CARB National Action Plan Update – Department of Defense

Dr. Paige Waterman
Walter Reed Army Institute of Research

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Combating Antibiotic Resistant Bacteria (CARB) National Action Plan Objectives

2. Surveillance – of targeted multidrug-resistant bacteria

3. Diagnostics – rapid testing for AMR bacteria

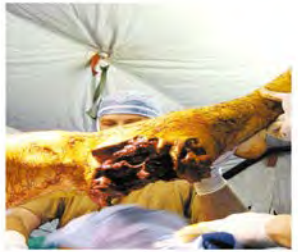
4. Therapeutics – new and novel approaches to treating AMR bacteria

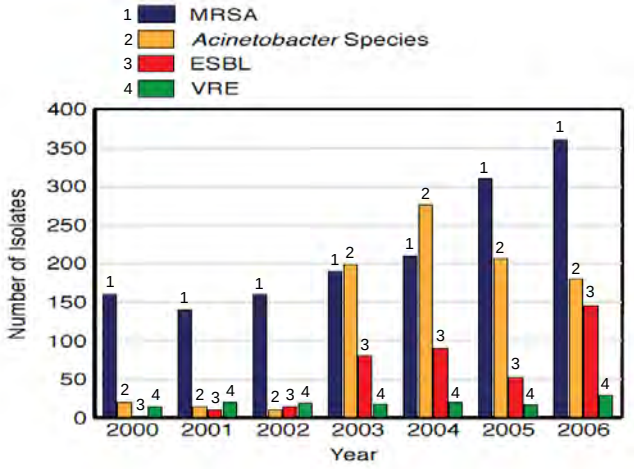
5. International Collaboration – for surveillance, collection, dissemination, and sharing of best practices re: AMR

AMR and the DoD

Multidrug Resistant organism Repository and Surveillance Network (MRSN) launched in 2009 as an infection control/quality improvement initiative

- Address gap in US and DoD response to AMR crisis
- Ensure safe, high-quality care within the MHS





Lesho EP et. al. *Med Aspects of Biol Warfare*. DoD, Army OTSG, Borden Institute. 201

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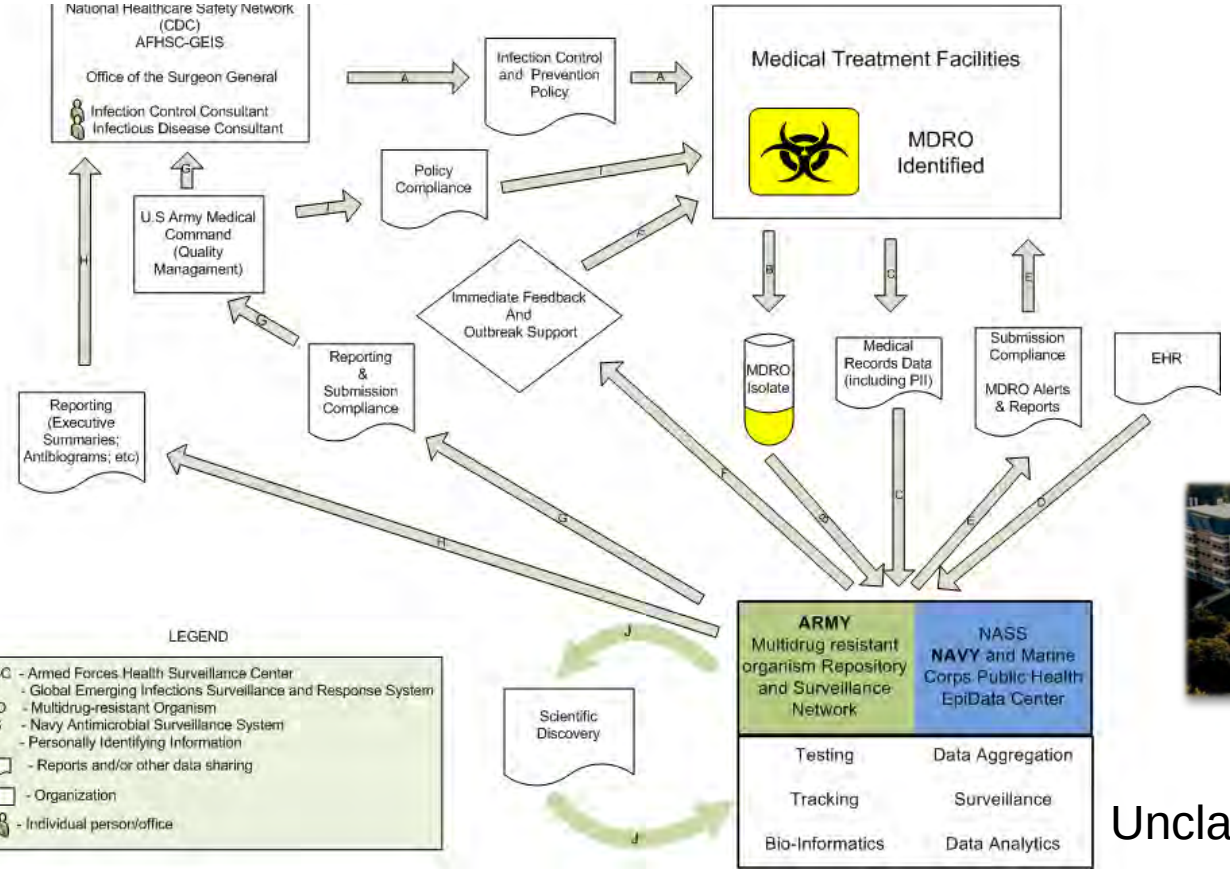
MRSN



Certified by the College of American Pathologists (CAP)

Unclassified

ARMoR (Antimicrobial Resistance Monitoring and Research)

VIEWPOINTS

The Antimicrobial Resistance Monitoring and Research (ARMoR) Program: The US Department of Defense Response to Escalating Antimicrobial Resistance

Emil P. Lesho,[1,3] Paige E. Waterman,[1,2,3] Uzo Chukwuma,[4] Kathryn McAuliffe,[4] Charlotte Neumann,[4] Michael D. Julius,[1] Helen Crouch,[5] Ruvani Chandrasekera,[2] Judith F. English,[6] Robert J. Clifford,[1] and Kent E. Kester[3]

[1]Multidrug-Resistant Organism Repository and Surveillance Network, Walter Reed Army Institute of Research, and [2]Armed Forces Health Surveillance Center, Global Emerging Infections Surveillance and Response System, Silver Spring, and [3]F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland; [4]Navy and Marine Corps Public Health, EpiData Center Department, Portsmouth, Virginia; [5]Brooke Army Medical Center, San Antonio, Texas; and [6]Navy Bureau of Medicine and Surgery, Falls Church, Virginia

(See the Editorial Commentary by Doron and Boucher on pages 398–400.)

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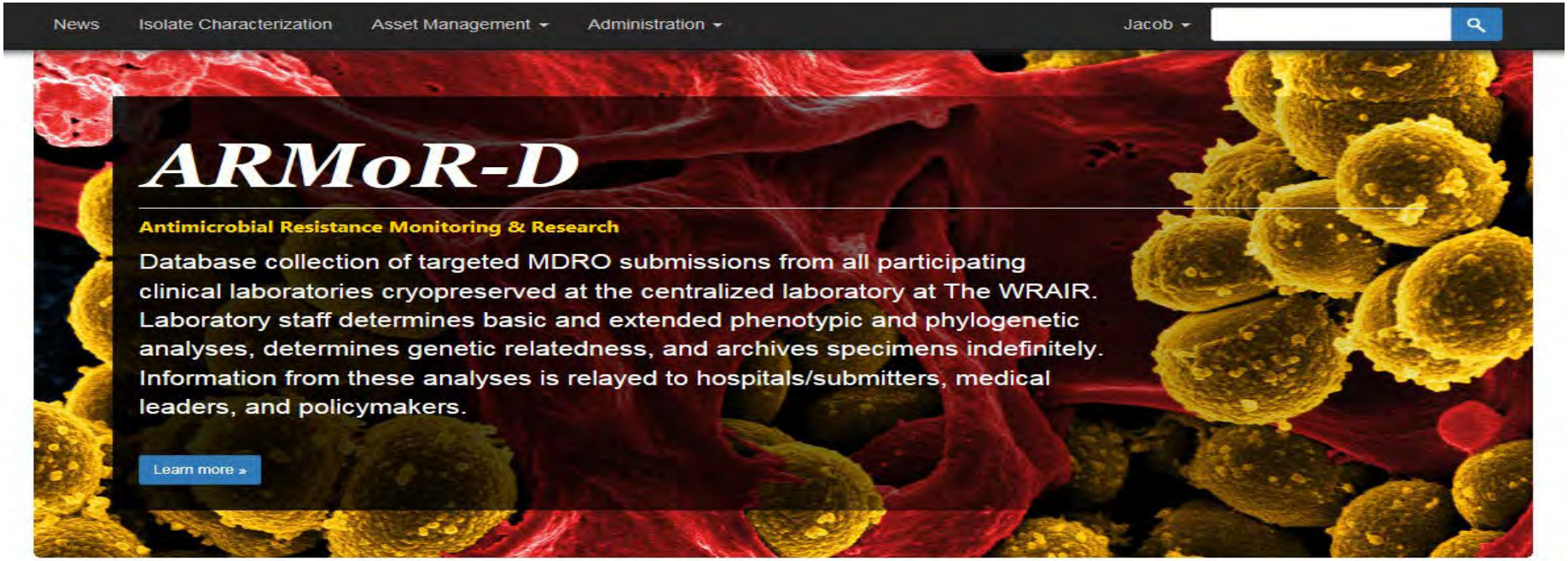


Responding to the epidemic of Gram-negative multidrug-resistant organism (MDRO) nosocomial and wound infections in the U.S. Military Health System, the Walter Reed Army Institute of Research (WRAIR) launched the Multidrug-resistant Organism Repository and Surveillance Network (MRSN) in July 2009.

Until then, no agency within the Department of Defense collected and characterized these organisms across the enterprise to inform best clinical practices, influence policy, and enhance infection prevention and control efforts.

The MRSN currently comprises a microbiology laboratory, organism repository and enterprise-wide network of military hospitals, to include those in combat zones. The network also receives participation by the Naval and Air Force medical facilities, in addition to other foreign military medical partners.

Pathogens of Interest

- **"MDR" ESKAPE+** pathogens
  - ***E****nterococcus faecium (vancomycin-resistant)*
  - ***S****taphylococcus aureus (methicillin-resistant)*
  - ***K****lebsiella pneumoniae*
  - ***A****cinetobacter spp*
  - ***P****seudomonas aeruginosa*
  - ***E****nterobacter spp*, ***E****scherichia coli*
- Carbapenem resistance; colistin resistance (mainly, enterobacteriaceae)
- *Clostridium difficile*

- Other clinically relevant organisms
  - Problematic identification or outbreak/transmission investigations

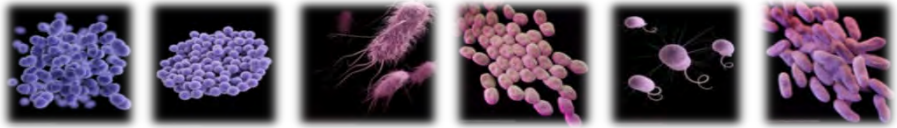
Ranked Tiered List of Infectious Disease Threats (2015)

Tier 1 - High user need, High operational risk

Rank	Disease
1	Malaria (all types)
2	Diarrhea - bacterial
3	Dengue fever
4	Influenza (Emerging high pathogenic with pandemic potential)
5	Chikungunya/Onyong-nyong, Ross River Fever
6	Norovirus
7	Mers-CoV and other Emerging Inf. Diseases
8	[illegible]
9	MDR Bacteria

Infectious Disease Threats to the US Military Prioritization Panel 2015

"MDR" definition: non-susceptible to 1+ drug from 3+ classes



Source: http://www.cdc.gov/media/subtopic/library/diseases.htm

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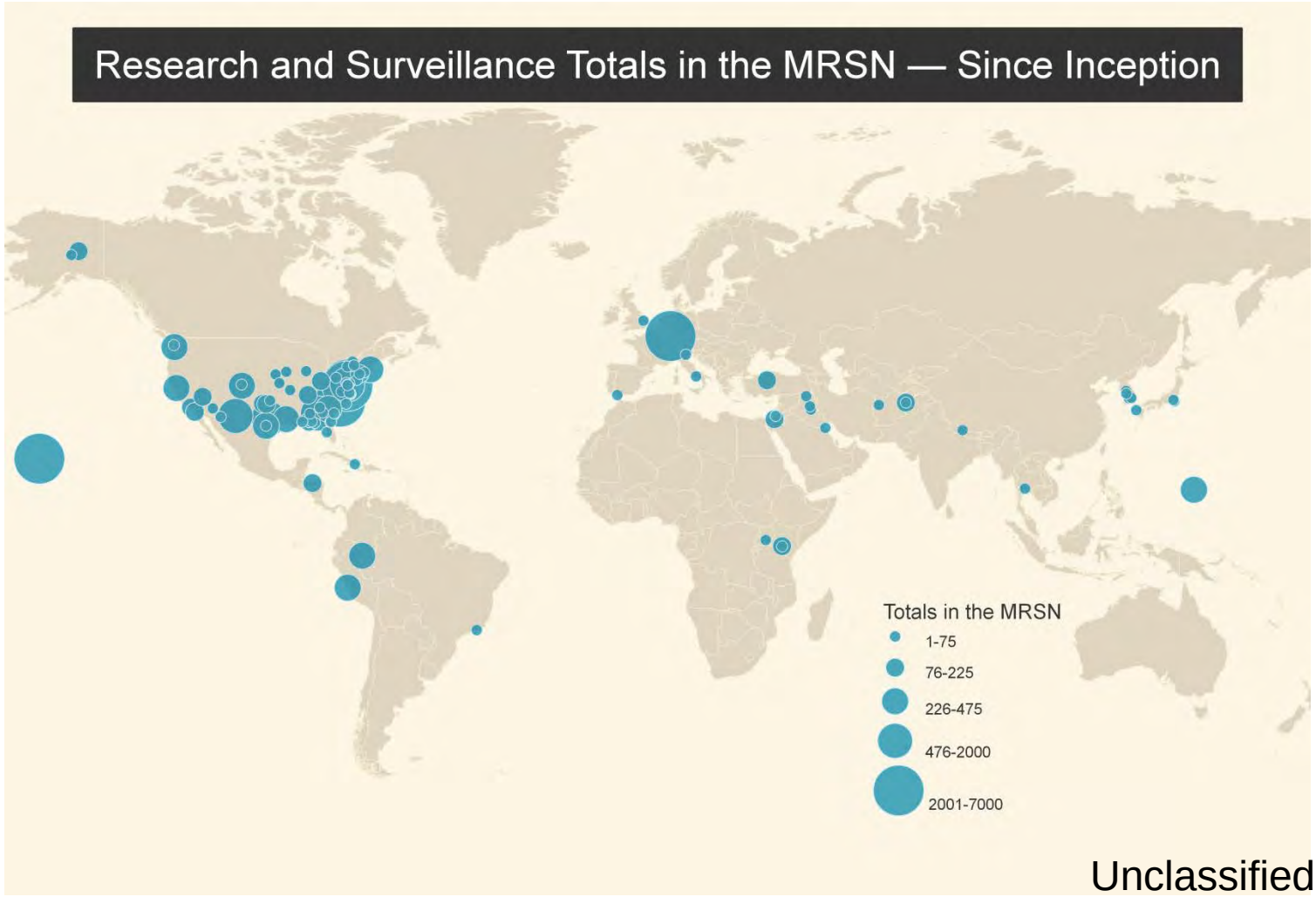
Research and Surveillance Totals in the MRSN — Since Inception



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ARMoR-Database (ARMoR-D)

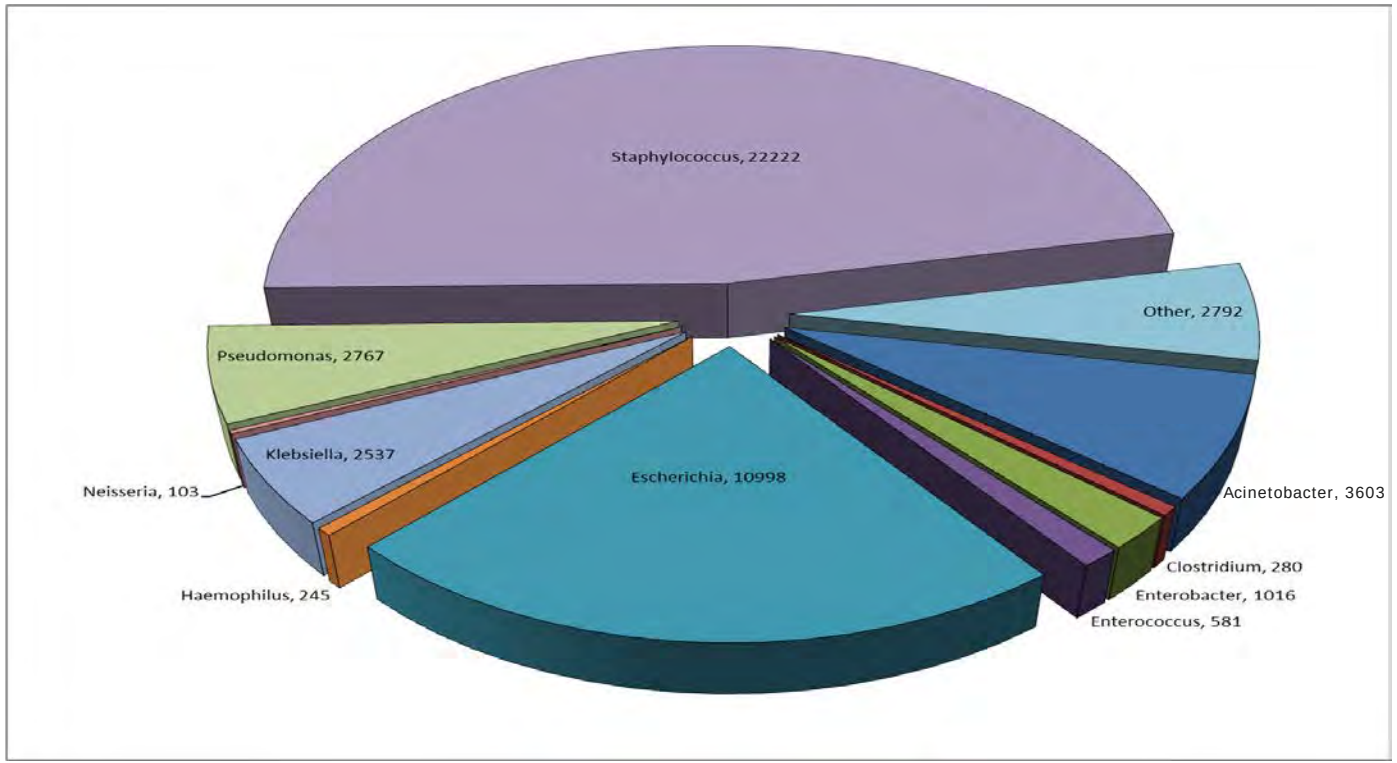
- Clinical and demographic data for each isolate
- Identification and susceptibility results from 3 platforms + any additional testing needed
- Multiplex PCR results
- Sequence data (16s ID, AMR and virulence genes)

As of August 31, 2017:

- **47,851 isolates from 34,082 patients**
- **122 facilities throughout the world**
- **1,175,255 tests performed**
- **2,841,964 results generated**

Repository contents

Over 47,000 isolates and 120 distinct species



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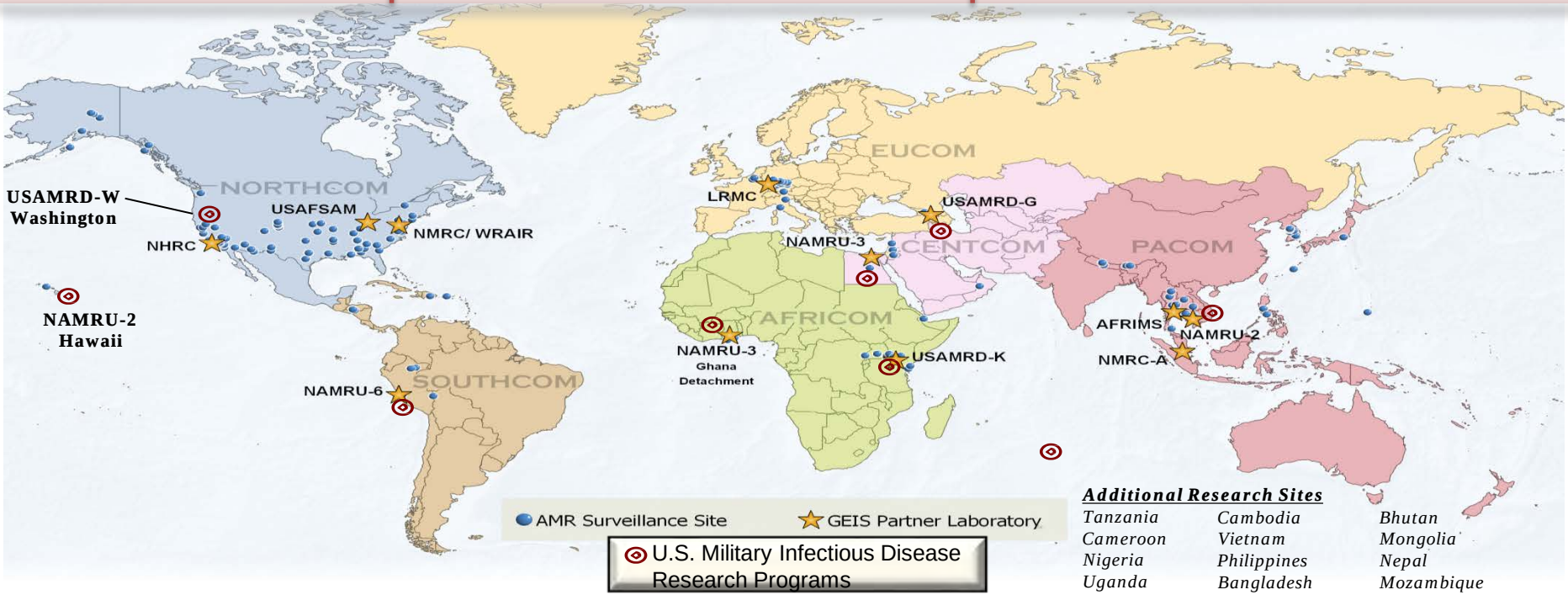
FY17 DoD AMR Activities

Number of Countries: 24	Number of Workplan Activities: 101	Number of Competed Proposals: 10



Global Emerging Infectious Diseases (GEIS)

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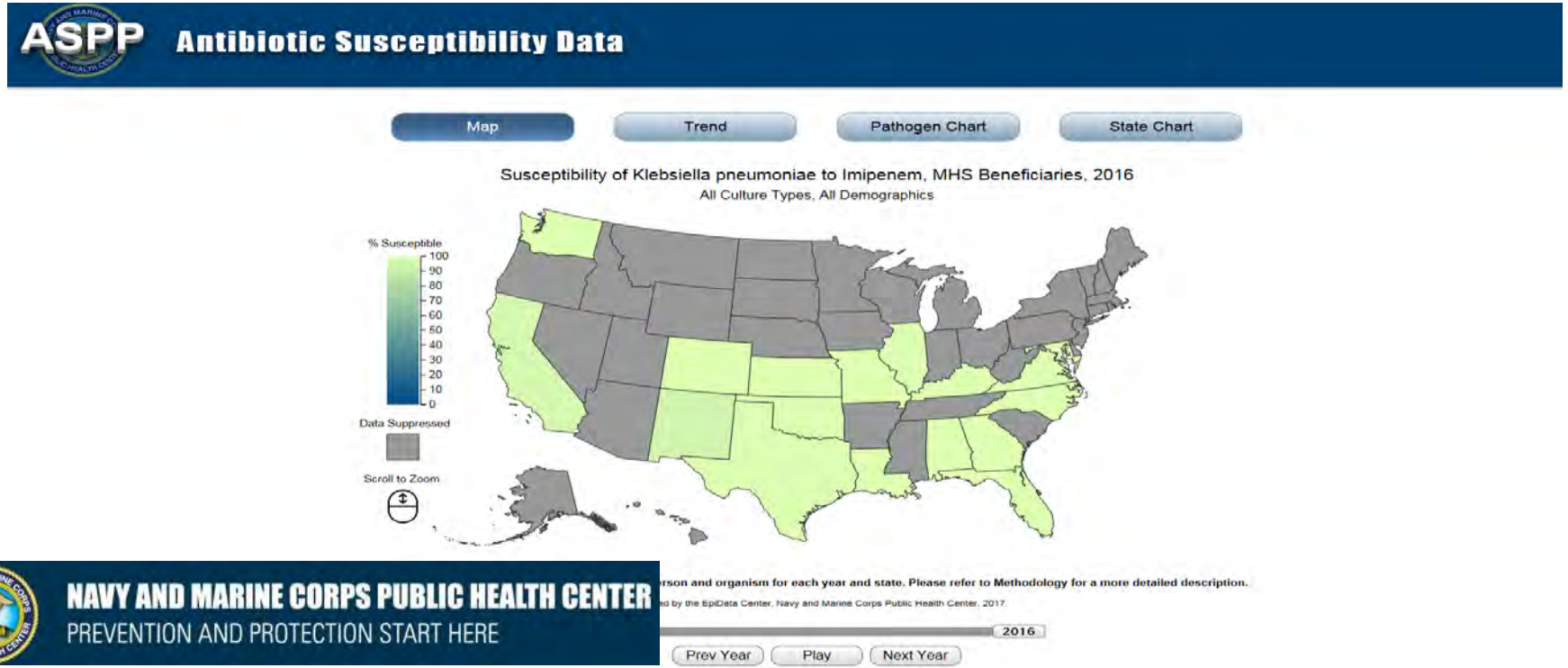
Regional Susceptibility Map



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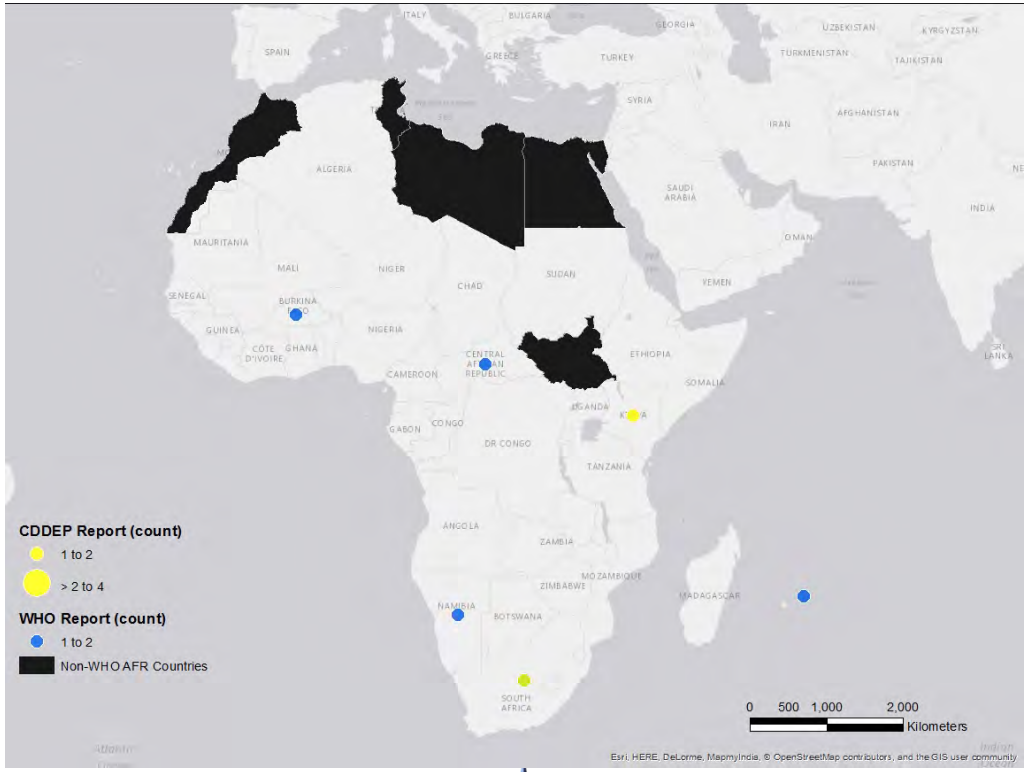
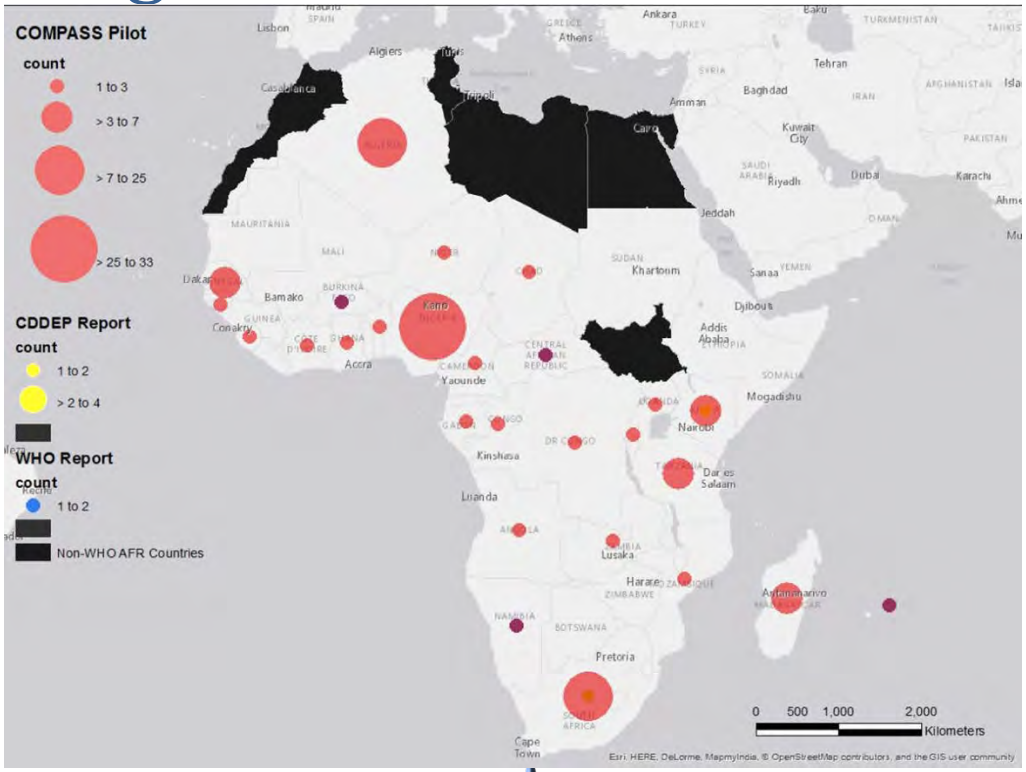
WHO and CDDEP reports: sparse data 6/47 WHO AFR countries



GEIS/Georgetown COMPASS

Discovered ~ 140 additional data sources/studies including on 21 more WHO AFR nations



GEIS/Georgetown COMPASS

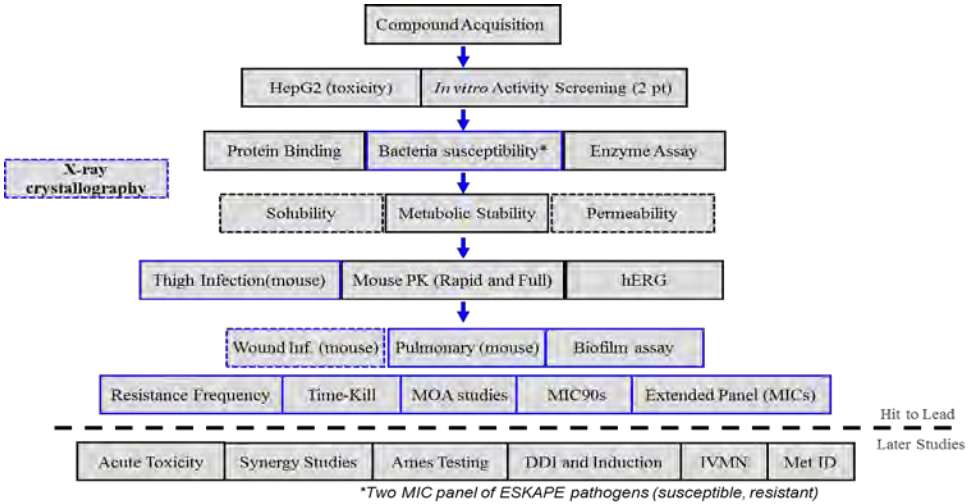
Goal 3: Therapeutics

WRAIR – Small Molecule AB Drug Discovery

FY16-20 Objectives:

- Discover agents effective against military relevant strains and biofilms
- Deliver 1-2 viable compounds by FY20 that can be transitioned into advanced development

Gated-Tier Test Strategy:

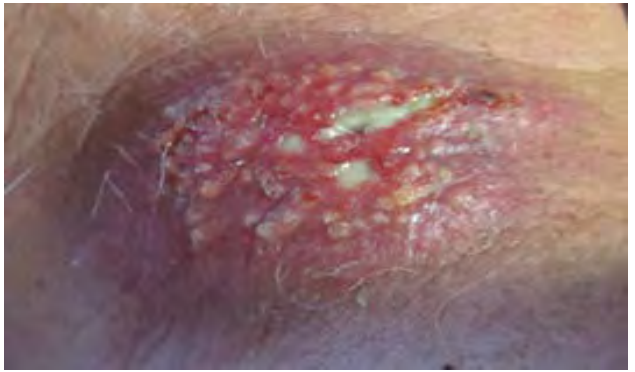


FY 17 Accomplishments:

- Completed 60% screening of the proprietary AB compound collection, "Bugbox", identifying promising chemical series
  - Evaluated late-stage pre-clinical candidate *in vivo* models of potential military use
- NCATS - Identified combination of three FDA-approved drugs that demonstrated efficacy against MDR KP, currently evaluating *in vivo* efficacy
- Initiated Year 1 activities with 3 industry/academic entities in DEC16
- Results from three internal programs nearing decision points in 1st QTR FY18

Staphylococcus aureus vaccine

- For the prevention of SSTI
- Basic trainees (Ft. Benning)
- 1st Phase I trial vaccination planned 2018



IDCRP

Uniformed Services University

NIH National Institute of Allergy and Infectious Diseases

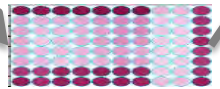
Intravenous Phage Therapy to Overcome Multi Drug Resistant *A. baumannii* Infection in Human

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

Robert T. Schooley, M.D.[1*], Biswajit Biswas, Ph.D.[2,3*], Jason J. Gill, Ph.D.[4,5], Adriana Hernandez-Morales, M.S.[6], Jacob Lancaster[2], Lauren Lessor[2], Jeremy J. Barr, Ph.D.[7,15], Sharon L. Reed, M.D.[1,8], Forest Rohwer, Ph.D.[7], Sean Benler, Ph.D.[7], Anca M. Segall, Ph.D.[7], Randy Taplitz, M.D.[1], Davey M. Smith, M.D., M.A.S.[1], Kim Kerr, M.D.[1], Monika Kumaraswamy, M.D.[1], Victor Nizet, M.D.[9,10], Leo Lin, Ph.D.[9], Melanie D. McCauley, M.D.[1], Steffanie A. Strathdee, Ph.D.[1], Constance A. Benson, M.D.[1], Robert K. Pope, Ph. D.[11], Brian M. Letson[11], Andrew C. Pieczl, M.D.[12], Alfred J. Mateczun, M.D.[2], Katherine E. Citwn, Ph.D.[13], James M. Regeimbal, Ph.D.[2], Luis A. Estrella, Ph.D.[2], David M. Wolfe, Ph.D.[2], Matthew S. Henry, M.S.[2,3], Javier Quinones, M.S.[2,3], Scott Salka[14], Kimberly A. Bishop-Lilly, Ph.D.[2,3], Ry Young, Ph.D.[3,0], Theron Hamilton, Ph.D.[2]

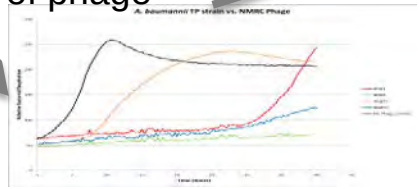
Development and use of personalized bacteriophage-based therapeutic cocktails to patient with a disseminated resistant *Acinetobacter baumannii* infection

Build library

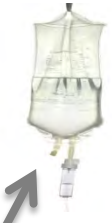


Screen pathogen

Identify efficacious individual phage and combinations of phage



Amplify and purify phage



Selection of therapeutic phages: within 18 hours of receiving the clinical isolate

Phage therapy outcome: clinical recovery within 48 hours of intravenous administration of the phage

Courtesy of Drs. Biswas , Hamilton & Schooley, Department of Genomics & Bioinformatics, BDRD, NMRC, Fort Detrick, MD & UCSD, CA

Goal 5: International

Notable FY17 AMR Accomplishments

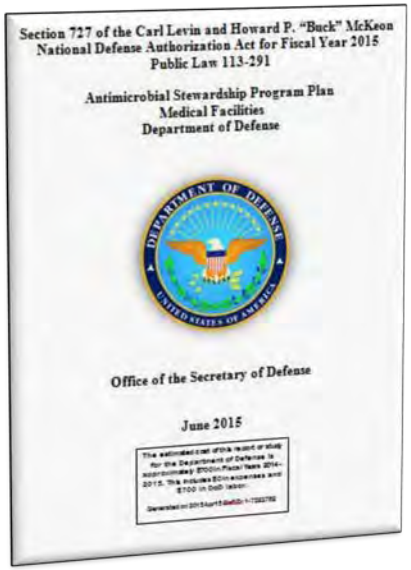
- The MRSN reported the **first U.S. human** *Escherichia coli* (*E. coli*) isolate carrying the **colistin resistance *mcr-1* gene** on a novel IncF plasmid (May, 2016).

- The Armed Forces Research Institute of Medical Sciences (AFRIMS), Thailand, identified ***mcr-1*** containing **colistin resistant gene in *Klebsiella pneumoniae*** from two patients in a medical facility in Thailand (confirmed, August, 2017).

- AFRIMS isolated **43 *bla*$_{NDM}$- and 2 *bla*$_{VIM}$-harboring *Enterobacteriaceae*** bacteria from patients in the Philippines from 2013-2016.

- The Naval Medical Research Unit-6 (NAMRU-6) identified the **first *Acinetobacter baumannii*** strain confirmed with **New Delhi metallo-beta-lactamase-1** (NDM-1) in Peru (August, 2017).

- Georgetown University piloted a **mapping tool** which captured highly diverse and potentially complementary streams of information to create and make publicly available a map of **CRE**, as well as to help identify and remedy gaps in data and understanding. The AFRICA pilot **substantially added to existing efforts to map CRE** spread and risks, including visibility into at least **10 additional nations**.



Summary

- Expand and standardize AMR surveillance program
- Develop and maintain active pipeline for small molecule discovery
- Develop programs for vaccines, bacteriophage to treat AMR
- Engage in collaborations for rapid **diagnostics**
- Continue Global Health Engagement with military/federal/civilian counterparts globally
- Provide feedback and technical assistance to researchers and clinicians