

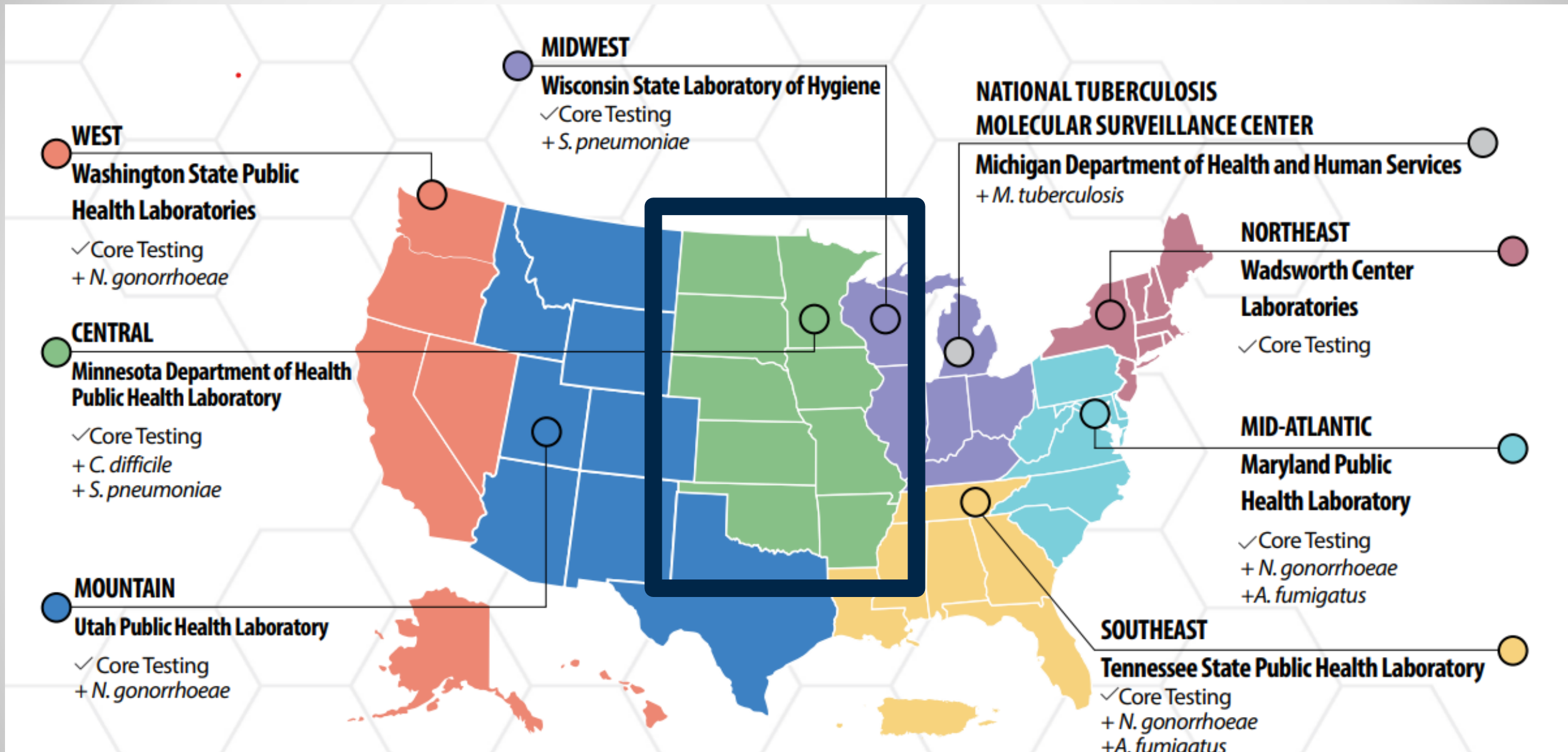


Regional and State Public Health Perspective on AMR Testing

Paula Snippes Vagnone | Coordinator, AR Lab Network Central Region

Objectives

- Describe the testing provide by AR Lab Network Regional and State labs to combat antibiotic resistance
- Demonstrate the AR Lab Network: “System in Action”

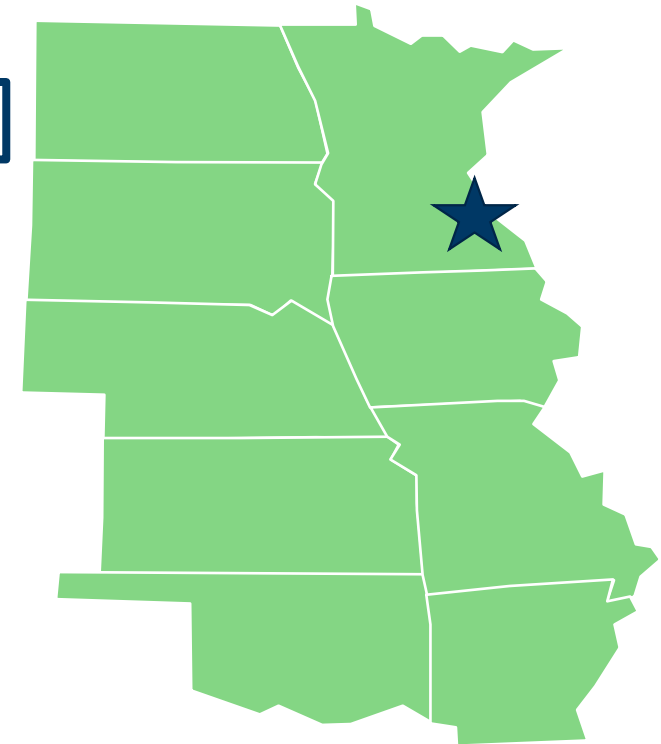


AR Lab Network – Central Region

Regional/State Lab Roles:

- Core Testing of Isolates:
 - CRE/CRPA detection and ID
 - Molecular carbapenemase ID
 - Carbapenem-resistant Acinetobacter (CRA)
 - Candida ID
 - AST and AFST
- Colonization Screening
 - CPOs
 - *Candida auris*
- Consultation and test onboarding assistance

Core Testing for State PHLs



- Optional for non-regional State PHLs
- SHARP funding increases capacity

AR Lab Network – Central Region

CRO Colonization Screening – Rectal Swabs

- Determine colonization of patient with one or more of the most common carbapenemase
 - Admission screening
 - Outbreak investigation
- Cepheid Xpert Carba-R assay
 - FDA-approved, real-time PCR assay
 - Quick turn-around-time; easy to use

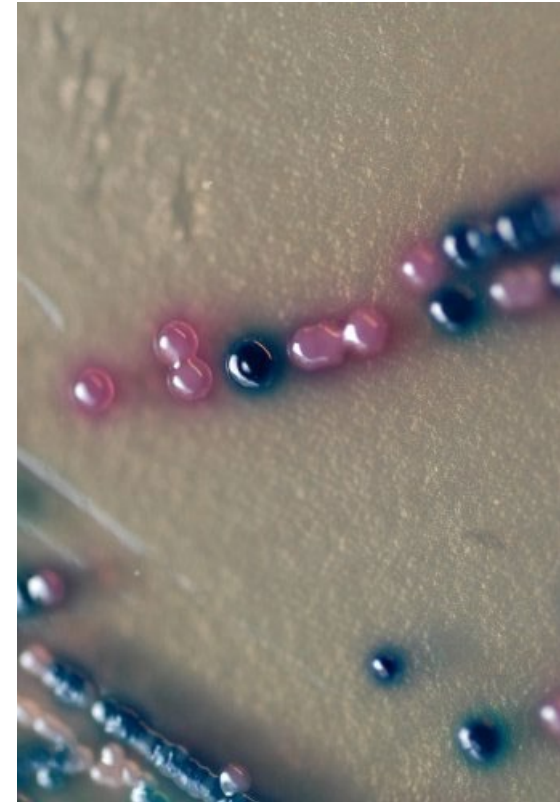
Free-of-Charge



AR Lab Network – Central Region

CRO Colonization Screening - Culture Method

- Isolation of organism(s) harboring the carbapenemase gene(s)
- Carba-R-positive specimens
- Recovered isolates tested by WGS to determine relatedness
 - Assist in infection prevention and response

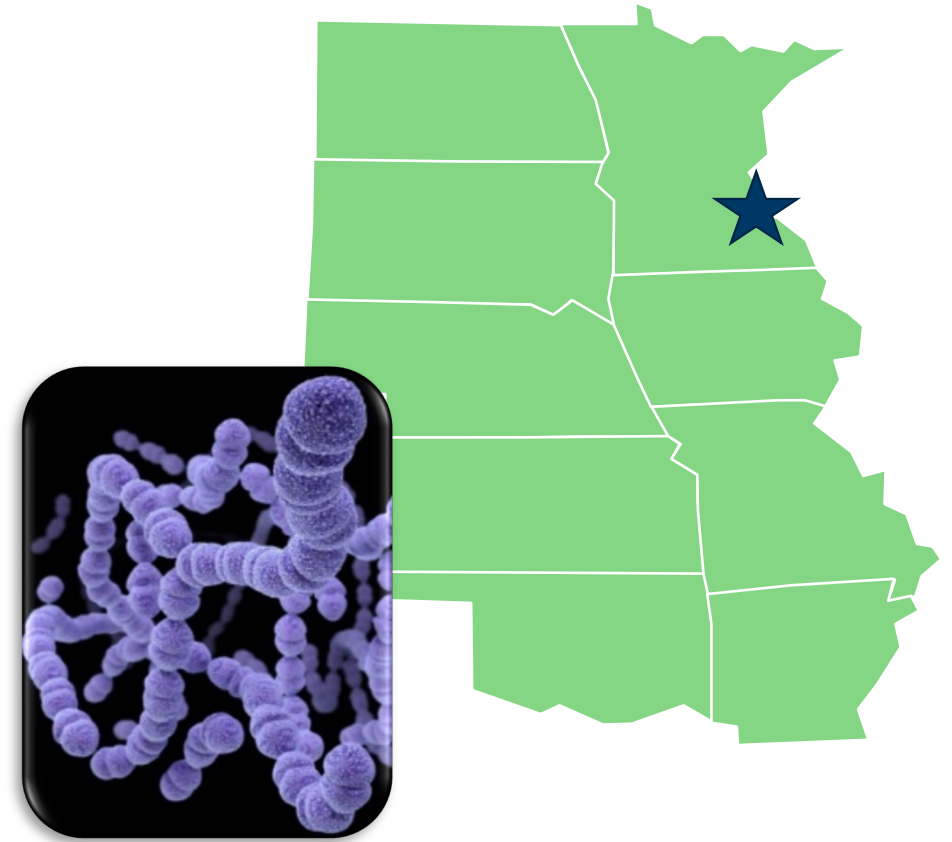


AR Lab Network – Central Region

Regional Lab Role:

Provide Supplemental Testing

- *Streptococcus pneumoniae*
 - 2 regional labs – Minnesota and Wisconsin
 - Provide serotyping results
 - **Purpose:** Identify antimicrobial resistance and emerging resistance traits – correlate with serotypes



AR Lab Network – Regional Labs



Provide Supplemental Testing – *N. gonorrhoeae*

- **4 regional labs:** Maryland, Tennessee, Utah, Washington
- **Testing:**
 - AST: agar-dilution
 - WGS
- **Purpose:** Build capacity for rapid detection, response, and monitoring of resistant *N. gonorrhoeae* through increased culturing and AST

AR Lab Network – Regional Labs

Provide Supplemental Testing – Expanded AST (ExAST)

- All Regions labs
- **Testing:** non-FDA cleared antibiotic combo
- **Purpose:** Provide antibiotic testing for serious infections where treatment options are very limited



AR Lab Network Expanded AST

Metallo- β -lactamase positive (NDM, VIM, IMP) Enterobacterales

- Among isolates collected in the AR Lab Network – approximately 4.5% of CRE and 13.7% of CP-CRE are NDM positive.
- 2018 Sanford Guide, and other guides such as “Up-to-Date”, recommend **ceftazidime-avibactam + aztreonam** for treatment of serious MBL infections – **key: aztreonam-avibactam**.
- Clinical labs are not able to test for susceptibility to this drug combination.

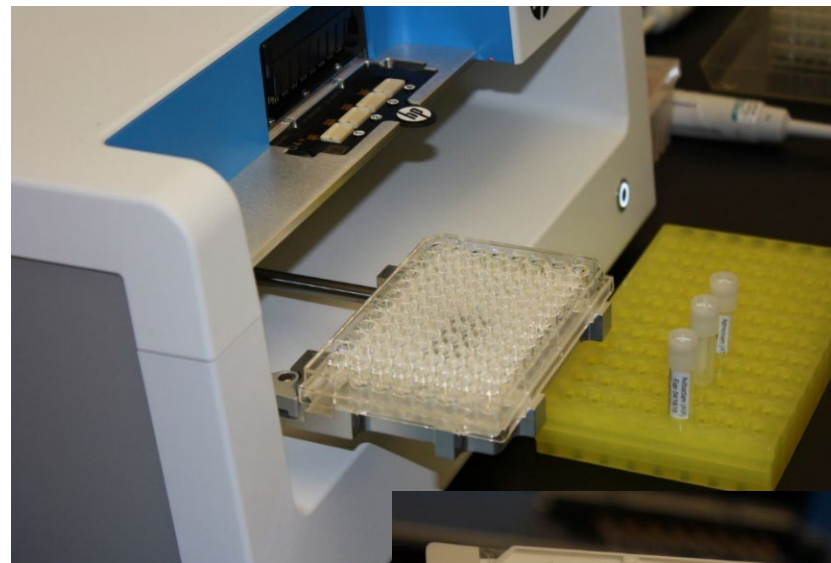
AR Lab Network Expanded AST

	Drugs for MDRO Gram-Negative Infections	Most Common CRE Types	
		KPC	NDM
FDA-Approved	Colistin	?	?
	Ceftazidime-Avibactam	✓	X
	Meropenem-Vaborbactam	✓	X
	Plazomicin	✓	?
	Imipenem-Relebactam	✓	X
Phase 3	Cefiderocol	✓	✓
	Aztreonam-Avibactam	✓	✓
	Cefepime-VNTR	✓	✓

- Colistin may be considered susceptible, but new data suggests colistin may provide little clinical benefit
- NDM-CRE usually carry a gene that confers resistance to all aminoglycosides including plazomicin
- **Aztreonam-avibactam** can be created by treating a patient with **ceftazidime-avibactam** and **aztreonam**

AR Lab Network Expanded AST

- Capacity found in AR Lab Network Regional Labs
- Closes the gap between new drug approval and the availability of testing methods in hospital labs
- Specialized inkjet printer allows for on-demand dispensing of reference AST panels containing new drugs
- Rapid reporting to improve care via AR Lab Network to hospitals for tailored patient treatment



AR Lab Network Expanded AST

Criteria for Testing

- Enterobacterales ONLY
 - Plans to expand to *P. aeruginosa* and possible *S. maltophilia*
- Non-susceptible to all β -lactams tested, including ceftazidime-avibactam or meropenem-vaborbactam
- MBL-producing isolates (NDM, VIM, or IMP) confirmed using molecular testing and are highly resistant to all, or majority, of antimicrobials tested

AR Lab Network Expanded AST

Antibiotics tested:

- **Ceftazidime-avibactam:** MIC and interpretations
- **Aztreonam:** MIC and interpretations
- **Aztreonam-avibactam:** MIC with no interpretations
- **Aztreonam-ceftazidime-avibactam combo:** NOT reported

CLIA-compliant testing

- AST results returned within 3 working days, upon isolate receipt, if testing is for guiding therapy

AR Lab Network Expanded AST

Expanded Antimicrobial Susceptibility Testing for Hard-to-Treat Infections

Antimicrobial susceptibility testing for Enterobacterales producing a metallo-beta-lactamase (MBL)

Clinicians and clinical and public health laboratories can request expanded antimicrobial susceptibility testing (ExAST) from CDC's Antibiotic Resistance Lab Network (AR Lab Network) to find potentially effective treatment options for their patients' most resistant infections.

- Resistance to new drugs used for treatment of carbapenem-resistant Enterobacterales (CRE) has been identified, specifically to ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-relebactam. However, these bacteria may be susceptible to the combination therapy ceftazidime-avibactam plus aztreonam, a combination of drugs that is an option in current IDSA guidance for treatment of serious infections caused by MBL-producing Enterobacterales.*
- Susceptibility testing is CLIA-compliant and is performed at no cost. MIC results will be reported within 3 business days for treatment of ceftazidime-avibactam, aztreonam, and aztreonam-avibactam to help assess utility of combination therapy.



- Southeast:** Tennessee Public Health Laboratory | ARLN.health@tn.gov
- Mid-Atlantic:** Maryland Public Health Laboratory | MDPHL.arln@maryland.gov
- Northeast:** Wadsworth Center Labs | ARLNcoreNY@health.ny.gov
- Midwest:** Wisconsin State Lab of Hygiene | wiARLN@slh.wisc.edu
- West:** Washington State Public Health Labs | ARLN@doh.wa.gov
- Central:** Minnesota Dept. of Health Public Health Lab | ARLNMN@state.mn.us
- Mountain:** Utah Public Health Lab | ARLNUtah@utah.gov

1. Isolates to submit:

Hospital laboratories and clinicians are encouraged to submit Enterobacterales isolates that:

- Test "not susceptible" to all beta lactams tested, including ceftazidime-avibactam, meropenem-vaborbactam, or imipenem-relebactam. These may be MBL-producing isolates with few treatment options.

-OR-

- Enterobacterales that test positive for NDM, VIM, or IMP genes.

2. What is the testing process?

- Isolates will be tested to confirm carbapenem resistance, carbapenemase production, and to identify the presence of specific carbapenemase genes.
- Isolates meeting the inclusion criteria will be tested against ceftazidime-avibactam, aztreonam, and avibactam-aztreonam.
- AST turn-around time is 3 business days after receipt of isolate.

3. How do I request ExAST and receive results?

- Please email your AR Lab Network Regional Laboratory (see map) to request testing and submission instructions. Please provide prior laboratory testing results, including organism identification and AST.
- Please confirm that Infection Prevention and Infectious Diseases services are aware of this patient and isolate.

- Southeast:** Tennessee Public Health Laboratory | ARLN.health@tn.gov
- Mid-Atlantic:** Maryland Public Health Laboratory | MDPHL.arln@maryland.gov
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<https://www.cdc.gov/drugresistance/pdf/drug-susceptibility-tests-508.pdf>

For more information on CDC's AR Lab Network, visit:
www.cdc.gov/drugresistance/laboratories.html

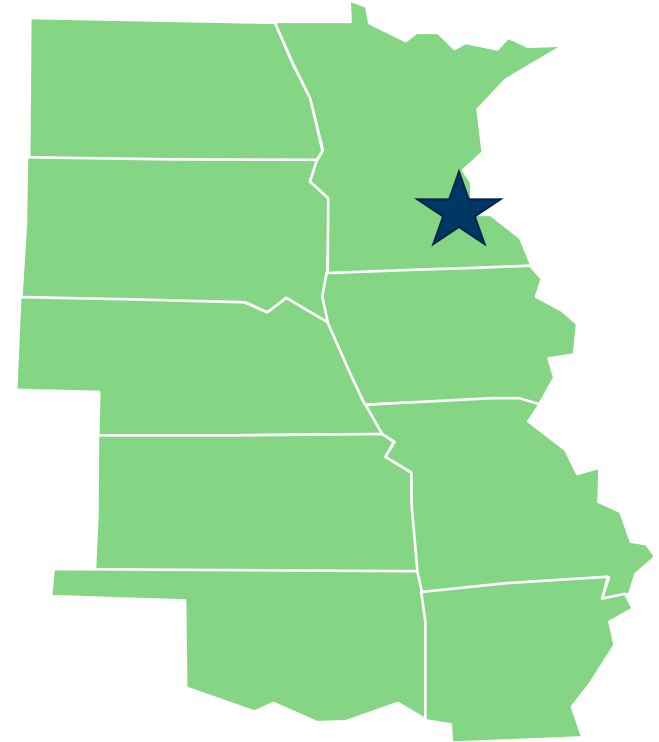


U.S. Department of
Health and Human Services
National Center for Injury
Prevention and Control

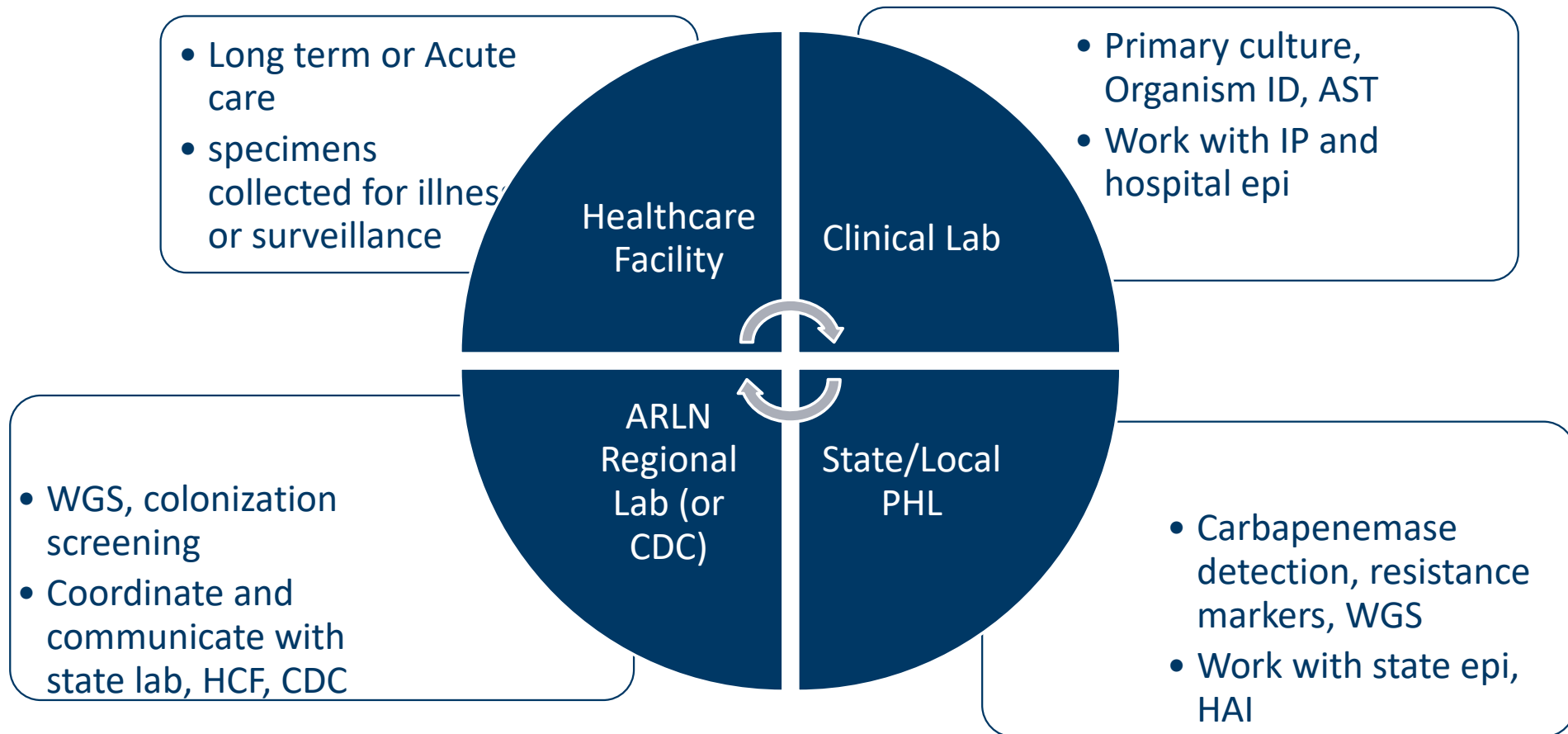
AR Lab Network – Central Region

Recruiting AR Lab Network Partner Laboratories

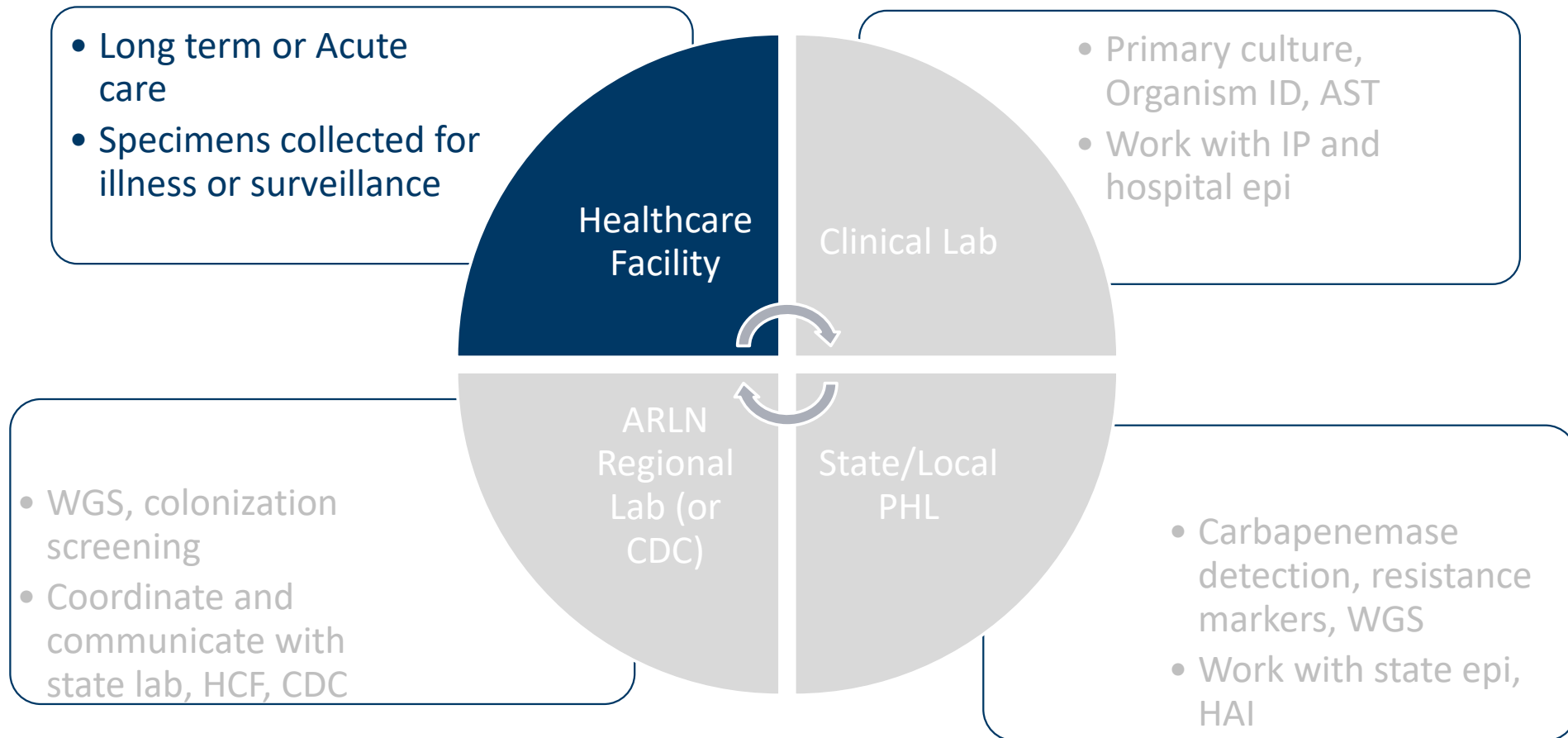
- PHLs working within each state to recruit and establish a network of clinical labs willing to submit isolates for further characterization
 - Carbapenem-resistant *Acinetobacter* - CRA
 - Yeast – *C. auris* and other yeast (ID and AFST)
 - *Streptococcus pneumoniae* (serotyping and AST)
 - *Aspergillus fumigatus* (azole resistance screening)



AR Lab Network: The System in Action

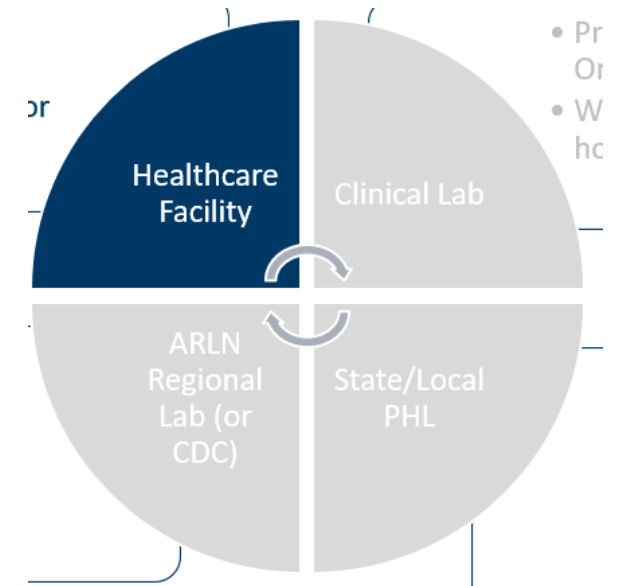


AR Lab Network: The System in Action Healthcare Facility



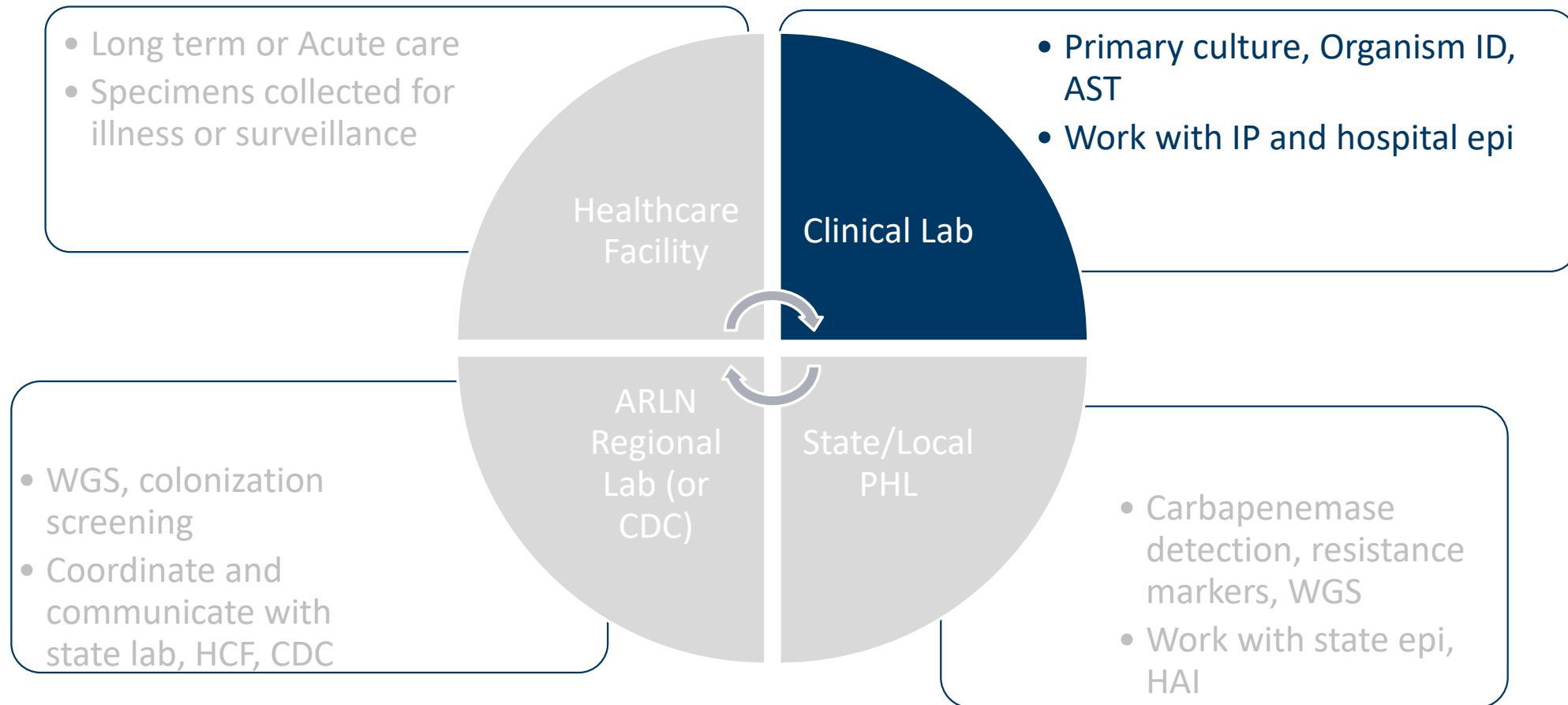
AR Lab Network: The System in Action Healthcare Facility

- 80 year-old female
- Resides in long-term care facility (LTCF)
- Wound care is done in this LTCF by a contracted wound care company
- Wound culture collected and sent to affiliated hospital laboratory



AR Lab Network: The System in Action

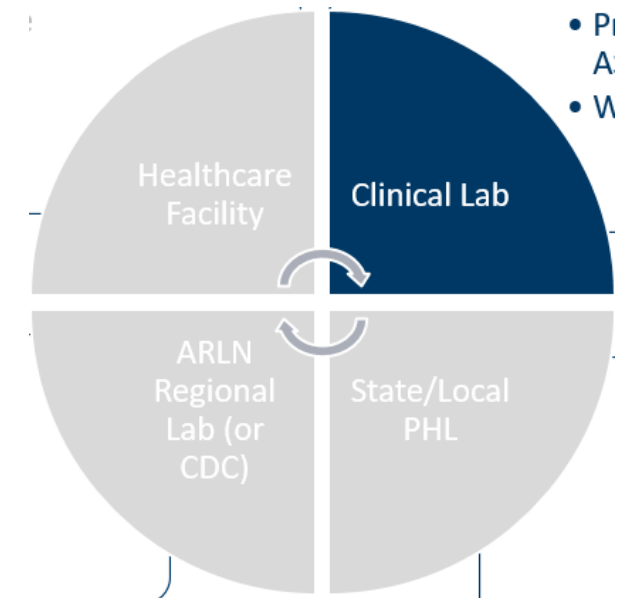
Hospital/clinical Laboratory



AR Lab Network: The System in Action

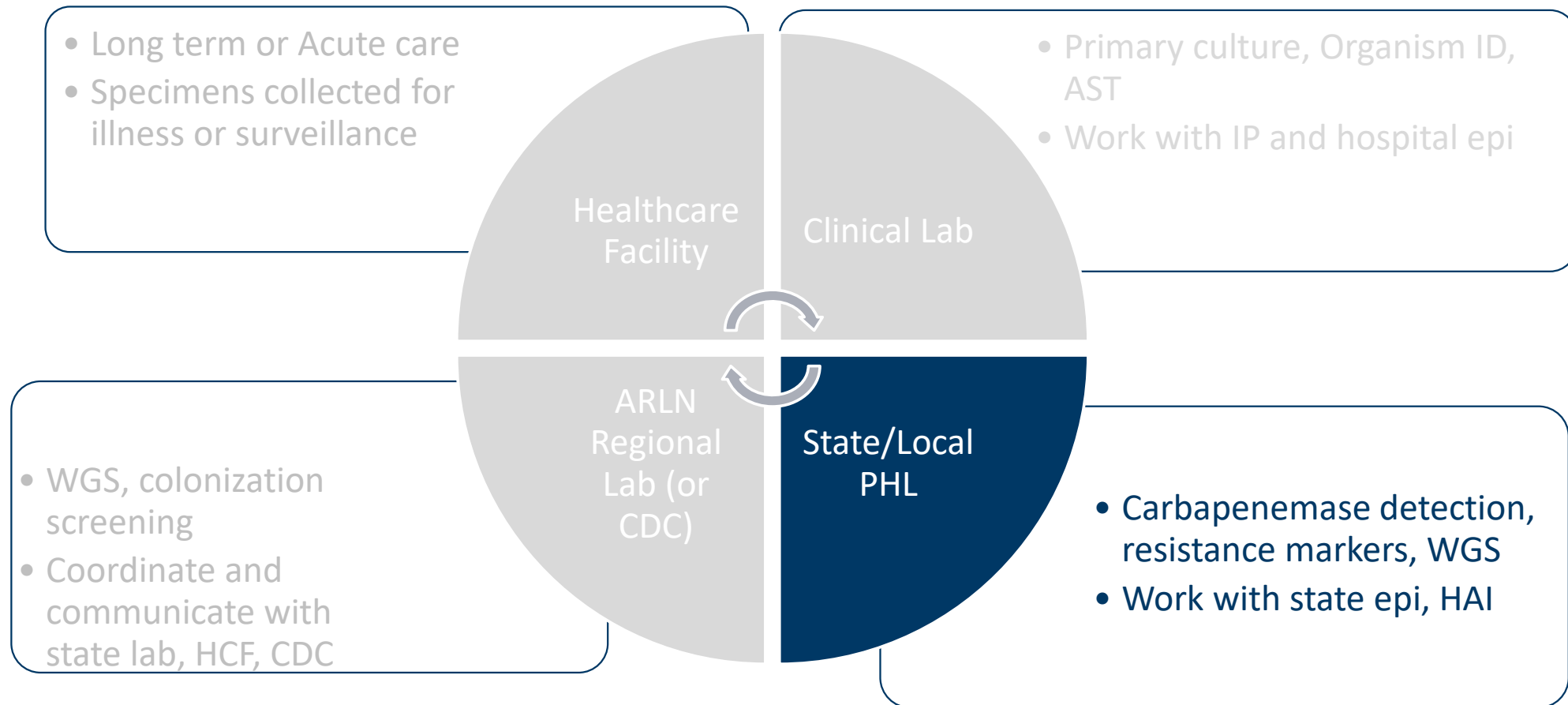
Hospital/clinical Laboratory

- Wound culture grows out an *Acinetobacter baumannii* and a *Staphylococcus aureus*
- AST results: meropenem and imipenem both have MICs ≥ 8 $\mu\text{g/mL}$ (R)
- Carbapenem resistant *A. baumannii* (CRA) are reportable and isolate is submittable to their state public health lab (PHL)
- Isolate is sent to state PHL



AR Lab Network: The System in Action

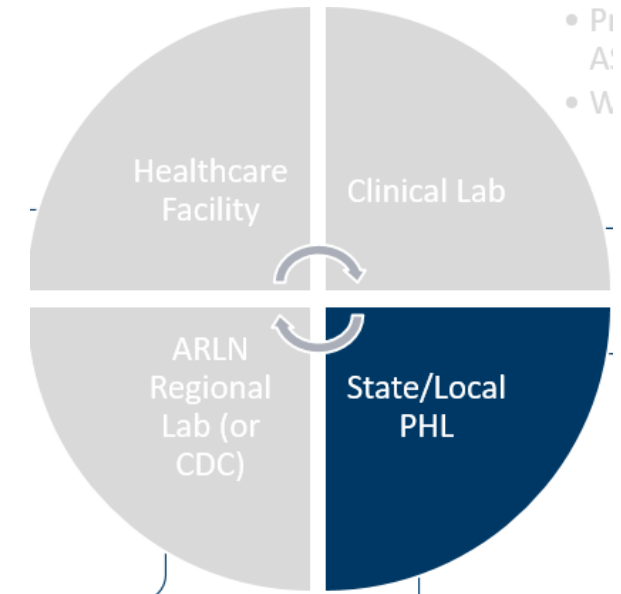
State/Local Public Health Lab



AR Lab Network: The System in Action

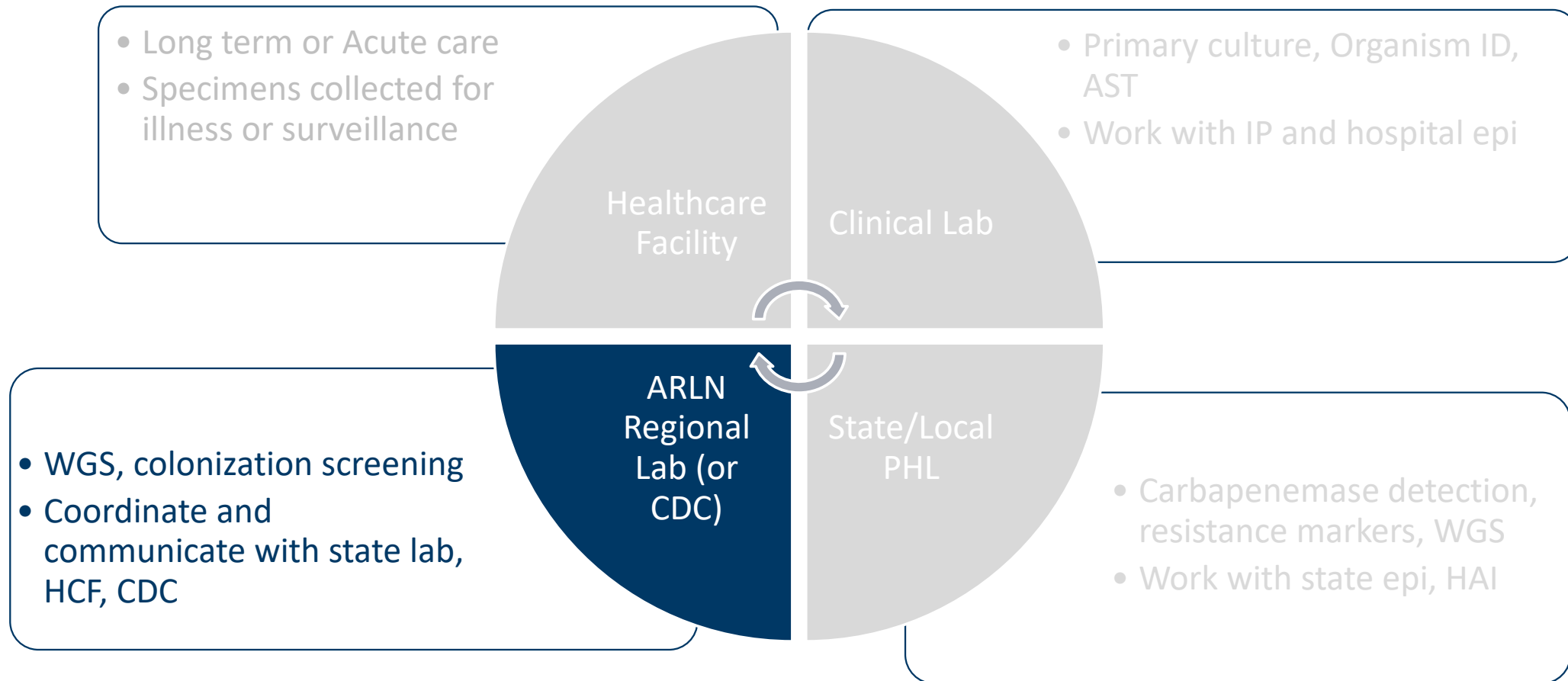
State/Local Public Health Laboratory

- State PHL does not yet have the capability to perform CRA testing – isolate is forwarded to the regional AR Lab Network PHL
- Note: SHARP funding is helping to increase the regional capacity



AR Lab Network: The System in Action

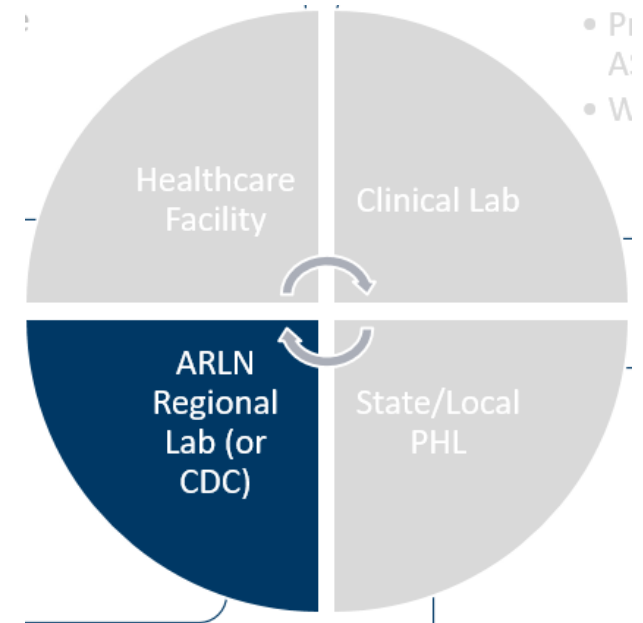
AR Lab Network Regional Lab



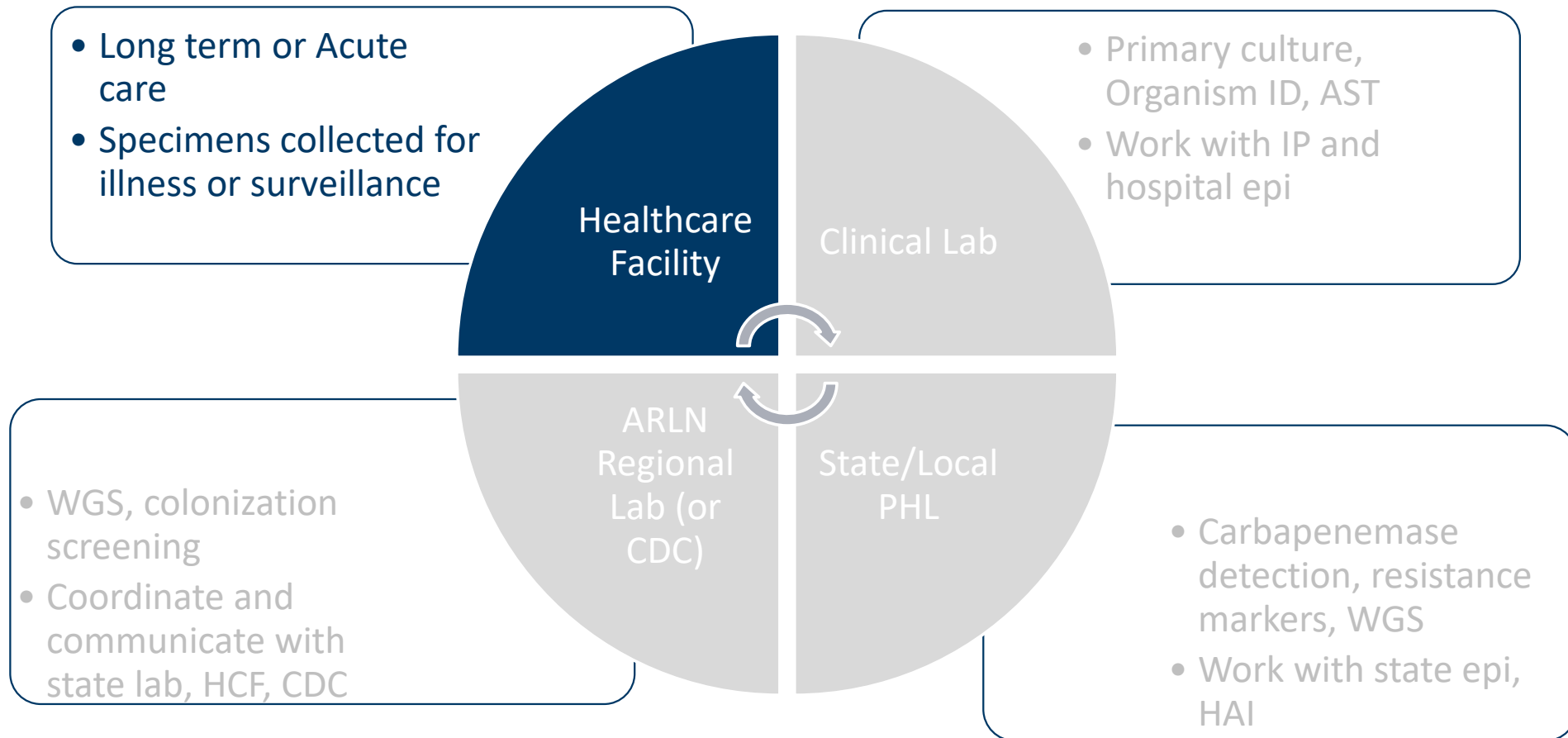
AR Lab Network: The System in Action

AR Lab Network Regional Laboratory

- Isolate is tested by PCR for the “Big-5” carbapenemases: KPC, NDM, VIM, IMP, OXA-48
- Isolate is tested by PCR for OXA variants: OXA-23, OXA-24, OXA-58, OXA-51
- Isolate is positive for **OXA-24**
- Results reported to submitting State PHL
- Alert notification sent to: State PHL, HAI epidemiologists and CDC

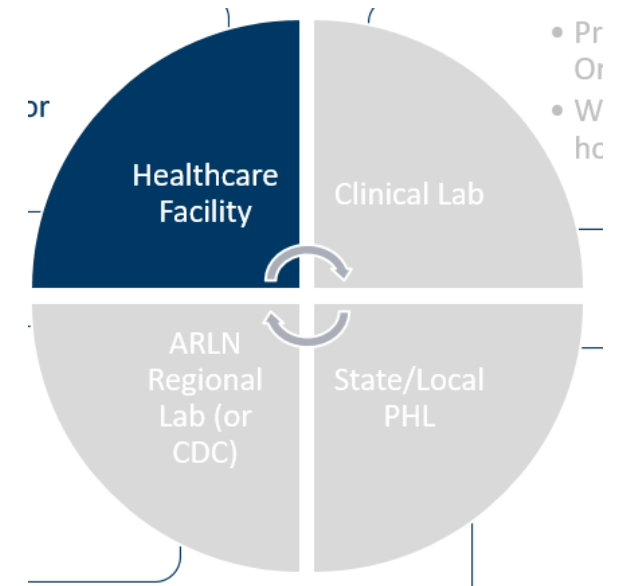


AR Lab Network: The System in Action Healthcare Facility



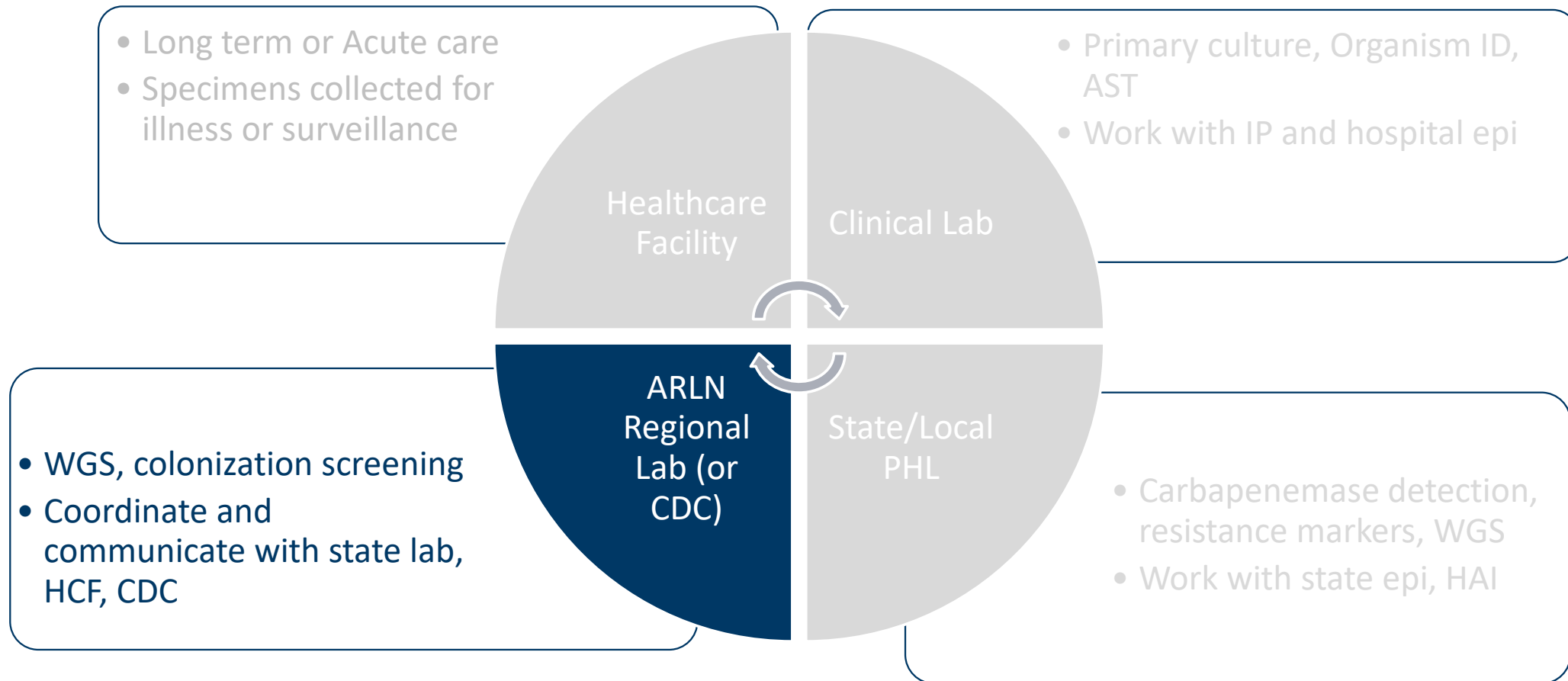
AR Lab Network: The System in Action Healthcare Facility

- HAI epidemiologist works with LTCF infection control and other staff to assess situation
- Develop a plan for screening other residents for CRA
- Specimens collected in coordination with AR Lab Network Regional Lab

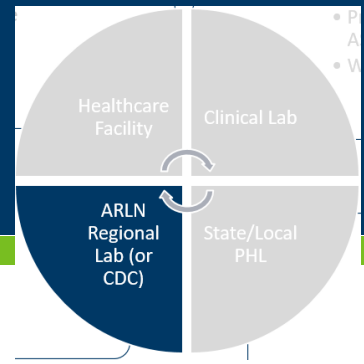


AR Lab Network: The System in Action

AR Lab Network Regional Lab

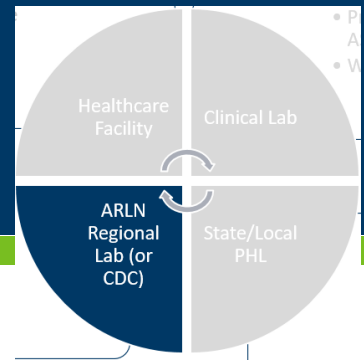


AR Lab Network: The System in Action Healthcare Facility



- AR Lab Network Regional lab performs culture-based screening for CRA
- Selective media, real-time PCR
- 2 additional patients found to have positive cultures for **OXA-24**

AR Lab Network: The System in Action Healthcare Facility



- Whole genome sequencing is performed to inform relatedness of the isolates
- All 3 patient isolates are found to be within 10 single nucleotide polymorphism (SNP) of each other, suggesting the isolates are related

	210095644	210095646	210095651
210095644	-	0	2
210095646	0	-	2
210095651	2	2	-

- Epidemiology + WGS indicates that transmission has probably occurred



The System in Action – Acute Care Facility

System in Action from the Central Region

- Acute care hospital – 1,265 beds, 70 operating rooms, 10 ICUs

Sept 28, 2020

Case #1

Source: Sputum
Isolated: KPC+ *P. aeruginosa*
Patient: ICU; ventilator-associated pneumonia; cardiac surgery
IPC: contact precautions, private room, private bathroom

Dec 12, 2020

Case #3

Source: Urine
Isolated: KPC+ *P. aeruginosa*
Patient: ICU; foley catheter; perforated intestine; hernia repair; peripherally inserted central catheter; gastrostomy tube
IPC: contact precautions, private room, private bathroom

Oct 10, 2020

Case #2

Source: Blood
Isolated: CRPA; Carba NP+
Patient: ICU; pancreatic cancer; central venous catheter
IPC: contact precautions, private room, private bathroom

Feb 2021

WGS analysis performed

IP continues investigation

System in Action from the Central Region

- MDH epidemiologists followed-up with the facility for each case
 - Requested WGS analysis on Cases #1-3

MDH Lab ID	Species ID	Specimen source	MLST	KPC Variant
Case #1	<i>Pseudomonas aeruginosa</i>	Sputum (clinical)	235	blaKPC-2
Case #2	<i>Pseudomonas aeruginosa</i>	Blood (clinical)	235	blaKPC-2
Case #3	<i>Pseudomonas aeruginosa</i>	Urine (clinical)	235	blaKPC-2

	Case #1	Case #2	Case #3
Case #1	-	1	2
Case #2	1	-	1
Case #3	2	1	-

- SNP analysis provided evidence there was a link between cases so IPs could investigate further

System in Action from the Central Region

Sept 28, 2020

Case #1

Source: Sputum
Isolated: KPC+ *P. aeruginosa*
Patient: ICU; ventilator-associated pneumonia; cardiac surgery
IPC: contact precautions, private room, private bathroom

Dec 12, 2020

Case #3

Source: Urine
Isolated: KPC+ *P. aeruginosa*
Patient: ICU; foley catheter; perforated intestine; hernia repair; peripherally inserted central catheter; gastrostomy tube
IPC: contact precautions, private room, private bathroom

Apr 14, 2021

Case #4

Source: Sputum
Isolated: CRPA
Devices: vent; foley; G-tube (temp); PICC (temp)
Procedures: none

Oct 10, 2020

Case #2

Source: Blood
Isolated: CRPA; Carba NP+
Patient: ICU; pancreatic cancer; central venous catheter
IPC: contact precautions, private room, private bathroom

Feb 2021

WGS analysis performed

IP continues investigation

Apr 17, 2021

Case #5

Source: BAL
Isolated: KPC+ *P. aeruginosa*
Devices: vent
Procedures: esophageal cancer surgery

System in Action from the Central Region

Sept 28, 2020

Case #1

Source: Sputum
Isolated: KPC+ *P. aeruginosa*
Patient: ICU; ventilator-associated pneumonia; cardiac surgery
IPC: contact precautions, private room, private bathroom

Dec 12, 2020

Case #3

Source: Urine
Isolated: KPC+ *P. aeruginosa*
Patient: ICU; foley catheter; perforated intestine; hernia repair; peripherally inserted central catheter; gastrostomy tube
IPC: contact precautions, private room, private bathroom

Epidemiological finding:

common endoscope used for all 5 cases
*No *P. aeruginosa* recovered from scope
Scope physical damage noted; discontinued

Apr 14, 2021

Case #4

Source: Sputum
Isolated: CRPA
Devices: vent; foley; G-tube (temp); PICC (temp)
Procedures: none

May 21, 2021

Case #6

Source: Sputum
Isolated: KPC+ *P. aeruginosa*
Patient: international residence and healthcare
Procedure w/ implicated endoscope Aug 2020
*presumed index case

Oct 10, 2020

Case #2

Source: Blood
Isolated: CRPA; Carba NP+
Patient: ICU; pancreatic cancer; central venous catheter
IPC: contact precautions, private room, private bathroom

Feb 2021

WGS analysis performed

IP continues investigation

Apr 17, 2021

Case #5

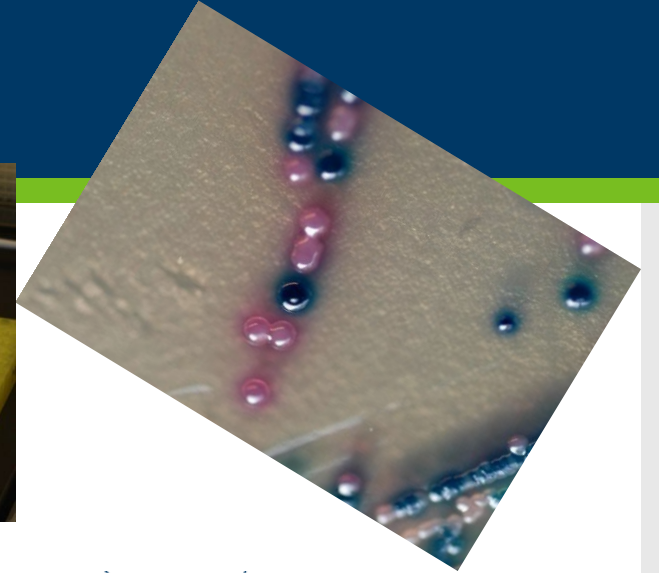
Source: BAL
Isolated: KPC+ *P. aeruginosa*
Devices: vent
Procedures: esophageal cancer surgery

System in Action from the Central Region

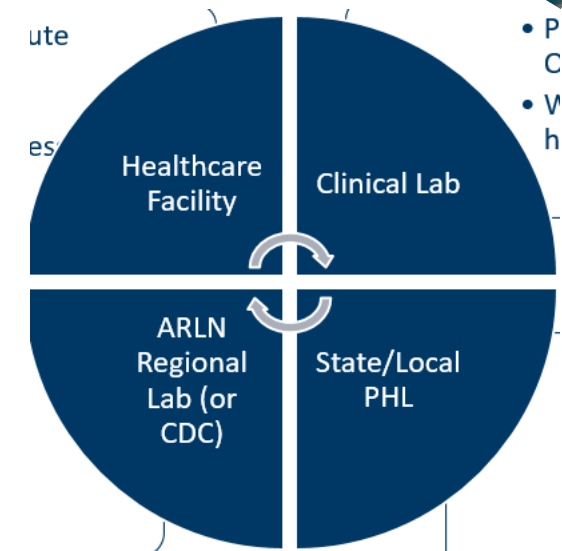
- **Endoscope identified by hospital IP during Apr/May cases**
 - Removed from service and contacted manufacturer
 - Only 1 endoscope used among all cases
 - Other endoscopes were cleaned and put back into service
- **Patient notification letters sent out for individuals who had procedures with implicated endoscope**
 - 225 letters/calls
 - 28 patients screened
 - 1 patient KPC+ CP-CRPA

	Case #1	Case #2	Case #3	Case #4	Case #5	Case #6	Case #7	Outlier
Case #1	-	1	2	0	1	3	8	47447
Case #2	1	-	1	2	3	5	11	47551
Case #3	2	1	-	3	4	6	11	46429
Case #4	0	2	3	-	1	3	8	47496
Case #5	1	3	4	1	-	4	9	47482
Case #6	3	5	6	3	4	-	11	47550
Case #7	8	11	11	8	9	11	-	47594
Outlier	47447	47551	46429	47496	47482	47550	47594	-

Conclusions



- **Variety of testing provide by AR Lab Network Regional and State labs**
- **AR Lab Network: “System in Action”**



Thank You!

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555-555-5555