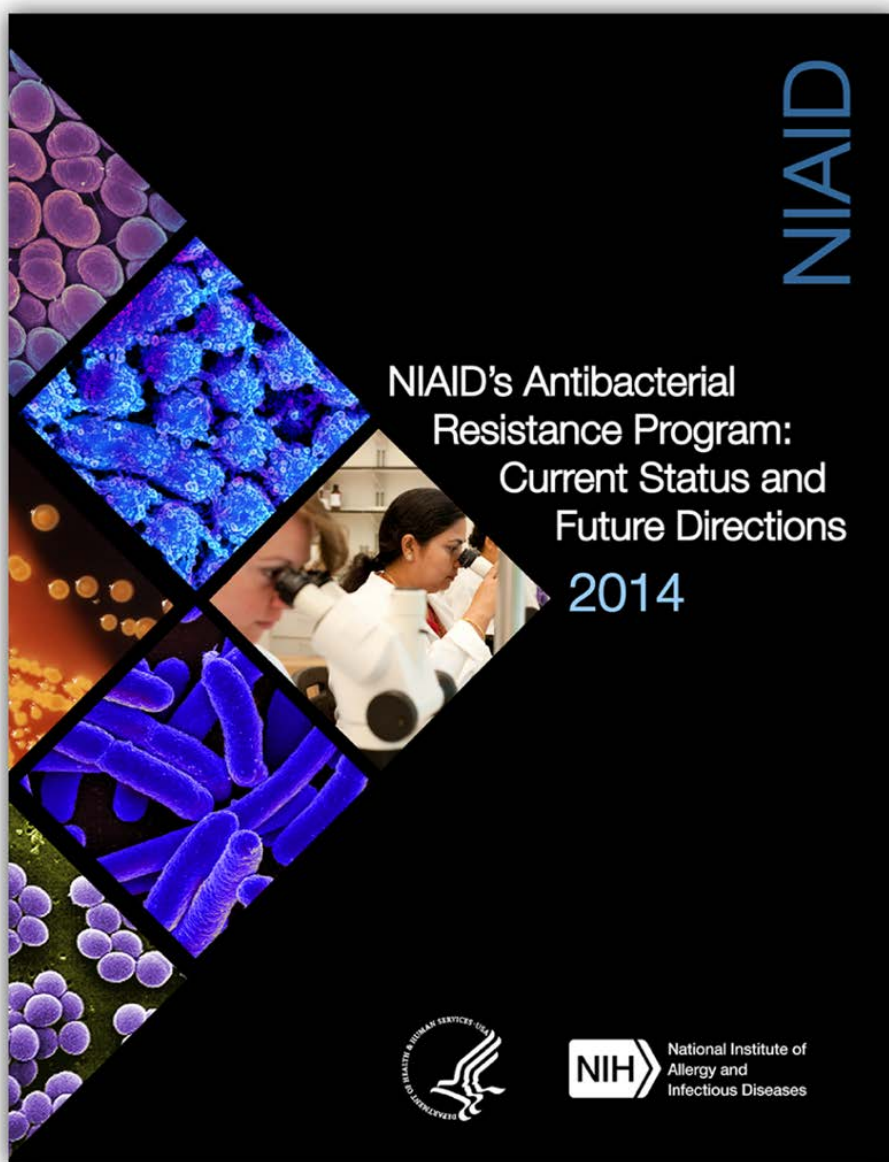

NIH/NIAID

Dennis M. Dixon, PhD
Chief, Bacteriology and Mycology Branch
Division of Microbiology and Infectious Diseases
NIAID, NIH, HHS

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



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

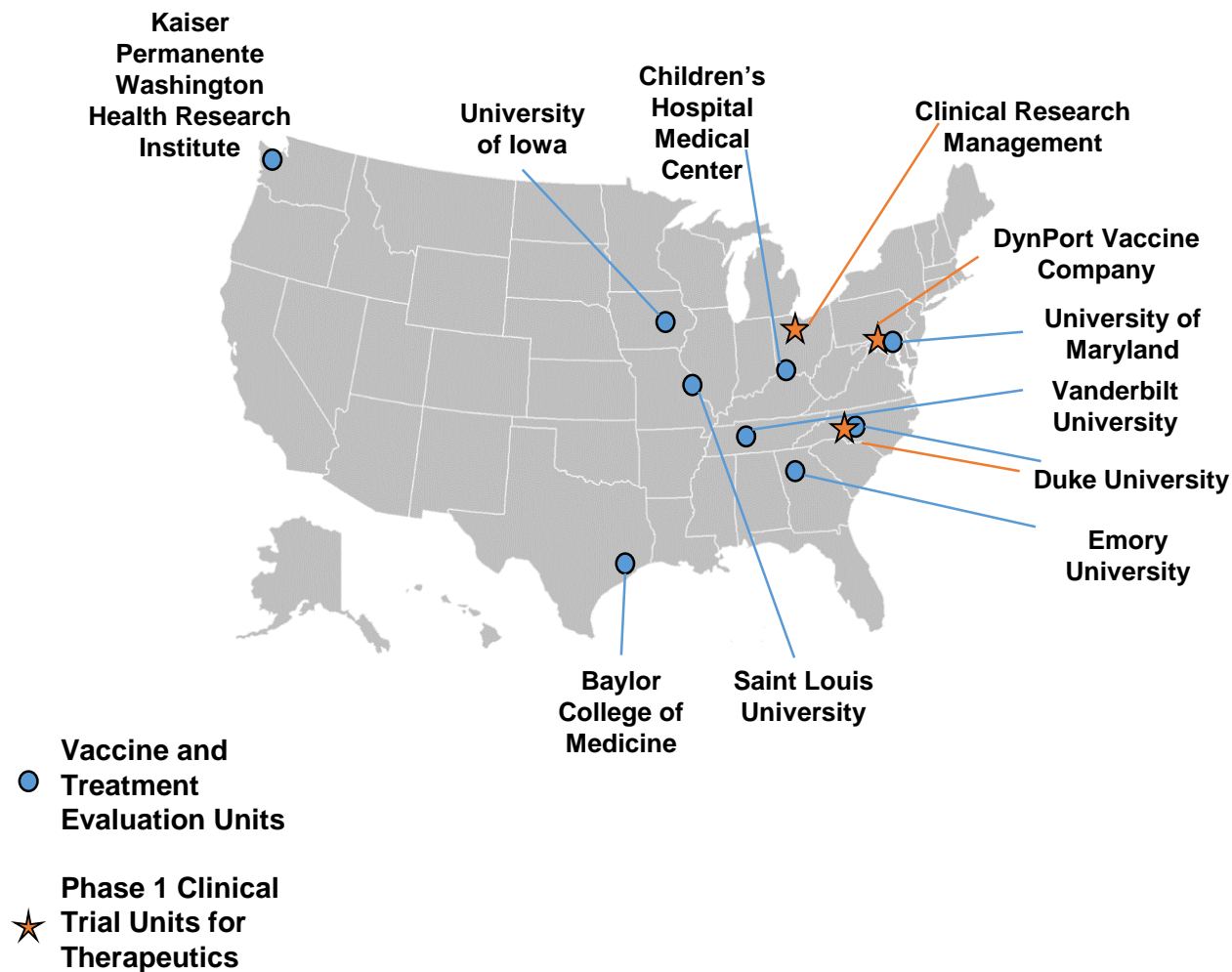
Suite of service contracts that provide a broad range of assays and capabilities to the extramural research community free-of-charge.

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
<ul style="list-style-type: none">• In Vitro Activity (MICs)• Synthesis and CMC• ADME Assays• Pharmacokinetics• Safety and Toxicity Testing	<ul style="list-style-type: none">• Assay Development• Safety and Toxicity Testing• Process Development• Pilot and GMP Manufacturing• Regulatory Activities	<ul style="list-style-type: none">• 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:

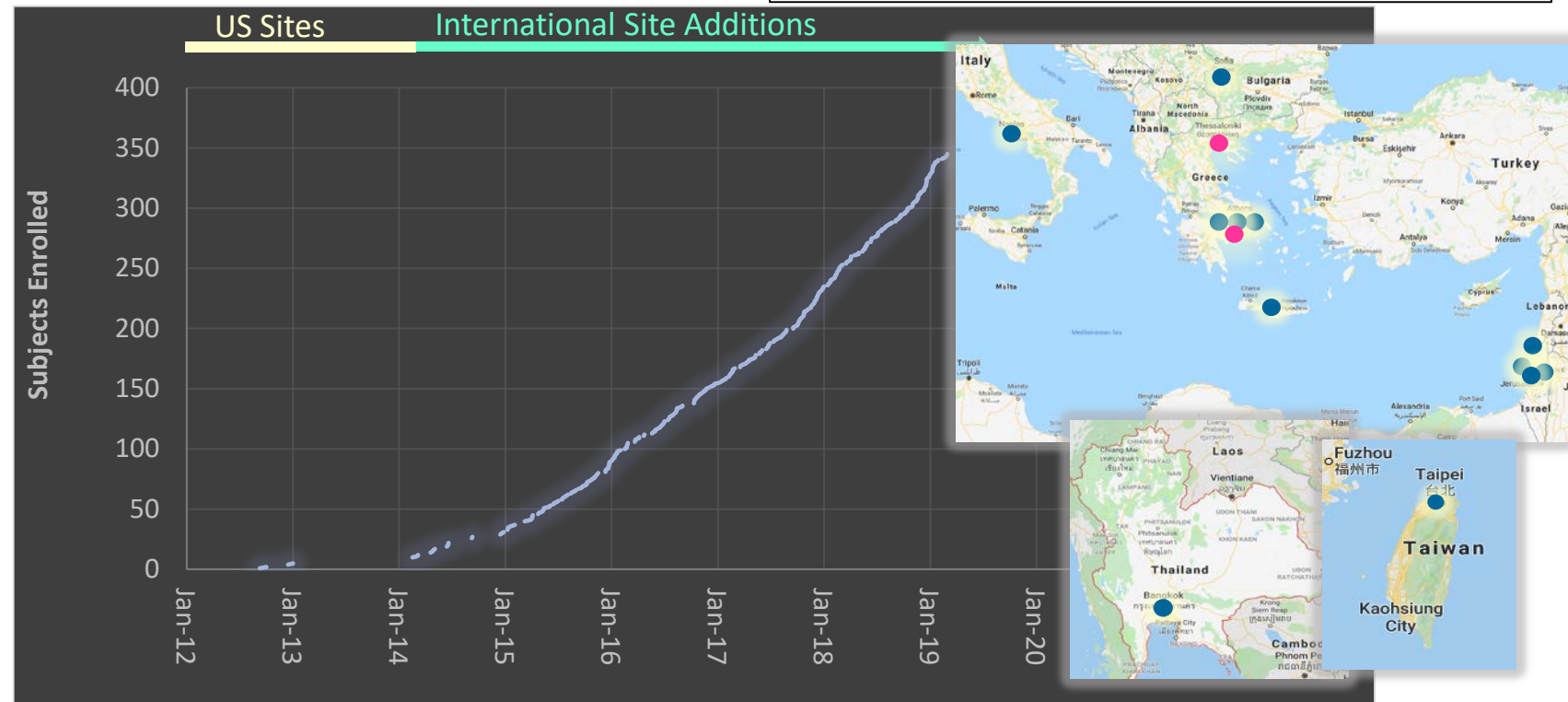
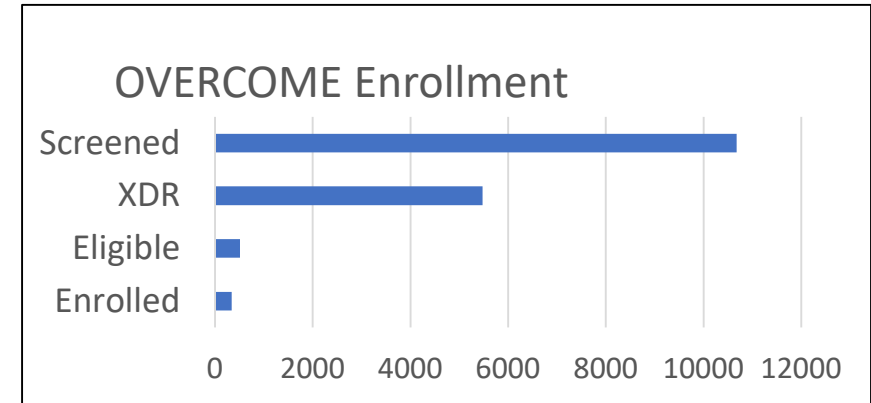
- Randomized, double-blind, placebo-controlled trial of Colistin vs. Colistin + carbapenem
- MDR *A. baumannii*, *P. aeruginosa* & CRE bloodstream infection and HAP/VAP
- N=444

Challenges:

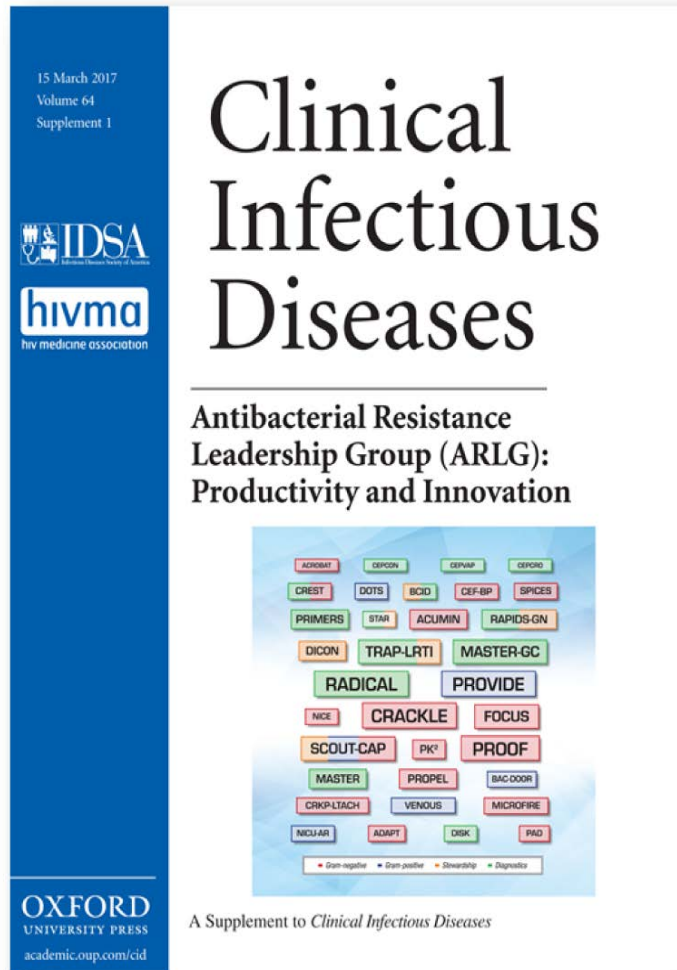
- Patients: critically ill
- Study Sites: total 13; US vs ex-US sites
- Regulatory requirement per region: Us vs. EU

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

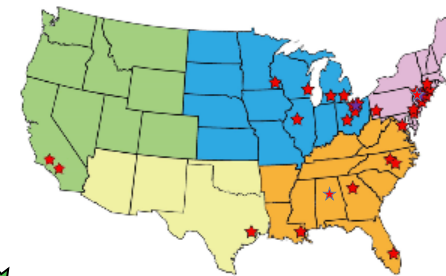
MDRO* Network Evolution



CRACKLE I:
8 sites/ 20 hospitals in 4 states

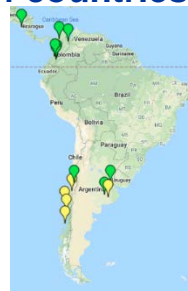


CRACKLE II:
32 sites/ 91 hospitals in 16 states + DC



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. Chambers¹³

 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>

 Taylor & Francis
Taylor & Francis Group

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

^aDepartment of Biostatistics, Harvard University, Boston, MA, USA; ^bCenter for Biostatistics in AIDS Research, Harvard University, Boston, MA, USA; ^cNational Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH), Bethesda, MD, USA.

CARB-X

Combating Antibiotic Resistant Bacteria

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

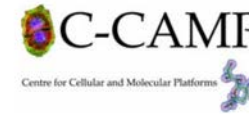
FUNDERS



ALLIANCE PARTNER

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GATES *foundation*

ACCELERATORS



Thank you

... For your interest