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# California Antimicrobial Resistance Laboratory Network

Presented by Webinar  
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# Objectives

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- Present the CDC's national Antibiotic Resistance Laboratory Network (ARLN)
  - Describe the CDC ARLN's "detect, respond, prevent, and innovate" strategy
  - Define the role of the Washington State Public Health Laboratory in the ARLN
  - Introduce the California AR Laboratory Network
  - Discuss how the California AR Laboratory Network will interface with the national ARLN
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# California Antimicrobial Resistance Laboratory Network – Kickoff Session

## Guests

### Centers for Disease Control

Jean Patel, PhD, D(ABMM)

Deputy Director, Office of Antimicrobial Resistance,  
National Center for Emerging Zoonotic and Infectious Diseases

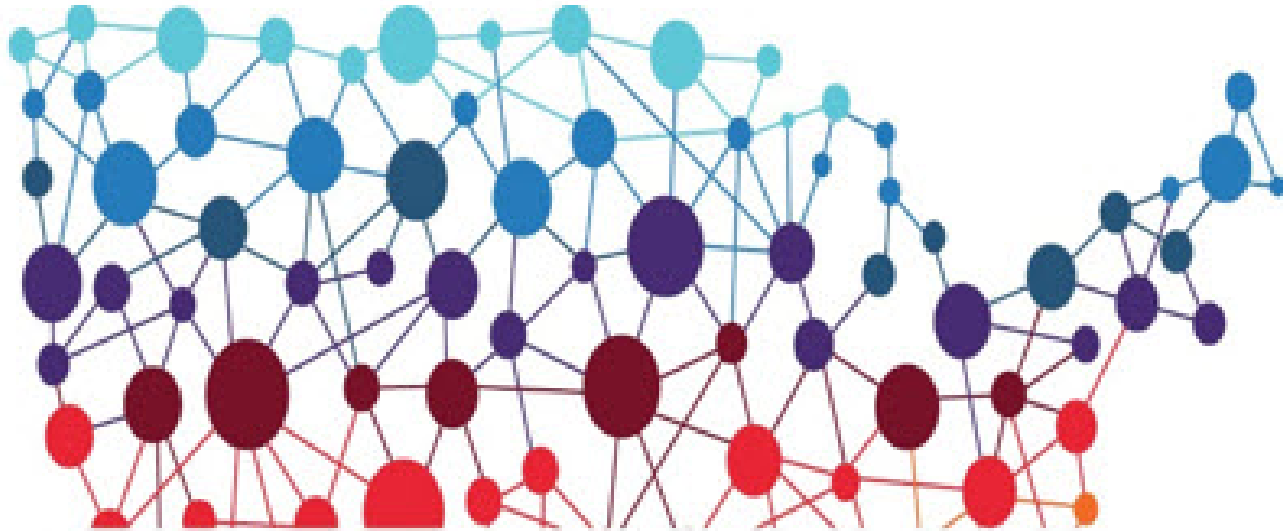
Allison C Brown, PhD, MPH

Lead, AR Capacities and Special Studies Team  
Clinical and Environmental Microbiology Branch  
Division of Healthcare Quality Promotion

### Washington State

Sopheay Hun, MBA, MLS(ASCP)

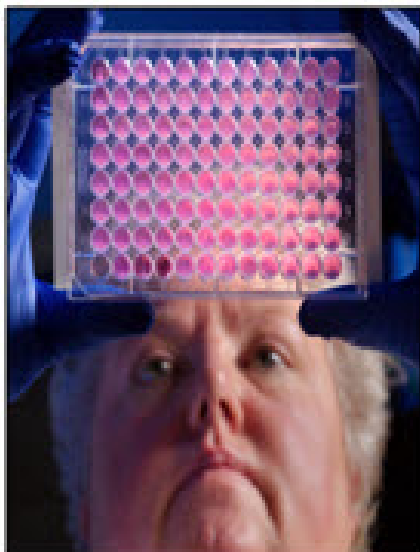
Antimicrobial Resistance Regional Laboratory (ARLN) Supervisor  
Washington State Department of Health  
Public Health Laboratories



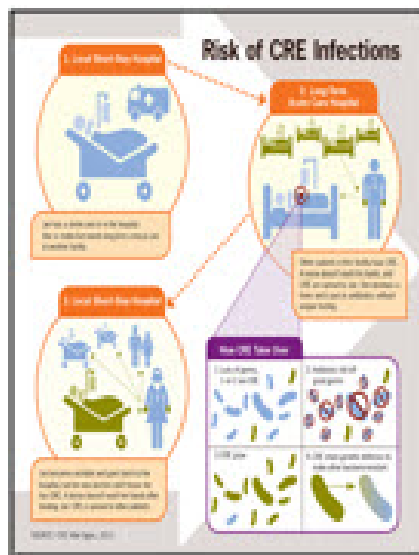
# ARLABnetwork

**Activities Focused on DHQP  
Pathogens**

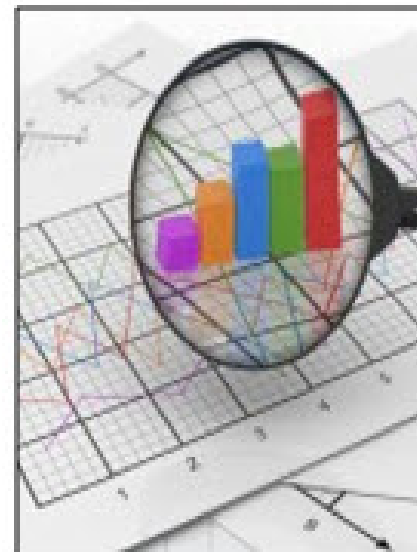
# Main Activities



Core Testing for CRE/CRPA



Colonization Testing

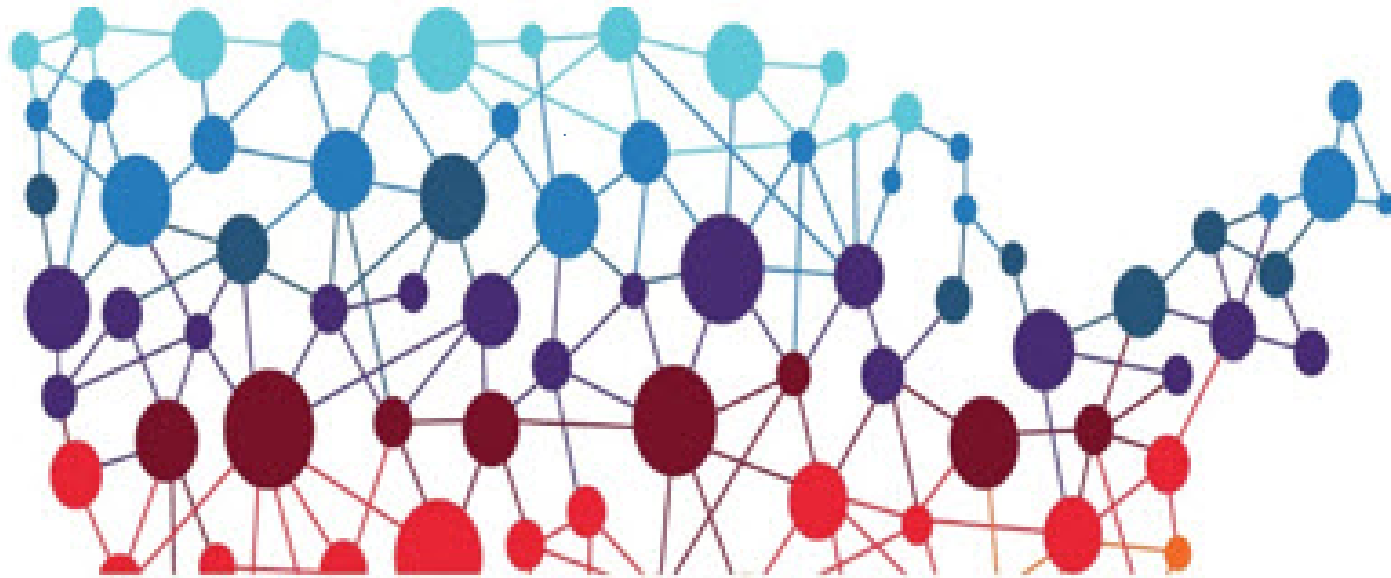


Enhanced Surveillance

# Objectives

- Increase testing capacities
  - 55 sites nationwide
  - 7 regional labs (overlap PulseNet regions)
- Improve infection control
  - Detect of CRE-infected/colonized patients
  - Isolate contacts to decrease transmission
- Characterize resistance mechanisms
  - Detect novel and emerging mechanisms
  - Understand distribution (facility, local, state, region)
- Estimate burden
  - Characterize colonizations, illnesses, transmission





# ARLABnetwork

**Core Testing for CRE/CRPA**

# Establishing a Network of Participating Facilities



## Goal

Establish network of clinical laboratories that provides isolates from all types of healthcare facilities

- At minimum, collect from laboratories serving short- and long-term acute care hospitals
- Ideally, include those serving long-term care facilities and other critical care settings



# Isolate Collection

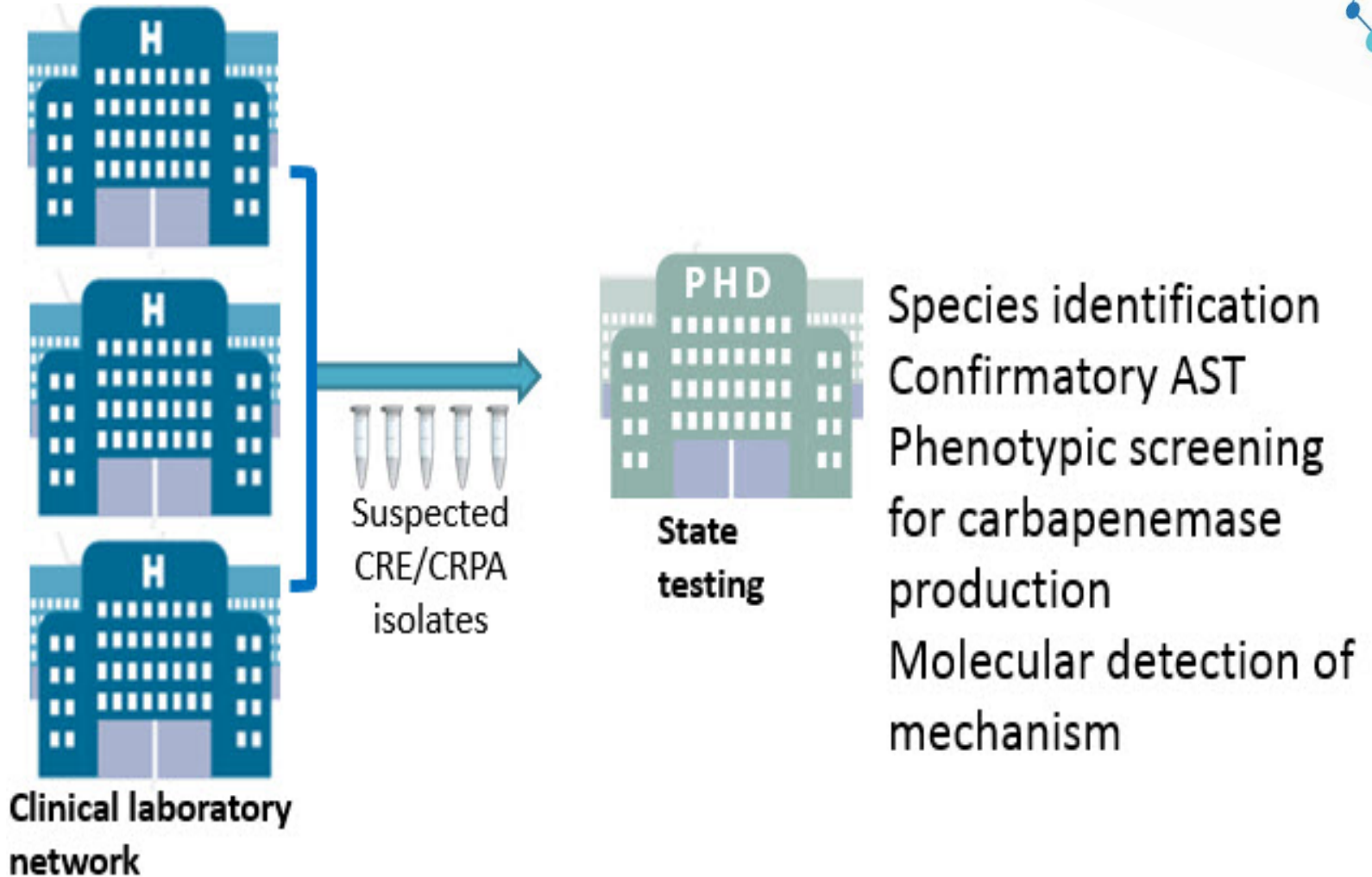
## CRE

- Target species: *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, and *Enterobacter* spp
- Resistant to imipenem, meropenem, doripenem, or ertapenem by standard AST methods

## CRPA

- All *Pseudomonas aeruginosa*
- Resistant to imipenem, meropenem, or doripenem by standard AST methods

# Methods



# Species Identification

Confirm species of Enterobacteriaceae and *Pseudomonas*

- MALDI-TOF mass spectrometry
- Automated instruments (VITEK 2, MicroScan, Phoenix, etc.)

# Antimicrobial Susceptibility Testing

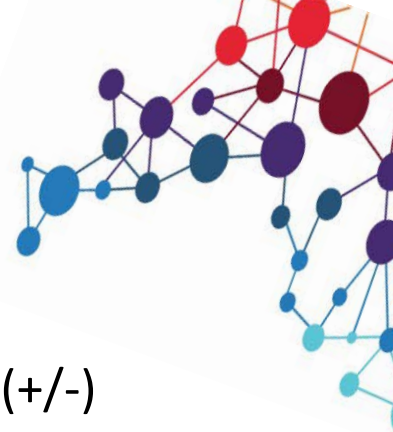


1. Confirm phenotypic detection of carbapenem resistance
2. Further characterize isolates (epidemiologically important resistance; possible mechanisms)
3. Method used should complement rather than duplicate those of submitting clinical laboratory

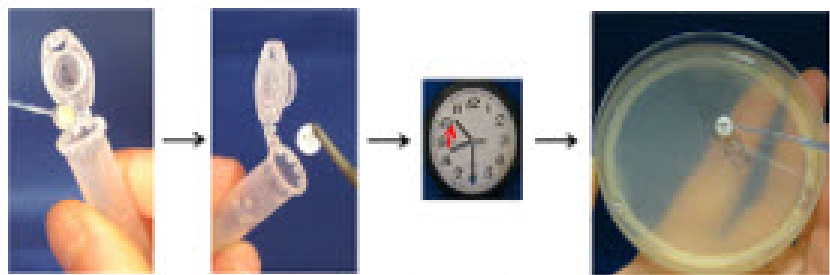
Drugs used to confirm and further characterize carbapenem-resistant Enterobacteriaceae (CRE) and carbapenem-resistant *P. aeruginosa* (CRPA)

Drug class	CRE	CRPA
Carbapenems	2 carbapenems (ertapenem and either imipenem, doripenem or meropenem)	2 carbapenems (selected from imipenem, doripenem and meropenem)
Cephems	Ceftazidime, ceftriaxone, and cefepime	ceftazidime and cefepime
B-lactam/B-lactamase inhibitor combinations	NA	piperacillin-tazobactam
Monobactams	aztreonam	aztreonam
Polymyxins	colistin	colistin

# Detection of Carbapenemase Production



- Determine whether an isolate produces a carbapenemase (+/-)
- Will not identify which one
- Carbapenem Inactivation Method (CIM) or CarbaNP assay



Suspend full loop of bacteria in H<sub>2</sub>O

Add 10 µg imipenem disk

Incubate for 2 hours 35°C

Place on Mueller Hinton agar inoculated with *E. coli* ATCC 25922



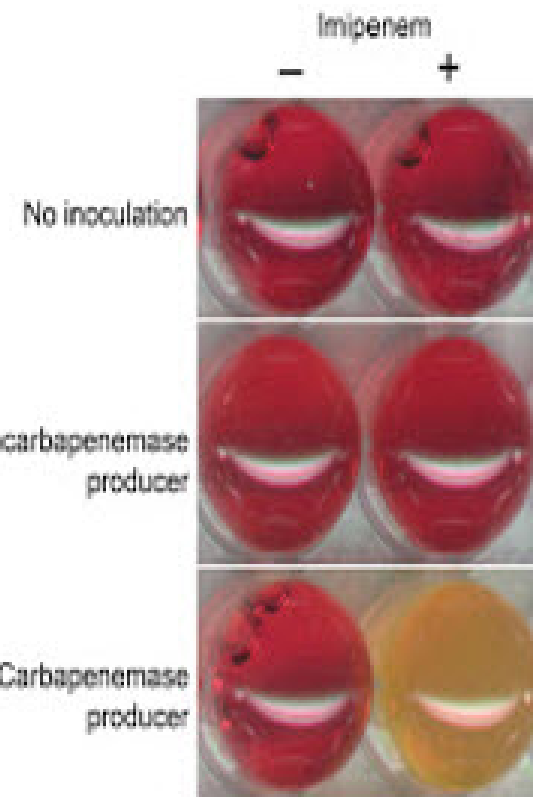
Incubate for at least 6 hours 35°C



Carbapenemase activity

No carbapenemase activity

Read presence or absence of inhibition zone





# Molecular Detection of Resistance Genes

Required and optional targets for CRE and CRPA

PCR	CRE	CRPA
<b>Required</b>	<i>bla</i> <sub>KPC</sub> , <i>bla</i> <sub>NDM</sub> , OXA-48-like genes	<i>bla</i> <sub>KPC</sub> , <i>bla</i> <sub>NDM</sub> , <i>bla</i> <sub>VIM</sub>
<b>Optional</b>	<i>bla</i> <sub>IMP</sub> , <i>bla</i> <sub>VIM</sub> , <i>mcr-1</i>	<i>bla</i> <sub>IMP</sub> , <i>mcr-1</i>

# Storage and Sending Isolates

- State labs will store all CRE and CRPA isolates with confirmed carbapenem resistance (one isolate per patient) for a **minimum of 2 years**
- When a novel and/or unusual mechanism is suspected, selected isolates will be submitted to designated AR regional lab **within 1 working day**
- CDC may request some isolates; requested isolates should be submitted to CDC **within 1 working day**

# Required Reporting



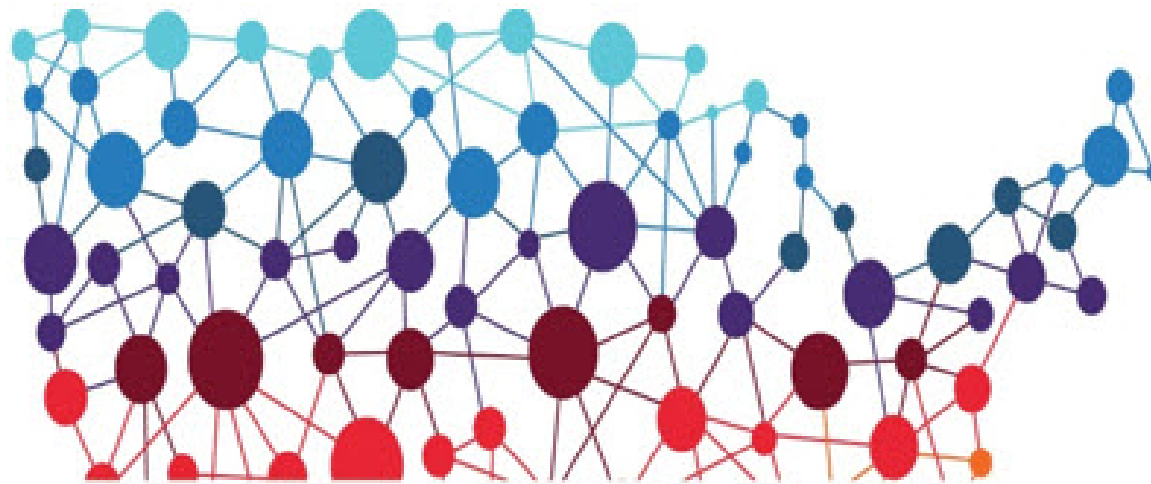
- **Within 1 working day of results:** Report any novel and/or unusual AMR in CRE or CRPA to CDC; send isolate to regional laboratory
  - Unusual AMR includes isolates with discordant results (phenotypic vs molecular) or unknown mechanisms of resistance
- **Within 2 working days of results:** Report results back to submitting clinical laboratories
  - Use secure communications
  - Include disclaimer that results can only be used to support infection prevention measures
  - Should not be a substitute for diagnostic procedures
  - Should not be used to guide clinical decisions



**Monthly:** Submit a report of all CRE and CRPA testing results to CDC







**ARLAB**network

## CRE Colonization Testing

# Colonization Testing: Rationale



- If patient isolate is carbapenem-resistant, facilities should consider screening for transmission
- Patients contacts might vary from setting to setting
- Minimum would include roommates of index patient for the duration of stay
- Longer stays may require broader group, point prevalence study(s) that includes unit or ward
- Colonization testing requires approval by state HAI coordinator and regional lab
- Appropriate uses should be approved unless capacity of regional lab has been/would be exceeded



# Colonization Testing Scenarios

Appropriate Use (One-Time Testing)	Non-Priority or Inappropriate Use (Ongoing Testing)
Screening roommates of new cases	Regional lab has exceeded capacity
Screening contacts of contaminated device	Routine inpatient screening
Point prevalence study (PPS) for new resistance or first identification of CRE	Admission screening
PPS when transmission suspected	Testing not linked to a facility or network prevention program

# Colonization Testing Turnaround

1 day turnaround time



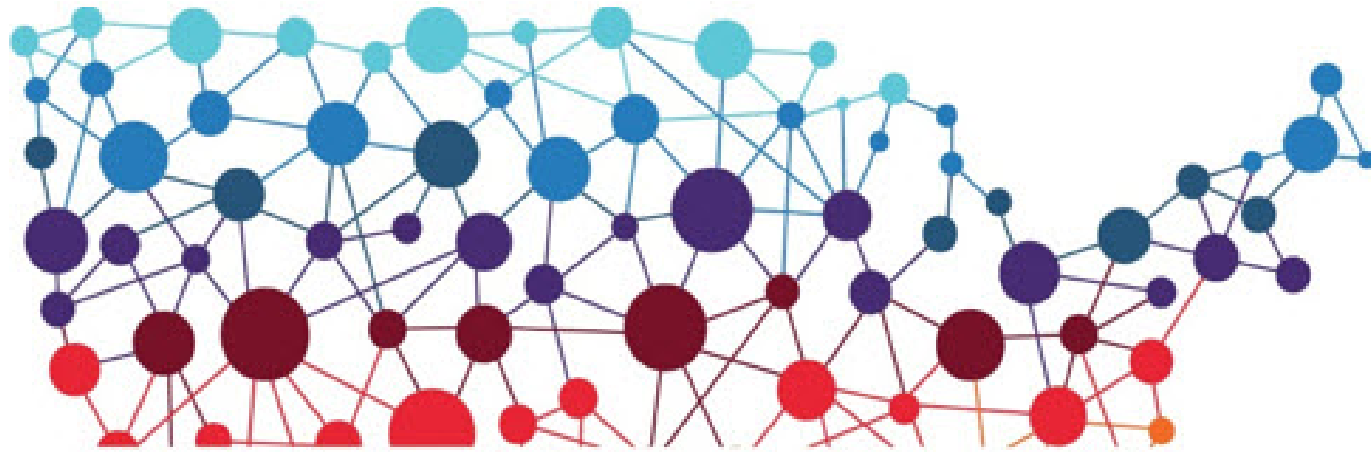
Initiate infection control/contact precautions

**Simultaneous reporting** to submitting facility and jurisdictional health department within **1 day** of results



Provide or request assistance; initiate investigation





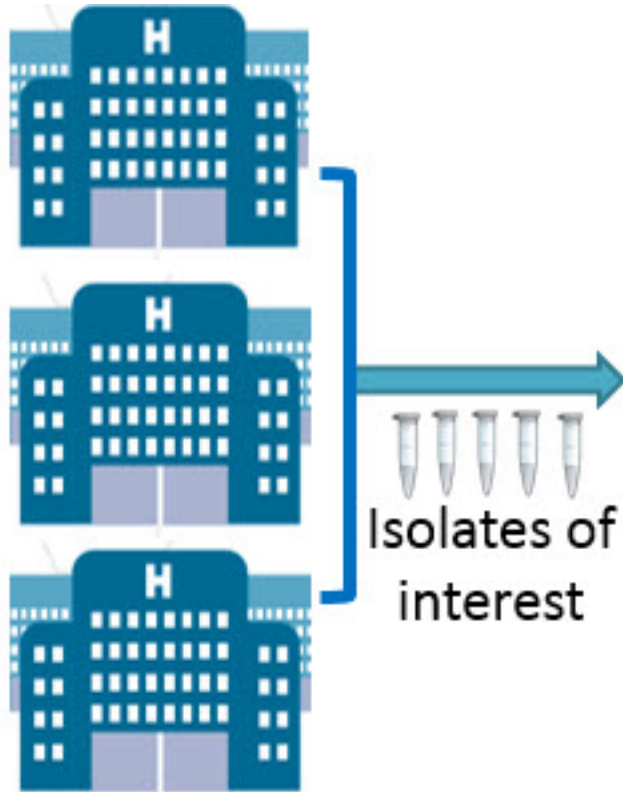
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## Enhanced Surveillance Activity

## K7 Activity 2

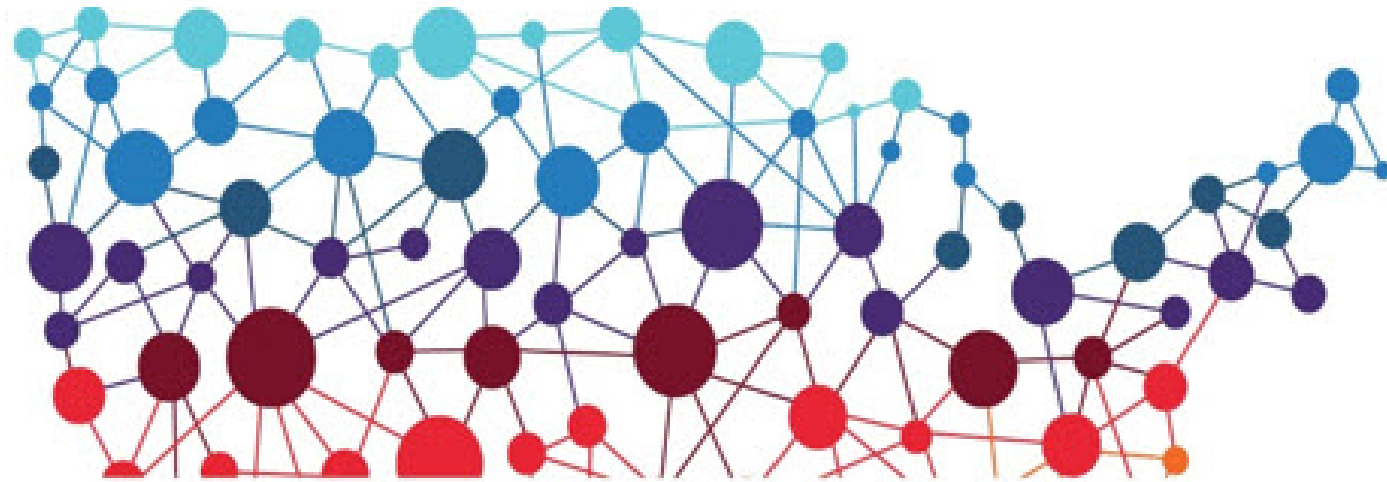
- Reference testing to better understand an emerging or changing AR threat
- Conducted by regional labs among network of collaborating clinical laboratories within jurisdictional states
- Flexible; may cover variety of different organisms
- Can assess utility and effectiveness of this system

# FY17: CR-Acinetobacter and mcr-1 genes in E. coli and Klebsiella spp.



- Species identification
- Confirmatory AST
- Phenotypic screening for carbapenemase production
- Molecular detection of mechanism

Regional network of clinical laboratories



# ARLABnetwork

## West Regional Lab



# West Regional Lab

- **Facility**

## ARLN West Region

Washington State Department of Health

Public Health Laboratories

1610 NE 150<sup>th</sup> Street

Shoreline, WA 98155

Phone (206) 418 – 5400

Fax (206) 418 – 5485



# West Regional Lab

- **ARLN West Region Leadership Team**

William A. Glover II, Ph.D., D(ABMM), MT(ASCP)  
Director of Science & Technology  
CLIA Director

Sopheay Hun, MBA, MLS(ASCP)  
ARLN Supervisor

Brian Hiatt  
Office Director for Microbiology

Marisa D'Angeli, MD, MPH  
Public Health & Epidemiologist



*Left to Right: Dr. William Glover, Maryann Watkins, Sopheay Hun  
November 2016*

# Overview

- **Update**
- **Testing**
- **Shipping**
- **Reporting**
- **Communication**



# Update



- **New ARLN lab construction started Nov. 1<sup>st</sup>**
- **Procurement process for capital equipment acquisitions**
- **Increase ARLN lab personnel capacity**
- **Working on IT infrastructure with APHL technical assistance support**
- **ARLN West Region lab team received training at CDC Nov. 1-4, 2016**

# West Regional Lab

- **CRE Surveillance Testing**

**State HAI  
approved  
CRE Colonization  
Testing**

*Infection Control  
Rapid One Day  
Reporting*

- Direct Molecular detection for most carbapenemase: KPC, NDM, VIM, OXA-48, IMP-1 group
- Only FDA-approved NAAT system at present for direct rectal swab
- Double swab allows use of 2<sup>nd</sup> swab for repeat PCR
- Stable for 5 days
- Quick visual reference job aids will be provided for proper collection



## West Regional Lab

- **Additional AR testing and emerging resistance detection**

State  
CRE  
Reference  
testing

State  
CRPA-  
Pseudomonas

State  
CR-  
Acinetobacter

Regional  
Candida  
susceptibility  
testing

Regional  
Candida ID  
confirmation,  
Candida auris

- 
- 
- **Training Assistance and Support for your State CRE program**

# West Regional Lab

- **Shipping**
- CDC paid for ARLN FedEx shipping account has been created for West region
- Quick reference instruction guide and login access for creating shipping labels for sending samples
- Shipping services are limited to FedEx Priority Overnight



FedEx®

# West Regional Lab

- **Reporting**



- Electronic Test Ordering and Resulting (ETOR) web-based portal in development for online reporting
- StarLIMS auto-fax results immediately to submitters and LHJ/public health upon completion of testing



# West Regional Lab

- **Communication**
- Regular state check-in conference calls
- Monthly ARLN West regional webinars
- Distribution email for ARLN West Region for questions, feedback and/or comments: [ARLN@doh.wa.gov](mailto:ARLN@doh.wa.gov)
- Any questions contact: Sopheay Hun  
[Sopheay.Hun@doh.wa.gov](mailto:Sopheay.Hun@doh.wa.gov)

# California Antimicrobial Resistance Laboratory Network

# California AR Lab Network Goals

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1. **Enhance situational awareness** of healthcare-associated AR pathogens by facilitating information and data sharing
2. **Connect healthcare facilities and laboratories to additional laboratory testing resources** to enhance patient care and infection control activities
3. **Strengthen collaboration** among clinical and public health laboratorians, infection control practitioners, and public health epidemiologists

# Laboratory Testing Resources – Initial Framework

Healthcare Providers and Laboratories	Local Public Health Laboratories	CDPH Microbial Diseases Laboratory	CDC ARLN (Washington State)
Work with local & state health department to understand when and where to submit isolates or specimens	CRE confirmation and characterization testing (e.g. CRE mechanism testing)*		CRE colonization testing of rectal swab specimens
Report outbreaks/clusters to local public health & L&C District Office	Genetic relatedness testing (e.g., whole genome sequencing)*		
			Characterization of novel/unusual resistance (e.g., <i>mcr-1</i> and other <i>mcr</i> variants, unusual <i>Candida</i> spp.)

\*Some testing may be available at local public health laboratories

# Los Angeles County Department of Public Health (LACDPH) Surveillance Project

- Enhanced lab surveillance to detect  $\beta$ -lactamases and carbapenem resistance mechanisms
  - Includes Maldi-TOF and modified Nanosphere BC-GN assay
  - Enrollment is open to labs currently not participating in enhanced surveillance
- Outbreaks should be reported to LACDPH Acute Communicable Disease Control
  - Isolates from healthcare facilities should be sent to LACDPH PHL
- For any enhanced surveillance enrollment or lab testing questions please contact Nicole Green, PhD, D(ABMM) at [nicgreen@ph.lacounty.gov](mailto:nicgreen@ph.lacounty.gov)

# California AR Lab Network – Data Sharing

- Aggregated reports
- Cumulative antibiograms
- Quarterly reports
  - Carbapenem Resistant Enterobacteriaceae
  - Multidrug Resistant (MDR) *Pseudomonas aeruginosa* and *Acinetobacter baumannii*
  - For labs that perform carbapenemase testing: numbers of carbapenemase-producing isolates, by specific carbapenemase (where possible)
- Any other unusual or novel resistance phenotype or mechanism

# Submission of Aggregated Data

- Annual Cumulative Antibiograms
- Include questions about development and design
  - Population-specific? Diagnosis specific?
  - How are repeat isolates represented?
  - How are <30 isolates per category handled?
  - If selective/cascade reporting, are suppressed results included?
  - Does your laboratory use the most updated CLSI breakpoints?

# Submission of Aggregated Data

- Proposed quarterly data collection templates for specific AR pathogens
- Excel-based, multiple submission options (fax, email)

Organism	Total Isolates Tested	No. Isolates Resistant to at Least one Carbapenem*	No. Isolates Documented to Possess Carbapenemase**
<i>Klebsiella pneumoniae</i>			
<i>Klebsiella oxytoca</i>			
<i>E. coli</i>			
<i>Enterobacter aerogenes</i>			
<i>Enterobacter cloacae</i>			
Other <i>Enterobacter</i> species			
	Total Isolates Tested	No. Isolates Multidrug Resistant (MDR)†	No. Isolates Documented to Possess Carbapenemase**
<i>Acinetobacter baumannii</i>			
<i>Pseudomonas aeruginosa</i>			

- \*Using updated CLSI Breakpoints
- \*\*If carbapenemase testing is performed; labs will be asked to indicate number of isolates identified with each carbapenemase(s), by organism
- †Multidrug resistance defined by Magiorakos et al. 2011



# Timeline

- December 2016
  - Participants submit 2015 cumulative antibiogram
  - Provide feedback on proposed data sharing template
  
- January-February 2017
  - Participants submit Q4 2016 aggregated data
  
- March 2017
  - Next quarterly conference call
  - Present preliminary reports of aggregated AR data

# Questions?

For more information, please contact  
the HAI Program at  
[HAIProgram@cdph.ca.gov](mailto:HAIProgram@cdph.ca.gov)

Thank you