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# Antibiotic use in US consumer-driven healthcare

Oct 10<sup>th</sup>, 2019  
Taiwan AMR Workshop  
Washington, DC

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Inpatient

Outpatient

- Medical offices
- Emergency department
- Urgent care
- Retail clinics
- Telemedicine

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## Unique\* challenges in retail healthcare



\*Depends on who you ask...

### Patient-provider relationship

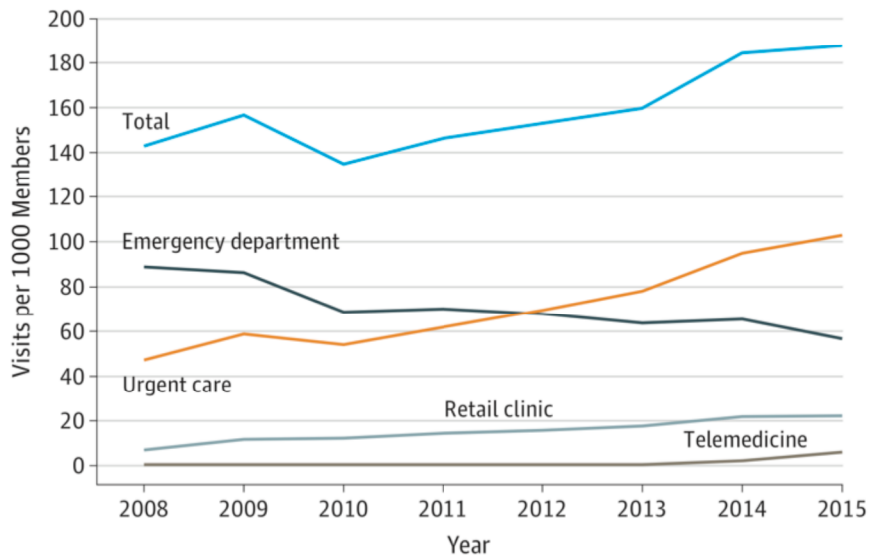
- Patients as consumers

### Pressures on providers

- Limited time
- Importance of patient satisfaction
- Lack of existing relationship

### Business pressures on operators

**Figure 1. Visits to Acute Care Venues for Treatment of Low-Acuity Conditions**



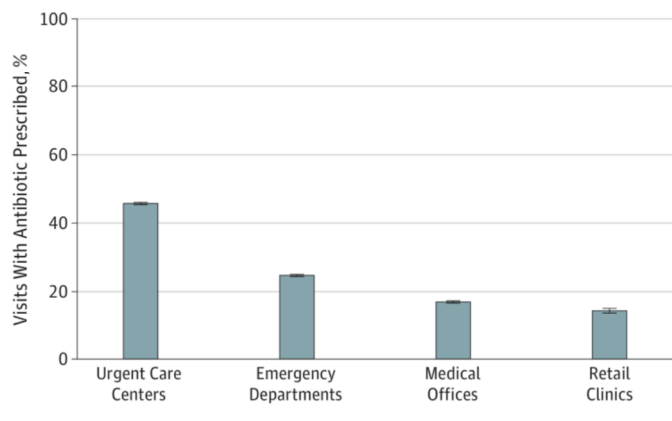
Poon et al, *JAMA Internal Medicine* 2018

## Urgent care and antibiotic use

1. Larger portion of low-acuity cases than medical offices or ED.
2. Higher rates of inappropriate prescribing.

Urgent care accounts for **~10%** of US outpatient visits but is likely responsible for **25-30%** of US outpatient antibiotic use.

**Figure. Percentage of Visits for Antibiotic-Inappropriate Respiratory Diagnoses Leading to Antibiotic Prescriptions**



Palms et al, *JAMA Internal Medicine* 2018



# Roadmap for Urgent Care Antibiotic Stewardship

## Multi-stakeholder summit

- Urgent care ecosystem: Payer, EHR, accrediting bodies, urgent care CEOs and CMOs, and professional societies

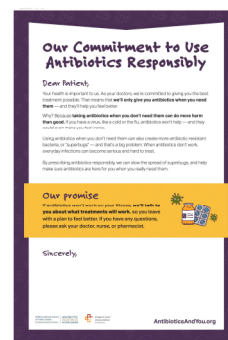
1. Industry-wide commitment
2. Original research to enable evidence-based practice
  - Benchmark
  - Assess interventions
3. Assess effect of social media on urgent care prescribing
4. Incorporate stewardship into urgent care accreditation & commendation
5. Stewardship for quality improvement
  - Maintenance of Certification: Antibiotic stewardship to meet Quality Improvement requirement

## Providers

Commitment poster

Communications training

Physician report card



## Patients

Delayed prescribing

Symptom prescription pad

Patient education materials



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## What's still missing

- National urgent care prescribing data
- Effective incentive structure for urgent care
- Accessible infrastructure for urgent care quality improvement

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## Our Wishlist

- National urgent care database
- Building a business case for good antibiotic stewardship
  - Aligning payer, accreditation, electronic health record company, and urgent care providers and operators
  - Incentive?
    - Positive: Carrots not sticks (e.g., based on achieving set goal or number of inappropriate prescribing averted, soft-steering)
    - Negative: Competition for one pot of funds, payment deduction, etc.
- Services to make easier for small businesses to practice stewardship

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# Addressing Antimicrobial Resistance through Research at NIH/NIAID

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

**9-11 October, 2019**  
**GWU, Washington DC**



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## NIH and NIAID

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### **NIH.** National Institutes of Health.

Largest public funder of biomedical research worldwide.

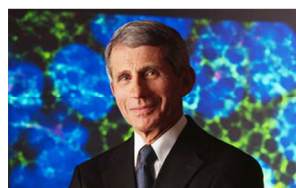
Director: Francis Collins, MD



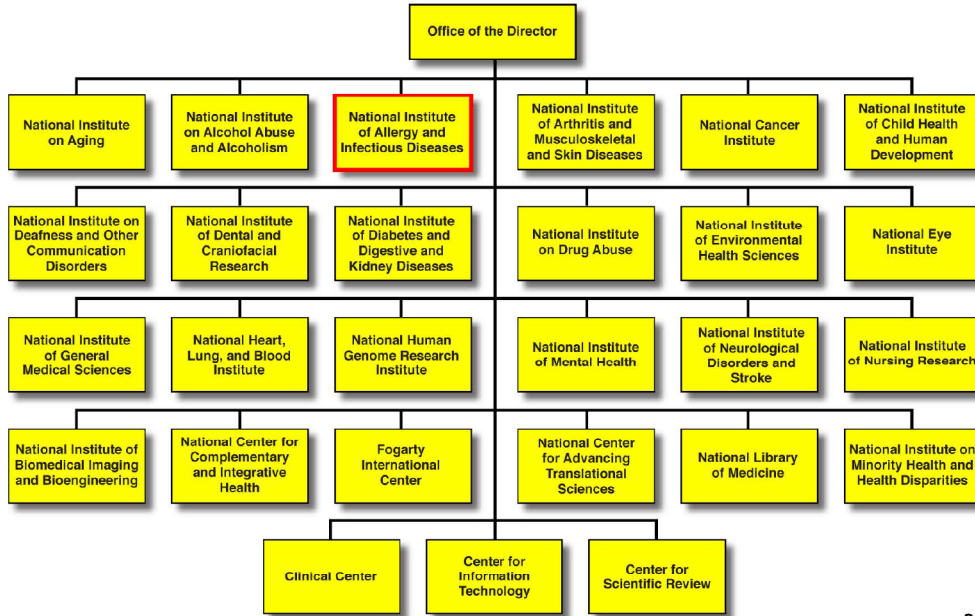
### **NIAID.** National Institute of Allergy and Infectious Diseases.

Lead institute on antimicrobial and antibacterial resistance.

Director: Anthony Fauci, MD

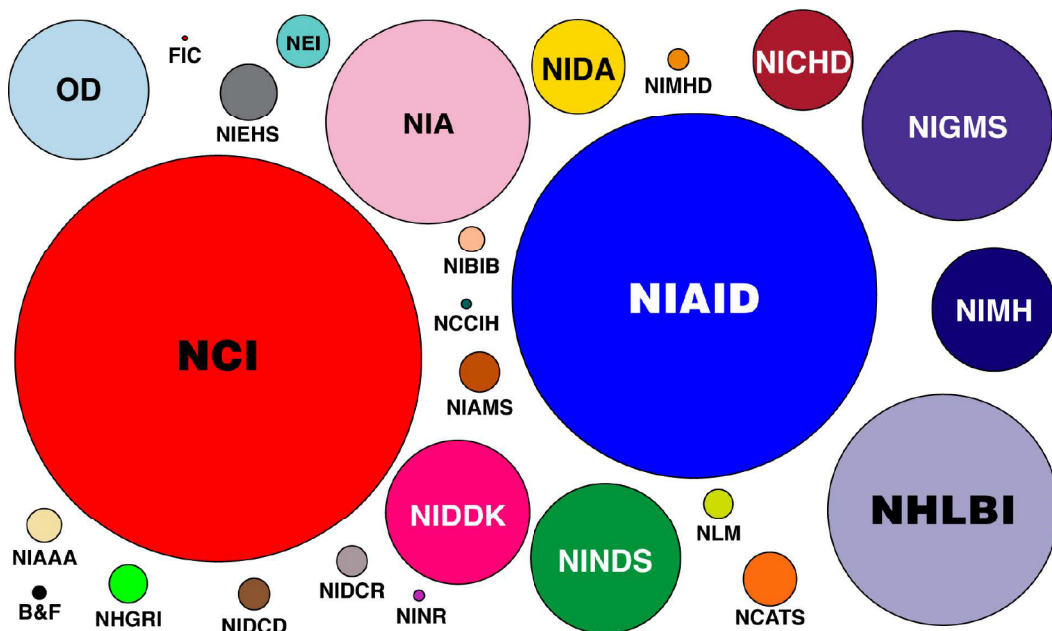


# National Institutes of Health



6/2018

# National Institutes of Health



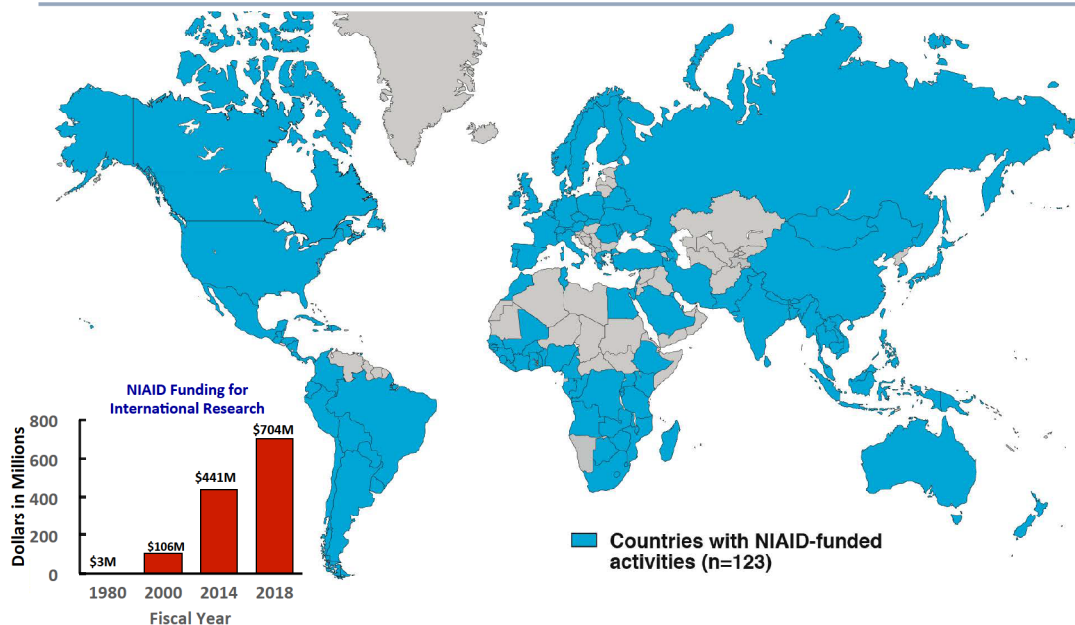
## FY 2019 Enacted Budget for 8 Largest NIH Institutes

NCI	\$6.1B
<b>NIAID</b>	<b>\$5.5B</b>
NHLBI	\$3.5B
NIA	\$3.1B
NIGMS	\$2.9B
NINDS	\$2.3B
NIDDK	\$2.2B
NIMH	\$1.9B

Total NIH Budget (enacted): \$39.3B

AS Fauci/NIAID

## NIAID Global Health Research, FY 2018



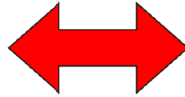
AS Fauci/NIAID



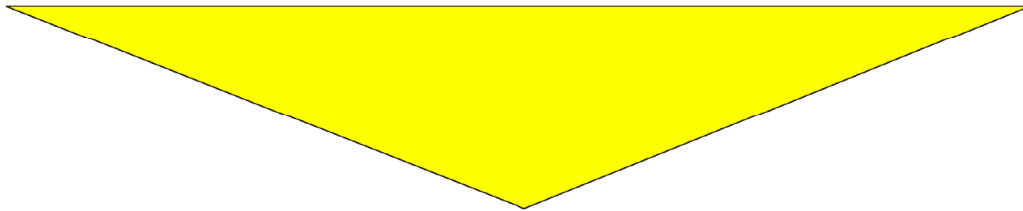
## NIAID Research: A Dual Mandate

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Maintain and “grow” a robust basic and applied research portfolio in microbiology, infectious diseases, immunology and immune-mediated diseases



Respond rapidly to emerging and re-emerging disease threats



**New/Improved Interventions**

AS Fauci/NIAID

## NIAID Strategic Priorities: FY 2019

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- Maintain a robust portfolio of basic research on infectious diseases and immunology
- Develop a safe and effective HIV vaccine, improved combination prevention strategies, optimization of treatment modalities, and novel approaches towards a cure for HIV infection
- Explore new multidisciplinary approaches to develop a universal influenza vaccine and enhance effectiveness of seasonal influenza vaccines
- Develop novel platform technologies and medical countermeasures for emerging and re-emerging infectious diseases such as tuberculosis, malaria, antibiotic-resistant bacteria, and biodefense
- Expand the study of human immunology and develop medical interventions for immune-mediated diseases with emphasis on immune tolerance strategies

AS Fauci/NIAID

# AMR Has Moved from Scientific to Political Discussions

- G7
- G20
- UN General Assembly

... among others

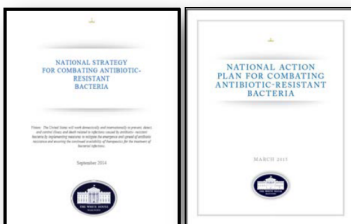
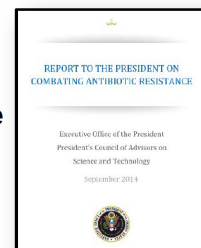


## US Government Response to the Public Health Threat of Antibiotic Resistance



**Presidential Executive Order 13676:**  
*Combating Antibiotic-Resistant Bacteria*

**President's Council of Advisors on Science and Technology (PCAST) Report**

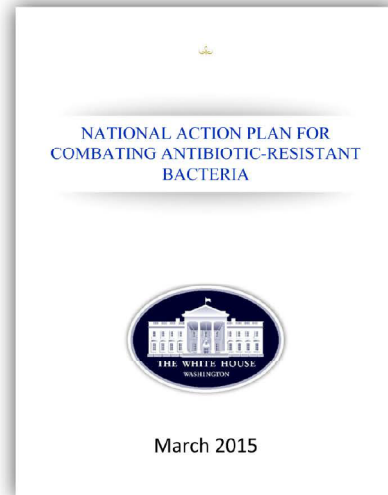


**National Strategy for Combating Antibiotic-Resistant Bacteria; National Action Plan for Combating Antibiotic-Resistant Bacteria**

# National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB)

## ■ Plan goals for CARB:

- Stewardship
- Surveillance
- Diagnostics
- Research
- International Collaboration



AS Fauci/NIAID

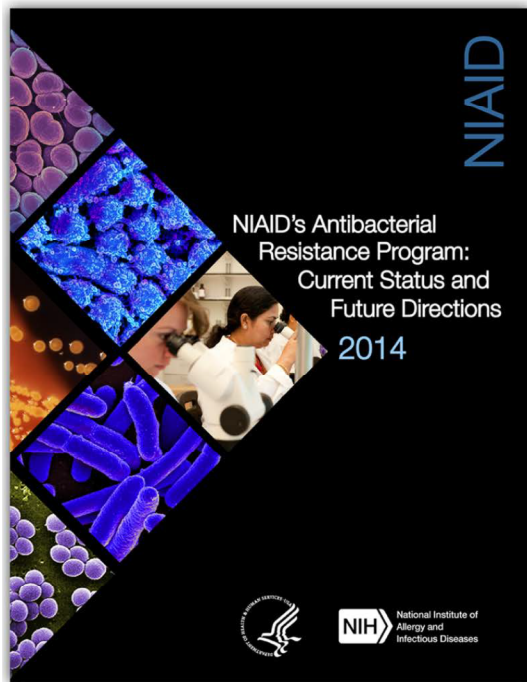
## NIAID Has a Key Role in Advancing the CARB National Action Plan Goals

- Expand clinical research efforts, including the Antibacterial Resistance Leadership Group
- Develop National Sequence Database of antibiotic-resistant bacteria
- Optimize treatment regimens to reduce emergence of resistance
- Conduct basic research to develop therapeutics
- Support pipeline of new drug candidates
- Incentivize development of diagnostic devices
  - “Prize” competition with BARDA, FDA, and CDC (up to \$20M)

	CARB \$
FY 16	\$100M
FY 17	\$50M
FY18	\$50M
FY19	\$37M
<b>TOTAL</b>	<b>\$237M</b>

# NIAID Antibacterial Resistance Program

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



**Diagnosis, Prevention and  
Treatment**

Web Search Term: **NIAID AR pdf**

## Seven Strategic Approaches to Antimicrobial Resistance Research

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- **Systems Biology and Antibacterial Resistance: New Directions for Drug Discovery**
- **Harnessing the Immune System to Combat Bacterial Infections**
- **Disarm, But Leave Unharmful: Exploring Anti-Virulence Strategies**
- **Synthetic Microbiota: An Ecobiological Approach**
- **Less is Better: Diagnostics to Guide Use of Narrow-Spectrum Therapeutics**
- **Exploiting Natural Predators: the Specificity of Phage Therapy**
- **Teaching Old Drugs New Tricks: Extending the Clinical Utility of Antibacterial Drugs**

# NIAID's Recent AR Review



## Antimicrobial Resistance

HD Marston, DM Dixon, JM Knisely, TN Palmore, AS Fauci

- AMR crisis must be addressed with a multi-faceted approach including basic, clinical and translational research



AS Fauci/NIAID

## 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"><li>▪ In Vitro Activity (MICs)</li><li>▪ Synthesis and CMC</li><li>▪ ADME Assays</li><li>▪ Pharmacokinetics</li><li>▪ Safety and Toxicity Testing</li></ul>	<ul style="list-style-type: none"><li>▪ Assay Development</li><li>▪ Safety and Toxicity Testing</li><li>▪ Process Development</li><li>▪ Pilot and GMP Manufacturing</li><li>▪ Regulatory Activities</li></ul>	<ul style="list-style-type: none"><li>▪ Free Reagents: <a href="https://www.beiresources.org/">https://www.beiresources.org/</a></li><li>▪ Structural Genomics Services: <a href="https://www.niaid.nih.gov/research/structural-genomics-centers">https://www.niaid.nih.gov/research/structural-genomics-centers</a></li></ul>



# CARB-X

Combating Antibiotic Resistant Bacteria

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

## FUNDERS



National Institute of Allergy and Infectious Diseases



Federal Ministry of Education and Research

## ALLIANCE PARTNER

BILL & MELINDA GATES foundation

## ACCELERATORS



## CARB-X is investing > \$500 million in 2016-2021\*

Supporting R&D from around the world to address the most serious drug-resistant bacteria

- 44 funded projects thus far in 7 countries
- **\$126** million in awards
- >15 approved projects not yet announced
- Non-dilutive funding and accelerator support for the early development of antibiotics, rapid diagnostics, and vaccines



\* As of June 29, 2019, since CARB-X was launched in July 2016

# CARB-X Portfolio currently has 29 Projects in 5 Countries



## North America

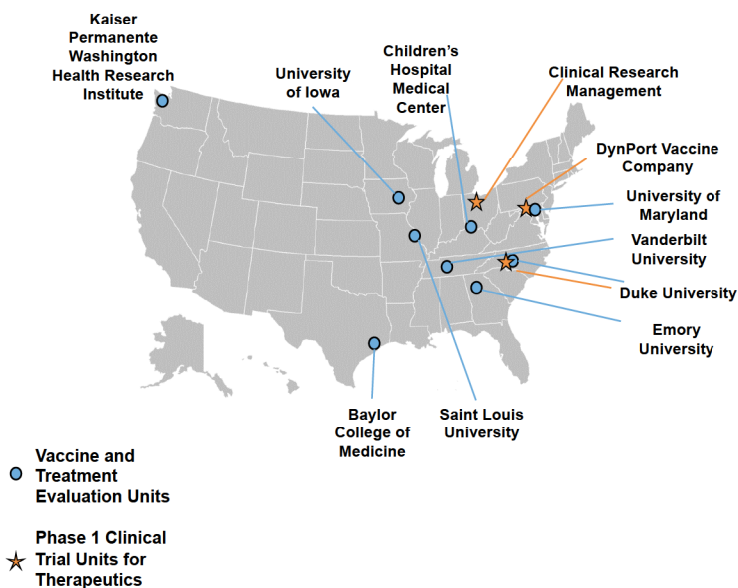
Forge Therapeutics** San Diego, CA	SciBac San Francisco, CA	T2 Biosystems Lexington, MA
Inhibrx La Jolla CA	Specific Diagnostics Mountain View, CA	Helixbind Inc. Marlborough, MA
Amicrobe Inc. Calsbad, CA	VenatoRx Pharmaceuticals Malvern, PA	Tetraphase Pharmaceuticals Watertown, MA
Talis Biomedical Menlo Park, CA	Integrated Biotherapeutics Rockville, MD	Zikani Therapeutics Watertown, MA
MicRx Pharmaceuticals Hayward, CA	Contrafect Corporation** Yonkers, NY	Entasis Therapeutics ** Waltham, MA
	Seres Therapeutics Cambridge, MA	Microbiotix Inc. Worcester, MA

## Europe and Asia

Proteus IRC Edinburgh, Scotland	Polyphor Allschwil, Switzerland
Oxford Drug Design Oxford, UK	Debiopharm International S.A.** Lausanne, Switzerland
Summit Therapeutics Oxford, UK	Bugworks Research India Pvt Ltd. Bangalore, India
Antabio Labège, France	
Idorsia Allschwil, Switzerland	

\* As of June 29, 2019  
\*\* More than 1 project funded

# Clinical Services



## 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

## Clinical Trial Themes: Examples

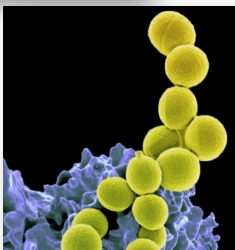
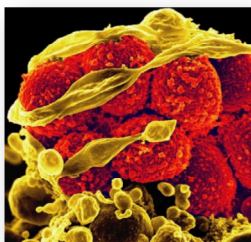
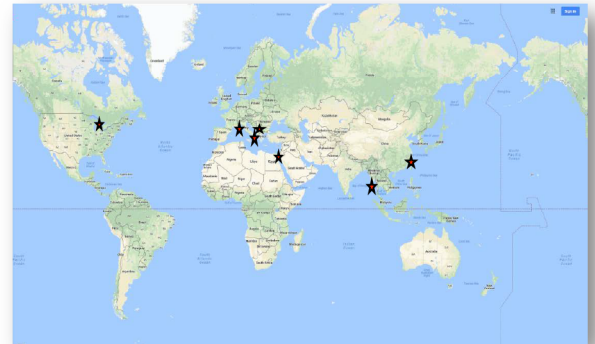


Photo Credits: NIAID Flickr

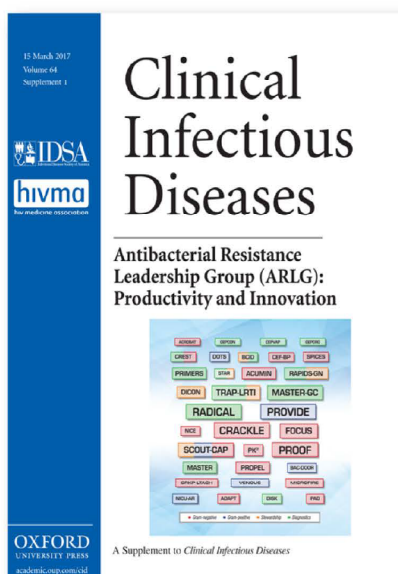
- Staphylococcal skin infections and bloodstream infections.
  - Do old drugs work? Are they needed? How long?
- Pediatric UTIs.
  - 10 vs 5 days
- Invasive Gram-negative infections (pneumonia or blood stream infections)
  - Issues:
    - Episodic and sporadic infections
    - Identifying quality sites with a steady stream and large number of infected patients

## Results: OVERCOME

- Randomized clinical trial to determine whether the treatment regimen of colistin combined with a carbapenem is associated with a decreased risk for all-cause mortality compared to colistin alone for patients with BSI and/or pneumonia due to XDR-GNB.
- US Sites: Detroit Medical Center/Wayne State University
- International sites: Israel-3, Thailand-1, Taiwan-1; Italy-1, Bulgaria-1; Greece-6.



## 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

# Translational/Product Development: Diagnostics

## Distinguish Viral Respiratory Infection



### A Host-Based RT-PCR Gene Expression Signature to Identify Acute Respiratory Viral Infection

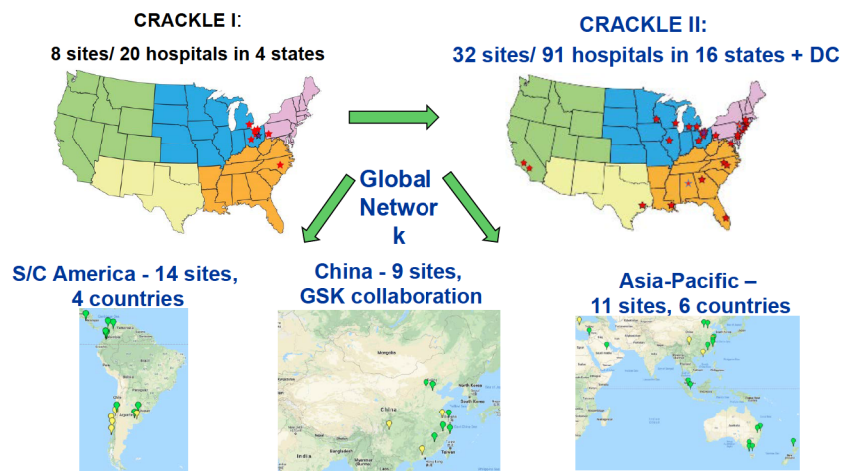
AK Zaas, GS Ginsburg et al.

18 September 2013

Vol. 5, Issue 203

- Duke University study, funded by NIAID
- RT-PCR test distinguishes viral from bacterial infection
- 102 emergency department patients, distinguished with 89% sensitivity, 94% specificity
- Could limit inappropriate prescription practices

## MDRO<sup>\*</sup> Network Evolution



\*MDRO = Multidrug-resistant organism



# The Power of Networking

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- Domestic Examples
  - US Interagency Task Force on AR
  - “CARB” Task Force;
  - Presidential Advisory Committee for “CARB”
- International Examples
  - TATFAR (Trans Atlantic Task Force on AR) currently US + European Union + Norway + Canada

## Transatlantic Task Force on Antimicrobial Resistance - TATFAR

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- US and EU membership
- Objective: Promote information exchange, coordination and co-operation between the US and the EU
- 2011: Report outlining 17 recommended areas for further collaboration
- 2014: Report on Implementation status
- [new 3<sup>rd</sup> bullet consolidate status timeline]



EU-US Summit –November 2009

# The Power of Networking

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- Domestic Examples
  - US Interagency Task Force on AR
  - “CARB” Task Force;
  - Presidential Advisory Committee for “CARB”
- International Examples
  - TATFAR (Trans Atlantic Task Force on AR) currently US + European Union + Norway + Canada
- TPTFAR - Trans Pacific Task Force on AR?

## NIH Testimony at Senate Hearing on Antimicrobial Resistance, 1999

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- February 25, 1999
- Antimicrobial Resistance: Solutions for this Growing Public Health Threat
- Testimony by Dr. Anthony S. Fauci to the Senate Committee on Health, Education, Labor, and Pensions; Subcommittee on Public Health and Safety



U.S. SENATE COMMITTEE ON  
Health, Education  
Labor & Pensions



## NIH Testimony at the Hearing on mcr-1, 2016

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- **June 14, 2016**
- **Combating Superbugs: U.S. Public Health Responses to AR**
- **Testimony by Dr. Dennis M. Dixon to the House Energy and Commerce Committee; Subcommittee on Oversight and Investigations**



## Thank you

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... For your interest