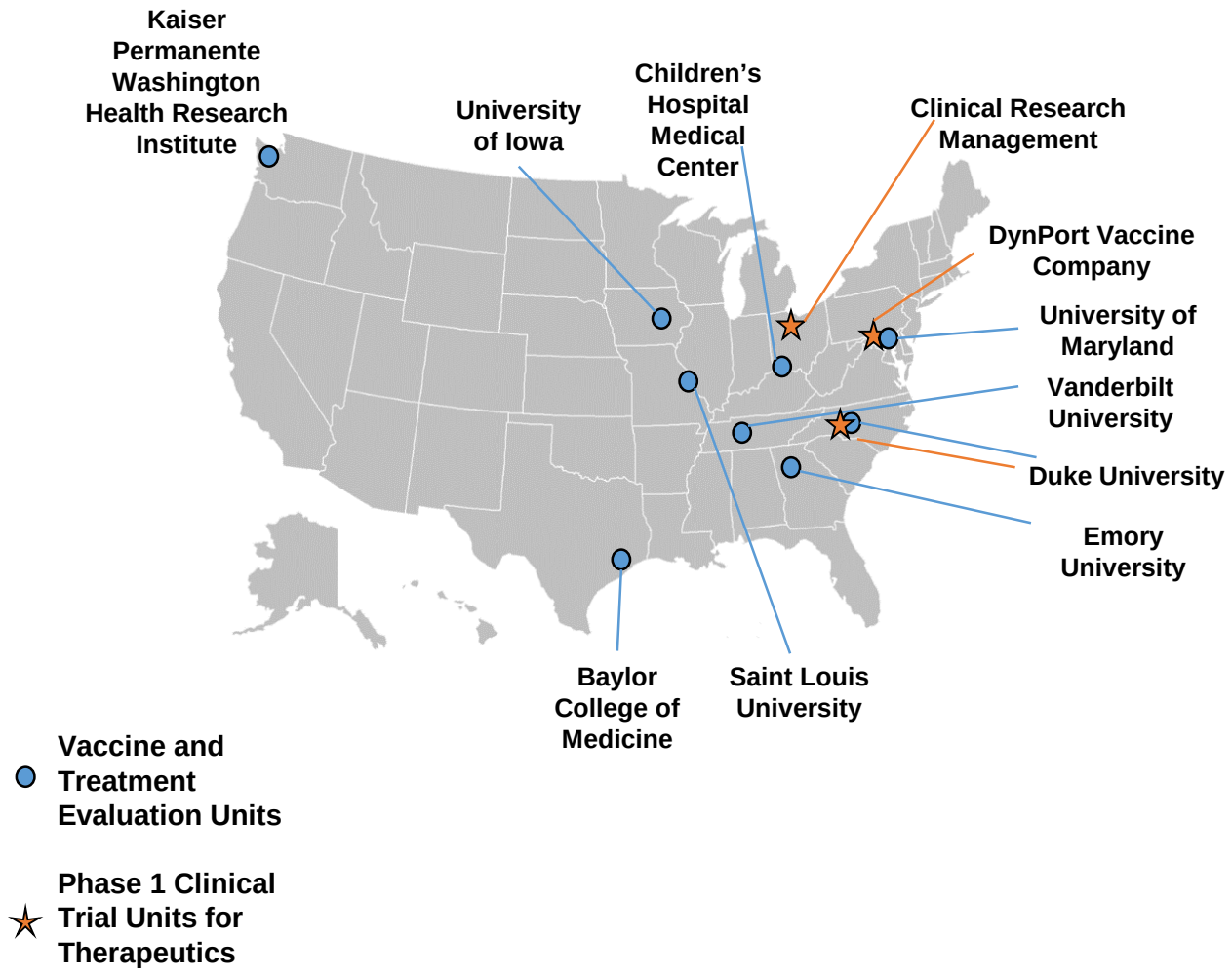
Suite of service contracts that provide a broad range of assays and capabilities to the extramural research community free-of-charge.

Who can apply for these services?

- Innovators from academia, non-profit organizations, industry, and government
- Domestic or foreign institutions
- Do not need to have NIH funding
- Simplified Request Process – available year-round

Therapeutics	Vaccines	Research Resources
• In Vitro Activity (MICs) • Synthesis and CMC • ADME Assays • Pharmacokinetics • Safety and Toxicity Testing	• Assay Development • Safety and Toxicity Testing • Process Development • Pilot and GMP Manufacturing • Regulatory Activities	• Free Reagents: https://www.beiresources.org/ • Structural Genomics Services: https://www.niaid.nih.gov/research/structural-genomics-centers

Clinical Services (Current Structure)



General Capabilities

- Contracts provide services, not direct funding, for all aspects of the clinical trial

Phase I Clinical Trial Units for Therapeutics

- Support Phase I clinical trials of new drugs

Vaccine and Treatment Evaluation Units (VTEUs)

- Phase I-IV clinical trials
- Prevention and treatment of DMID pathogens

Targeted Clinical Trials to Address Antimicrobial Resistance

- In 2007, NIAID launched a series of ***"strategy"*** trials designed to provide vital information on the optimal use of off-patent antibiotics to answer key questions:
  - Which drugs to use;
  - How much to give;
  - How long to give them.
- Ultimate goal: to find treatment regimens that limit the emergence of drug resistance.

Photo Credit: NIAID Flickr

COlistin Monotherapy VERsus COMbination ThErapy (OVERCOME)

Need:

- Effective clinical management of MDR-Gram-negative bacilli (GNB) infections

Design:

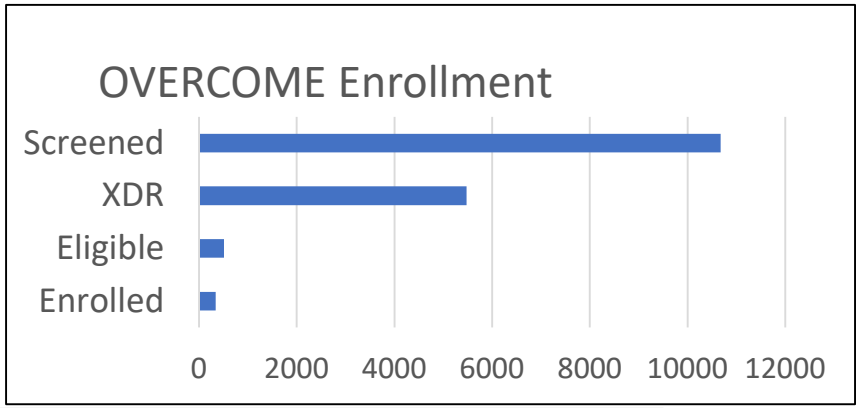
- Randomized, double-blind, placebo-controlled trial of Colistin vs. Colistin + carbapenem
- MDR *A. baumannii* , *P. aeruginosa* & CRE bloodstream infection and HAP/VAP
- N=444

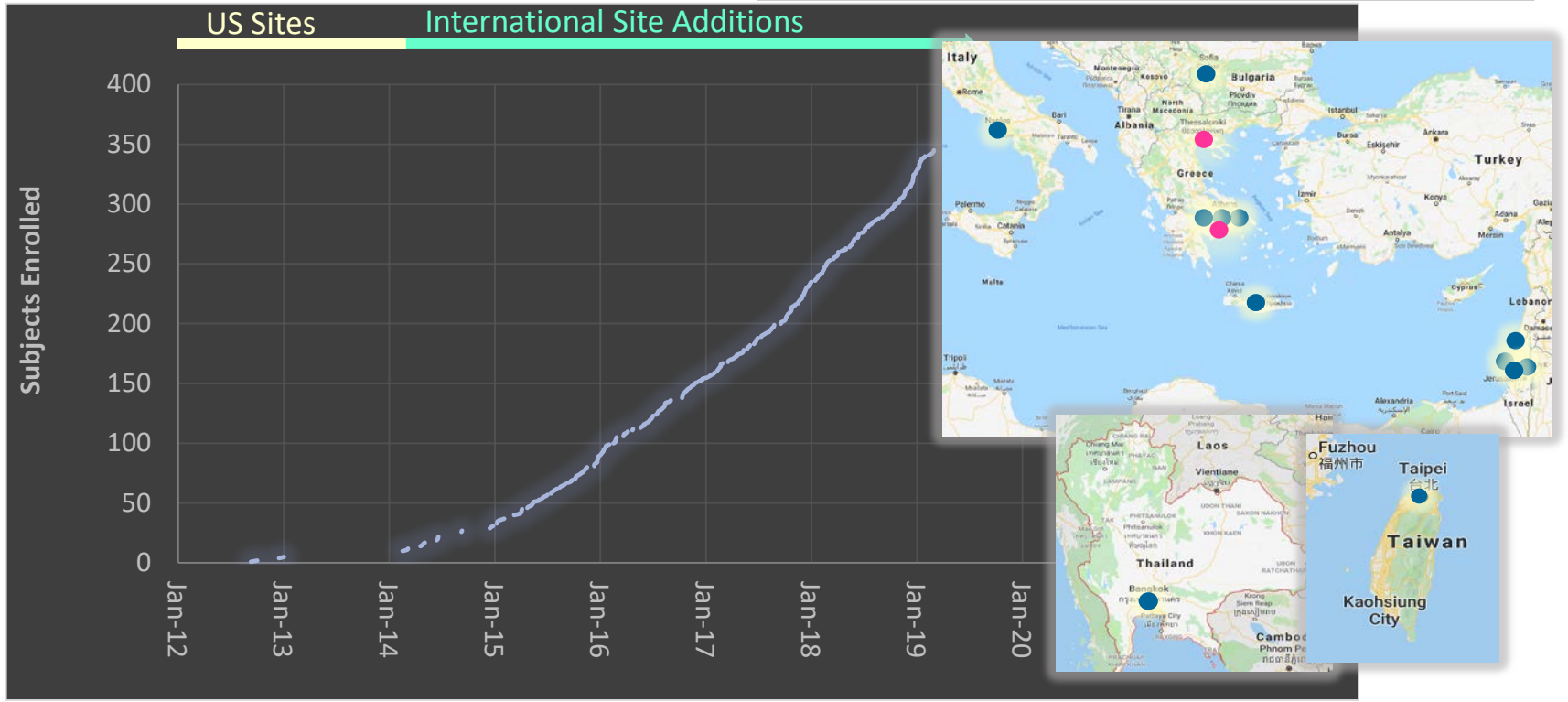
Challenges:

- Patients: critically ill
- Study Sites: total 13; US *vs* ex-US sites
- Regulatory requirement per region: Us vs. EU

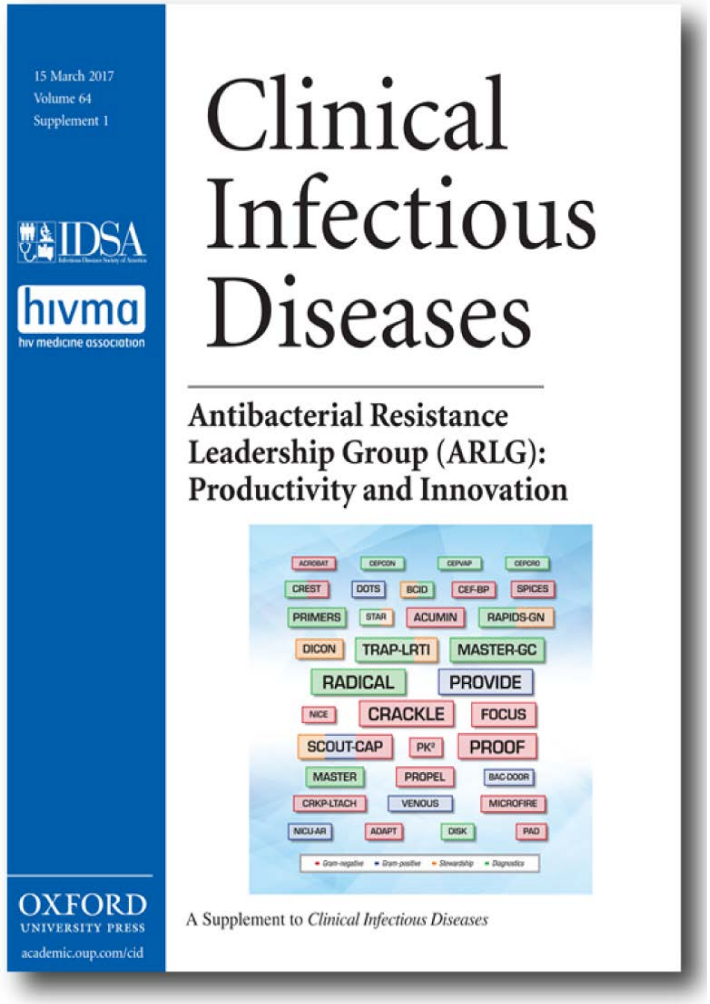
Collaboration:

- DMID/BMB
- PI
- PPD
- IMI's COMBACTE





Antibacterial Resistance Leadership Group (ARLG)



- Created in June 2013 to develop, prioritize, and implement a clinical research agenda on antibacterial resistance

- To date, the ARLG has:
  - reviewed >100 study proposals
  - initiated >45 studies
  - included data from >18,000 subjects
  - published >115 manuscripts

- Recompetes in 2019

MDRO* Network Evolution

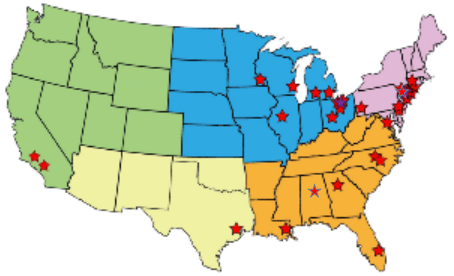
MDRO Network
Antibacterial Resistance Leadership Group

CRACKLE I:

8 sites/ 20 hospitals in 4 states

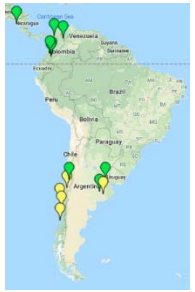
CRACKLE II:

32 sites/ 91 hospitals in 16 states + DC



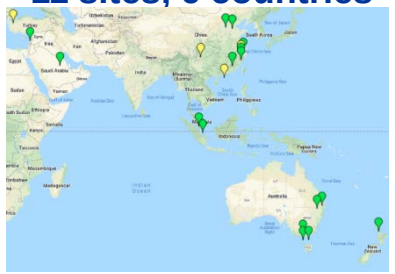
Global Network

S/C America - 14 sites, 4 countries



China - 9 sites, GSK collaboration

Asia-Pacific – 11 sites, 6 countries



*MDRO = Multidrug-resistant organism

Innovations in Antibacterial Trial Design

HEALTHCARE EPIDEMIOLOGY INVITED ARTICLE

Robert A. Weinstein, Section Editor

Desirability of Outcome Ranking (DOOR) and Response Adjusted for Duration of Antibiotic Risk (RADAR)

Scott R. Evans,[1] Daniel Rubin,[2] Dean Follmann,[3] Gene Pennello,[4] W. Charles Huskins,[5] John H. Powers,[6,7] David Schoenfeld,[8] Christy Chuang-Stein,[9] Sara E. Cosgrove,[10] Vance G. Fowler Jr,[11] Ebbing Lautenbach,[12] and Henry F. Chambers[13]

Statistics in Biopharmaceutical Research

ISSN: (Print) 1946-6315 (Online) Journal homepage: http://amstat.tandfonline.com/loi/usbr20

Comment: Fundamentals and Innovation in Antibiotic Trials

Scott R. Evans & Dean Follmann

STATISTICS IN BIOPHARMACEUTICAL RESEARCH
2016, VOL. 8, NO. 4, 386–393
http://dx.doi.org/10.1080/19466315.2016.1207561

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Using Outcomes to Analyze Patients Rather than Patients to Analyze Outcomes: A Step Toward Pragmatism in Benefit:Risk Evaluation

Scott R. Evans[a,b] and Dean Follmann[c]

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CARB-X

Combating Antibiotic Resistant Bacteria

A global public-private partnership supporting great science to fight drug-resistant bacteria

FUNDERS

ASPR – Assistant Secretary for Preparedness and Response

BARDA – Biomedical Advanced Research and Development Authority

Wellcome

NIH – National Institute of Allergy and Infectious Diseases

UKaid from the British people

Federal Ministry of Education and Research

ALLIANCE PARTNER

Bill & Melinda Gates foundation

ACCELERATORS

Basel Area. Swiss

BioInnovation Institute

CLSI – California Life Sciences Institute

C-CAMP – Centre for Cellular and Molecular Platforms

DZIF – German Center for Infection Research

FIND – Because diagnosis matters

ILSE – Institute for Life Science Entrepreneurship

MassBio – Massachusetts Biotechnology Council

RTI International

Wellcome

Thank you

… For your interest