CDPH
California Department of Public Health

County of Los Angeles Public Health

What's Happening with Carbapenem-Resistant Organisms in California in 2025? Making the Case for Carbapenemase Testing

Presented via webinar

December 10, 2025

Webinar Reminders

This session is being recorded.

The slides will be distributed following the webinar.

One hour of CEU for laboratorians available. You will receive information on how to receive them in a follow-up communication.

Please stay muted.

Type questions or comments in the Q&A box. We will try to answer live. Any questions not covered will be included in a follow-up Q&A document.

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Objectives

- List current recommendations for carbapenemase testing of carbapenem-resistant Enterobacterales (CRE), *Pseudomonas aeruginosa* (CRPA), and *Acinetobacter baumannii* (CRAB) in the clinical laboratory.
- Summarize recent trends in carbapenem-resistant organism (CRO) and carbapenemase-producing organism (CPO) prevalence in California.
- Describe the experiences of California clinical laboratories with CRO and CPO testing and reporting.
- Discuss antimicrobial susceptibility testing of last-resort agents recommended as therapeutic options for CROs.
- List current reporting requirements for CROs and CPOs, and identify public health resources, including those from the Antimicrobial Resistance Lab Network.

In brief, we will cover…

- Prevalence of CROs and CPOs in California.
- Current recommendations for carbapenemase testing.
- What three clinical laboratories within our California clinical laboratory community are doing for CROs.

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Prevalence of Carbapenem-resistant and Carbapenemase-producing Organisms in California

Sydney Loewen, PhD

AR Prevention and Response Supervisor, Healthcare-Associated Infections Program

California Department of Public Health

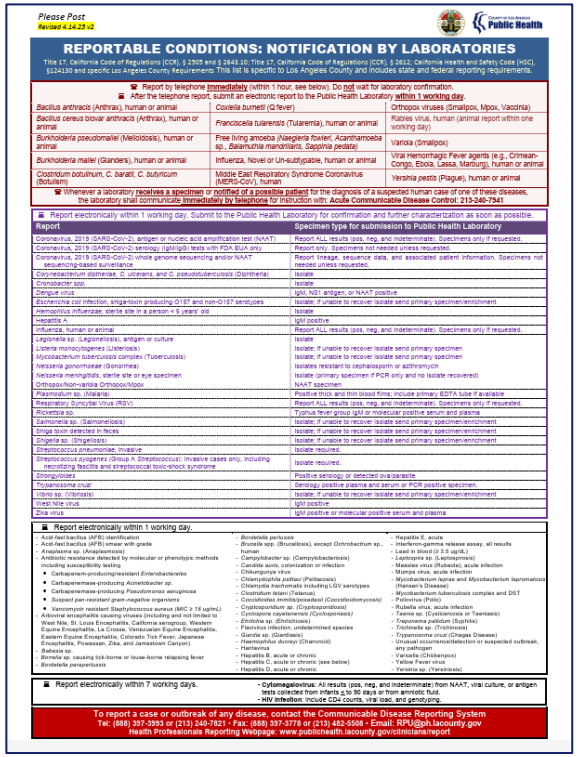
CRO and CPO Reporting Requirements

Statewide (Title 17) Reporting Requirements for CPOs

- **Labs** (clinical and public health) conducting carbapenemase testing report CPOs via electronic laboratory reporting.

Local Reporting Requirements for CROs

- Some local health departments (e.g., Alameda, LA, Orange, Sacramento) also have CRO submission and reporting requirements.
- For **LACDPH**, **healthcare providers** report CRE; there is **no laboratory reporting** requirement.



Please Post
Revised 4.14.25 v2

REPORTABLE CONDITIONS: NOTIFICATION BY LABORATORIES

Title 17, California Code of Regulations (CCR), § 2505 and § 2643.10; Title 17, California Code of Regulations (CCR), § 2612; California Health and Safety Code (HSC), §124130 and specific Los Angeles County Requirements. This list is specific to Los Angeles County and includes state and federal reporting requirements.

☎ Report by telephone immediately (within 1 hour, see below). Do not wait for laboratory confirmation.
🖷 After the telephone report, submit an electronic report to the Public Health Laboratory within 1 working day.

Bacillus anthracis (Anthrax), human or animal	*Coxiella burnetii* (Q fever)	Orthopox viruses (Smallpox, Mpox, Vaccinia)
Bacillus cereus biovar *anthracis* (Anthrax), human or animal	*Francisella tularensis* (Tularemia), human or animal	Rabies virus, human (animal report within one working day)
Burkholderia pseudomallei (Melioidosis), human or animal	Free-living amoeba (Naegleria fowleri, Acanthamoeba sp., *Balamuthia mandrillaris, Sappinia pedata*)	Variola (Smallpox)
Burkholderia mallei (Glanders), human or animal	Influenza, Novel or Un-subtypable, human or animal	Viral Hemorrhagic Fever agents (e.g., Crimean-Congo, Ebola, Lassa, Marburg), human or animal
Clostridium botulinum, C. baratii, C. butyricum (Botulism)	Middle East Respiratory Syndrome Coronavirus (MERS-CoV), human	*Yersinia pestis* (Plague), human or animal

☎ Whenever a laboratory receives a specimen or notified of a possible patient for the diagnosis of a suspected human case of one of these diseases, the laboratory shall communicate immediately by telephone for instruction with: **Acute Communicable Disease Control: 213-240-7941**

🖷 Report electronically within 1 working day. Submit to the Public Health Laboratory for confirmation and further characterization as soon as possible.

Report	Specimen type for submission to Public Health Laboratory
Coronavirus, 2019 (SARS-CoV-2), antigen or nucleic acid amplification test (NAAT)	Report ALL results (pos, neg, and indeterminate). Specimens only if requested.
Coronavirus, 2019 (SARS-CoV-2) serology (IgM/IgG) tests with FDA EUA only	Report only. Specimens not needed unless requested.
Coronavirus, 2019 (SARS-CoV-2) whole genome sequencing and/or NAAT sequencing/based surveillance	Report lineage, sequence data, and associated patient information. Specimens not needed unless requested.
Corynebacterium diphtheriae, C. ulcerans, and *C. pseudotuberculosis* (Diphtheria)	Isolate
Cronobacter spp.	Isolate
Dengue virus	IgM, NS1 antigen, or NAAT positive
Escherichia coli infection, shiga-toxin producing O157 and non-O157 serotypes	Isolate; if unable to recover isolate send primary specimen/enrichment
Hemophilus influenzae, sterile site in a person < 5 years' old	Isolate
Hepatitis A	IgM positive
Influenza, human or animal	Report ALL results (pos, neg, and indeterminate). Specimens only if requested.
Legionella sp. (Legionellosis), antigen or culture	Isolate
Listeria monocytogenes (Listeriosis)	Isolate; if unable to recover isolate send primary specimen
Mycobacterium tuberculosis complex (Tuberculosis)	Isolate; if unable to recover isolate send primary specimen
Neisseria gonorrhoeae (Gonorrhea)	Isolates resistant to cephalosporin or azithromycin
Neisseria meningitidis, sterile site or eye specimen	Isolate (primary specimen if PCR only and no isolate recovered)
Orthopox/Non-variola Orthopox/Mpox	NAAT specimen
Plasmodium sp. (Malaria)	Positive thick and thin blood films, include primary EDTA tube if available.
Respiratory Syncytial Virus (RSV)	Report ALL results (pos, neg, and indeterminate). Specimens only if requested.
Rickettsia sp.	Typhus fever group IgM or molecular positive serum and plasma
Salmonella sp. (Salmonellosis)	Isolate; if unable to recover isolate send primary specimen/enrichment
Shiga toxin detected in feces	Isolate; if unable to recover isolate send primary specimen/enrichment
Shigella sp. (Shigellosis)	Isolate; if unable to recover isolate send primary specimen/enrichment
Streptococcus pneumoniae, Invasive	Isolate required.
Streptococcus pyogenes (Group A Streptococcus): invasive cases only, including necrotizing fasciitis and streptococcal toxic-shock syndrome	Isolate required.
Strongyloides	Positive serology or detected ova/parasite
Trypanosoma cruzi	Serology positive plasma and serum or PCR positive specimen.
Vibrio sp. (Vibriosis)	Isolate; if unable to recover isolate send primary specimen/enrichment
West Nile virus	IgM positive
Zika virus	IgM positive or molecular positive serum and plasma

🖷 Report electronically within 1 working day.

- Acid-fast bacillus (AFB) identification
- Acid-fast bacillus (AFB) smear with grade
- *Anaplasma* sp. (Anaplasmosis)
- Antibiotic resistance detected by molecular or phenotypic methods including susceptibility testing
  - Carbapenem-producing/resistant *Enterobacterales*
  - Carbapenemase-producing *Acinetobacter* sp.
  - Carbapenemase-producing *Pseudomonas aeruginosa*
  - Suspect pan-resistant gram-negative organisms
  - Vancomycin resistant *Staphylococcus aureus* (MIC ≥ 16 ug/mL)
- Arboviral encephalitis causing viruses (including and not limited to West Nile, St. Louis Encephalitis, California serogroup, Western Equine Encephalitis, La Crosse, Venezuelan Equine Encephalitis, Eastern Equine Encephalitis, Colorado Tick Fever, Japanese Encephalitis, Powassan, Zika, and Jamestown Canyon)
- *Babesia* sp.
- *Borrelia* sp. causing tick-borne or louse-borne relapsing fever
- *Bordetella parapertussis*
- *Bordetella pertussis*
- *Brucella* spp. (Brucellosis), except *Ochrobactrum* sp., human
- *Campylobacter* sp. (Campylobacteriosis)
- *Candida auris*, colonization or infection
- Chikungunya virus
- *Chlamydophila psittaci* (Psittacosis)
- *Chlamydia trachomatis* including LGV serotypes
- *Clostridioides (Clostridium) difficile*
- *Coccidioides immitis/posadasii* (Coccidioidomycosis)
- *Cryptosporidium* sp. (Cryptosporidiosis)
- *Cyclospora cayetanensis* (Cyclosporiasis)
- *Ehrlichia* sp. (Ehrlichiosis)
- *Francisco* infection, undetermined species
- *Giardia* sp. (Giardiasis)
- *Haemophilus ducreyi* (Chancroid)
- Hantavirus
- Hepatitis B, acute or chronic
- Hepatitis C, acute or chronic (see below)
- Hepatitis D, acute or chronic
- Hepatitis E, acute
- Interferon-gamma release assay, all results
- Lead in blood (≥ 3.5 ug/dL)
- *Leptospira* sp. (Leptospirosis)
- Measles virus (Rubeola), acute infection
- Mumps virus, acute infection
- *Mycobacterium leprae* and *Mycobacterium lepromatosis* (Hansen's Disease)
- *Mycobacterium tuberculosis* complex and DST
- Poliovirus (Polio)
- Rubella virus, acute infection
- *Taenia* sp. (*T. saginata* or *T. solium*)
- *Treponema pallidum* (Syphilis)
- *Trichinella* sp. (Trichinosis)
- *Trypanosoma cruzi* (Chagas Disease)
- Unusual occurrence/detection or suspected outbreak, any pathogen
- Varicella (Chickenpox)
- Yellow Fever virus
- *Yersinia* sp. (Yersiniosis)

🖷 Report electronically within 7 working days.

- **Cytomegalovirus**: All results (pos, neg, and indeterminate) from NAAT, viral culture, or antigen tests collected from infants ≤ to 90 days or from amniotic fluid.
- **HIV infection**: include CD4 counts, viral load, and genotyping.

To report a case or outbreak of any disease, contact the Communicable Disease Reporting System
Tel: (888) 397-3993 or (213) 240-7821 • Fax: (888) 397-3778 or (213) 482-5500 • Email: RPH@ph.lacounty.gov
Health Professionals Reporting Webpage: www.publichealth.lacounty.gov/cli/hlcrtana/report

[Laboratory Reportable Conditions (PDF) | LACDPH](publichealth.lacounty.gov/acd/docs/LabList.pdf)
(publichealth.lacounty.gov/acd/docs/LabList.pdf)

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CDC Antimicrobial Resistance Laboratory Network (AR Lab Network) Carbapenemase Testing

Clinical labs voluntarily submit CRO isolates

CDC, regional, state and local public health labs conduct carbapenemase and other testing

Thank you for your support!!!

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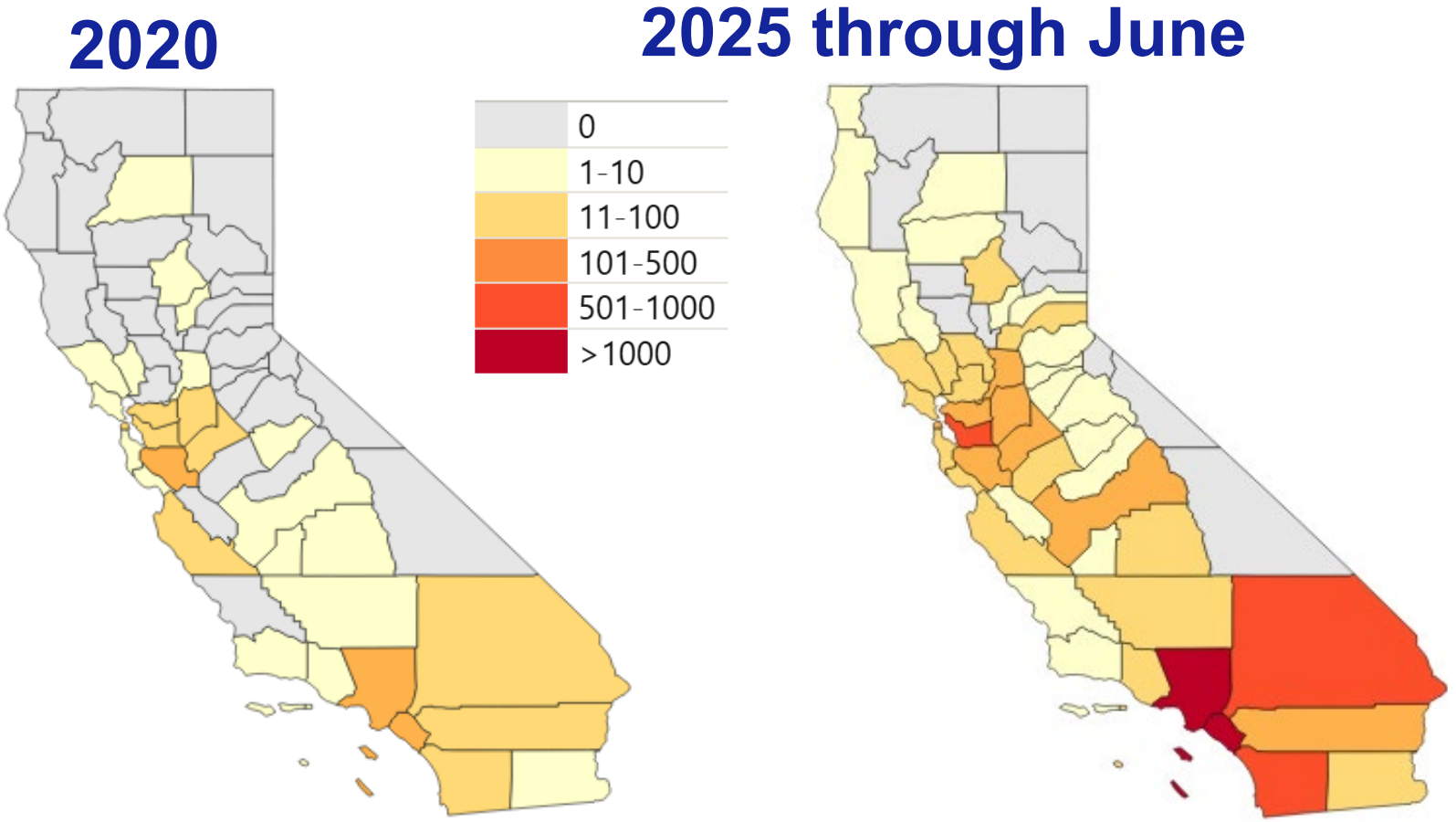
CPO cases in California are increasing and spreading

Cumulative CPO Cases Reported to CDPH (Preliminary Data)



Candida auris and CPO Dashboard | CDPH
(www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/ARDataReporting.aspx)

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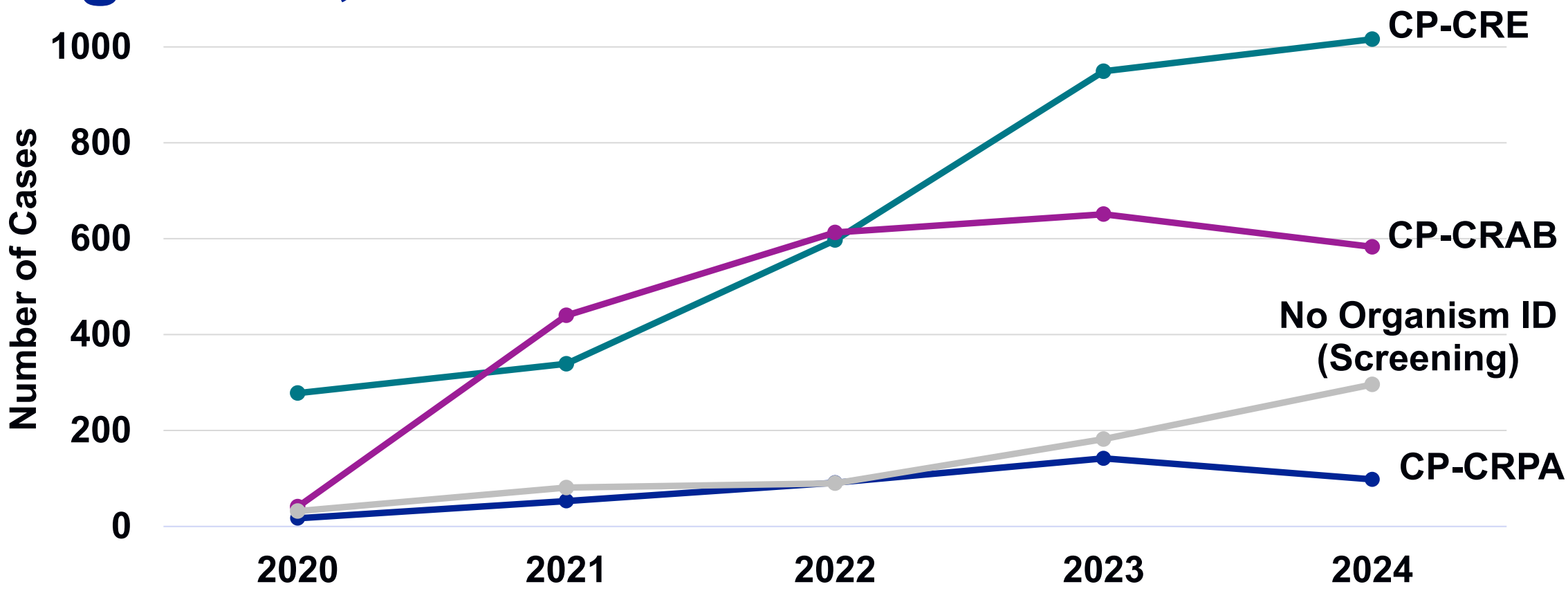
California CPO Cases Reported by Organism, 2020–2024



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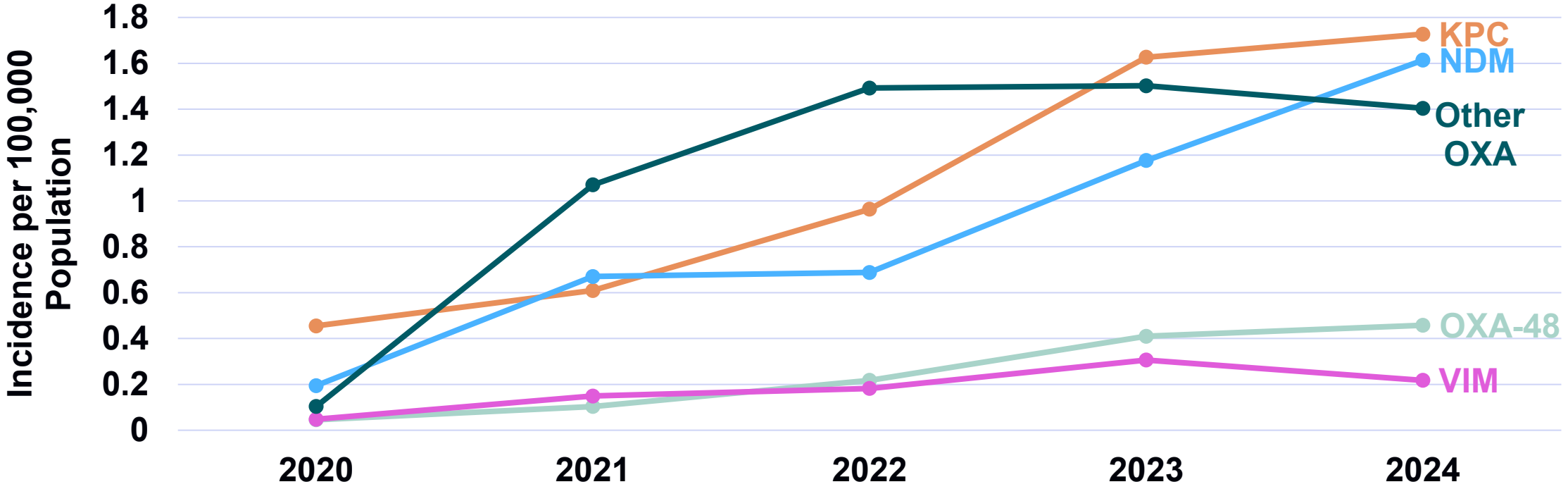
California CPO Incidence by Carbapenemase Type, 2020–2024*



*CPO cases reported to CDPH by carbapenemase type, alone or in combination with other carbapenemases. Other OXA includes OXA-23, 24/40, 58, 235-like variants.

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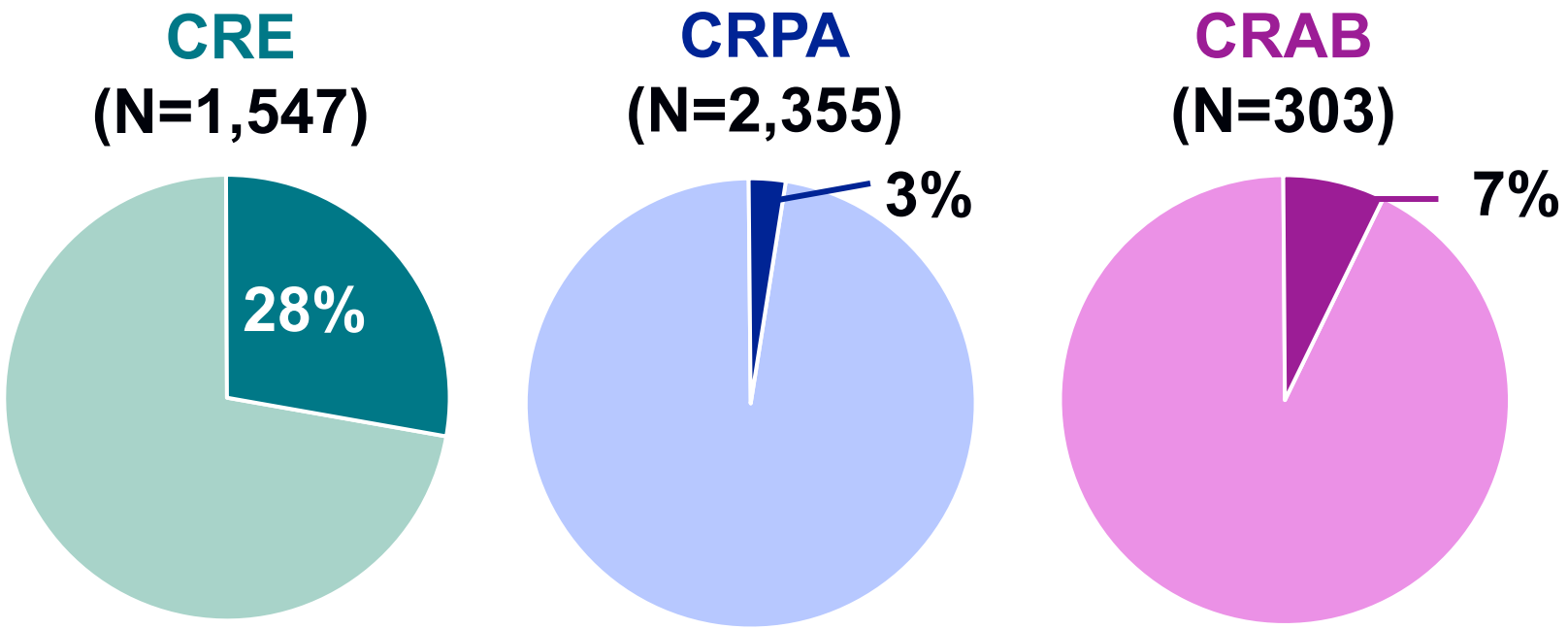
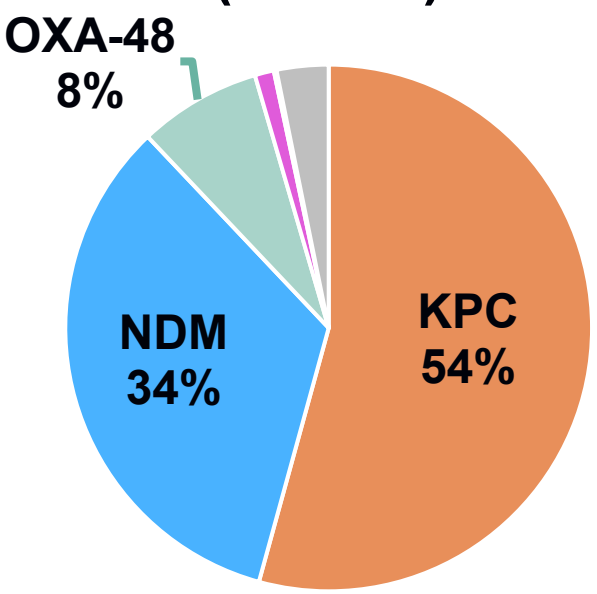
Percent Carbapenemase(s) Detected among CRO Isolates Tested at MDL, 2020–Jun 2025*



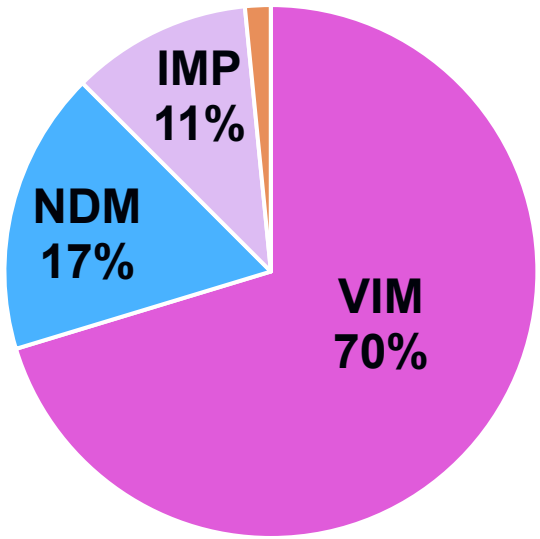
*CDPH Microbial Diseases Laboratory (MDL) tested CRE, CRAB, and CRPA isolates for KPC, NDM, OXA-48-like, VIM, and IMP carbapenemase genes

Carbapenemases Detected among CPO Isolates Tested at MDL, 2020–Jun 2025*

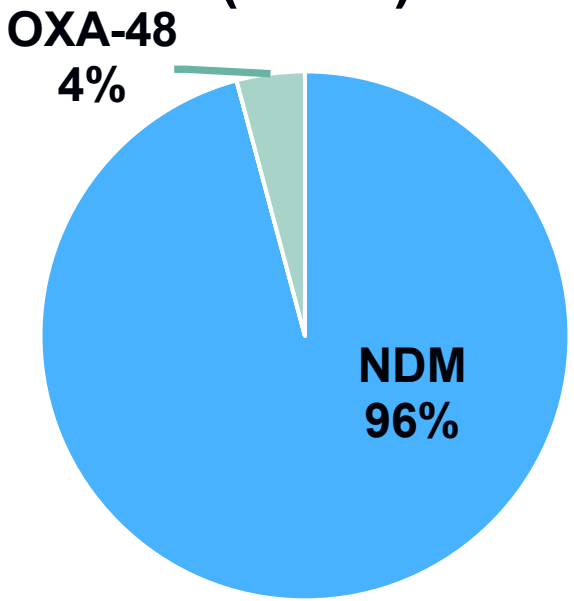
CP-CRE (N=597)



CP-CRPA (N=64)



CP-CRAB (N=24)



*CDPH Microbial Diseases Laboratory (MDL) tested CRE, CRAB, and CRPA isolates for KPC, NDM, OXA-48-like, VIM, and IMP carbapenemase genes

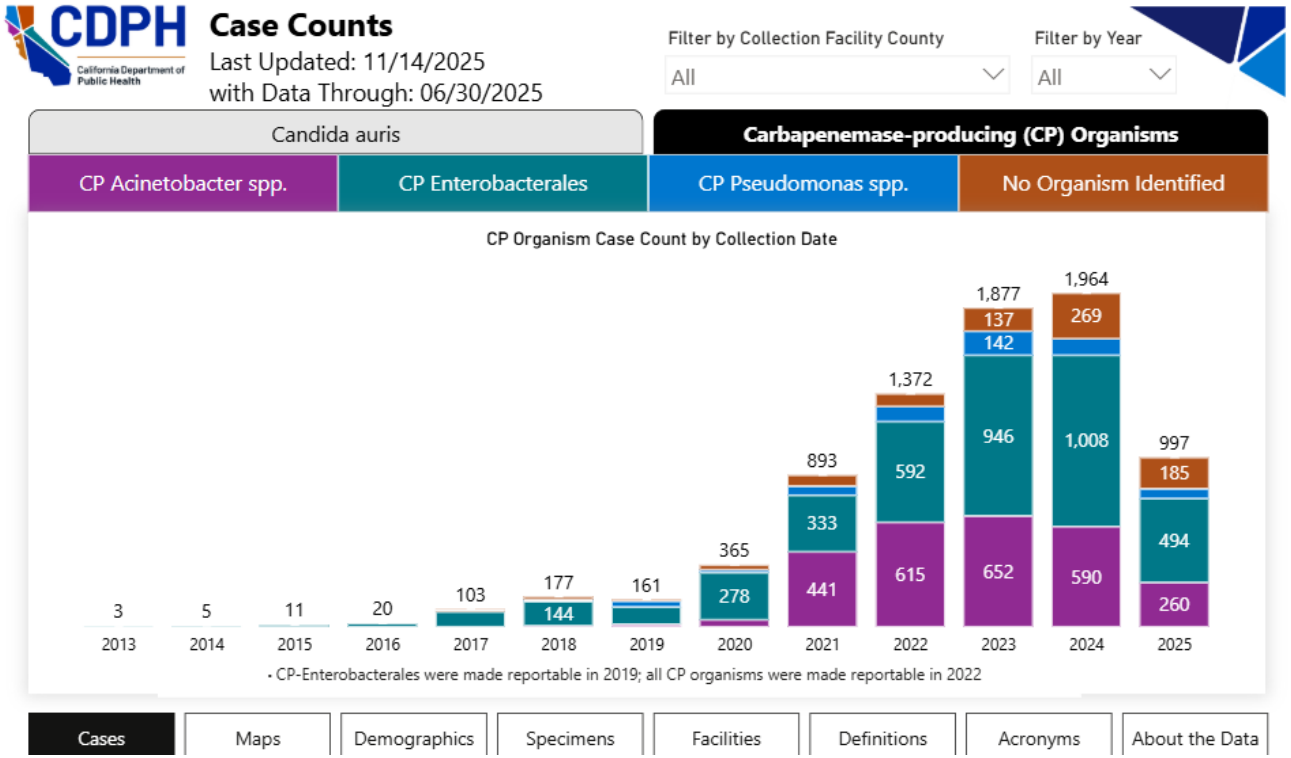
Learn more about CPO epidemiology in California

Check out our new dashboard!

(www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/ARDataReporting.aspx)

Candida auris & Carbapenemase-producing Organism Dashboard

Welcome to the *Candida auris* & Carbapenemase-producing Organism Dashboard, which provides summary information on cases identified in California healthcare facilities. Data in the dashboard are updated approximately every three to six months, and data from the 12 months prior to the last update should be considered preliminary.



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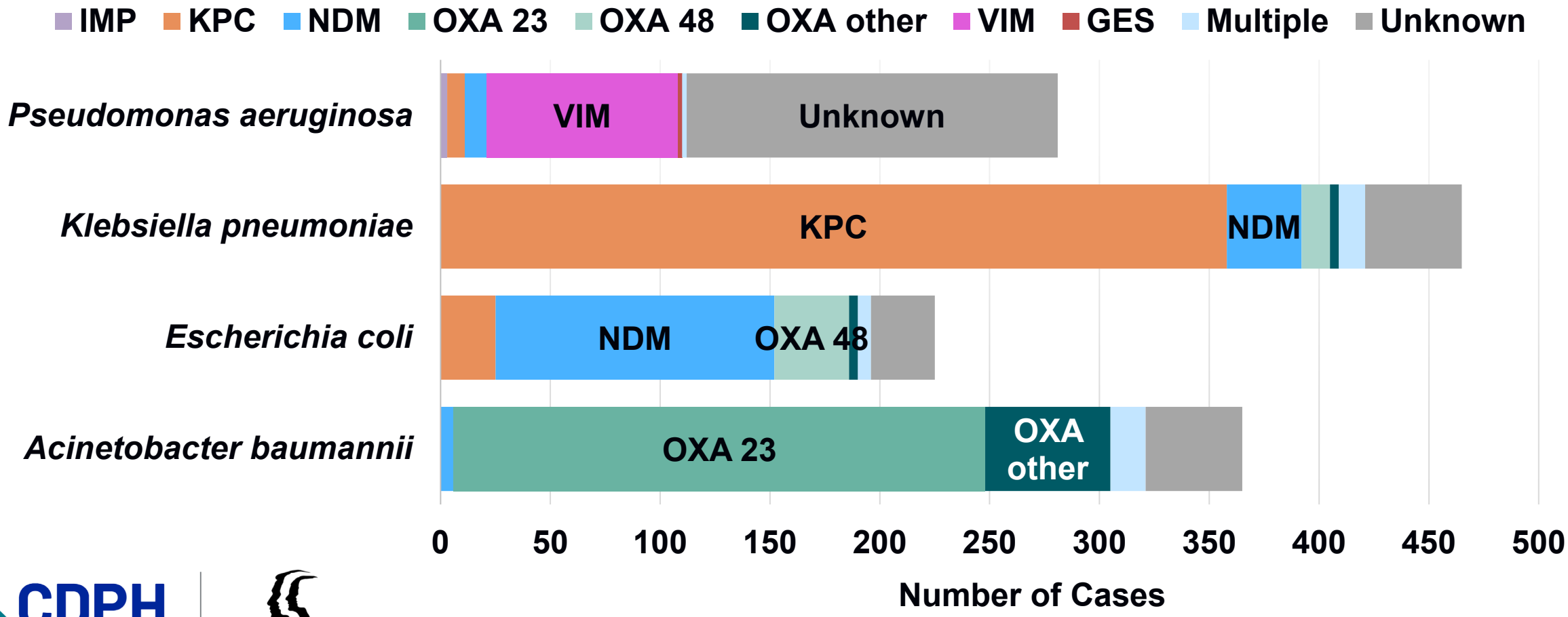
Prevalence of Carbapenem-resistant and Carbapenemase-producing Organisms in Los Angeles County

Wendy Knight, MPH, CIC
Epidemiologist, Healthcare Outreach Unit
Acute Communicable Disease Control
Los Angeles County Department of Public Health

LACDPH CPO Cases by Organism and Gene Detected, 2023-2025



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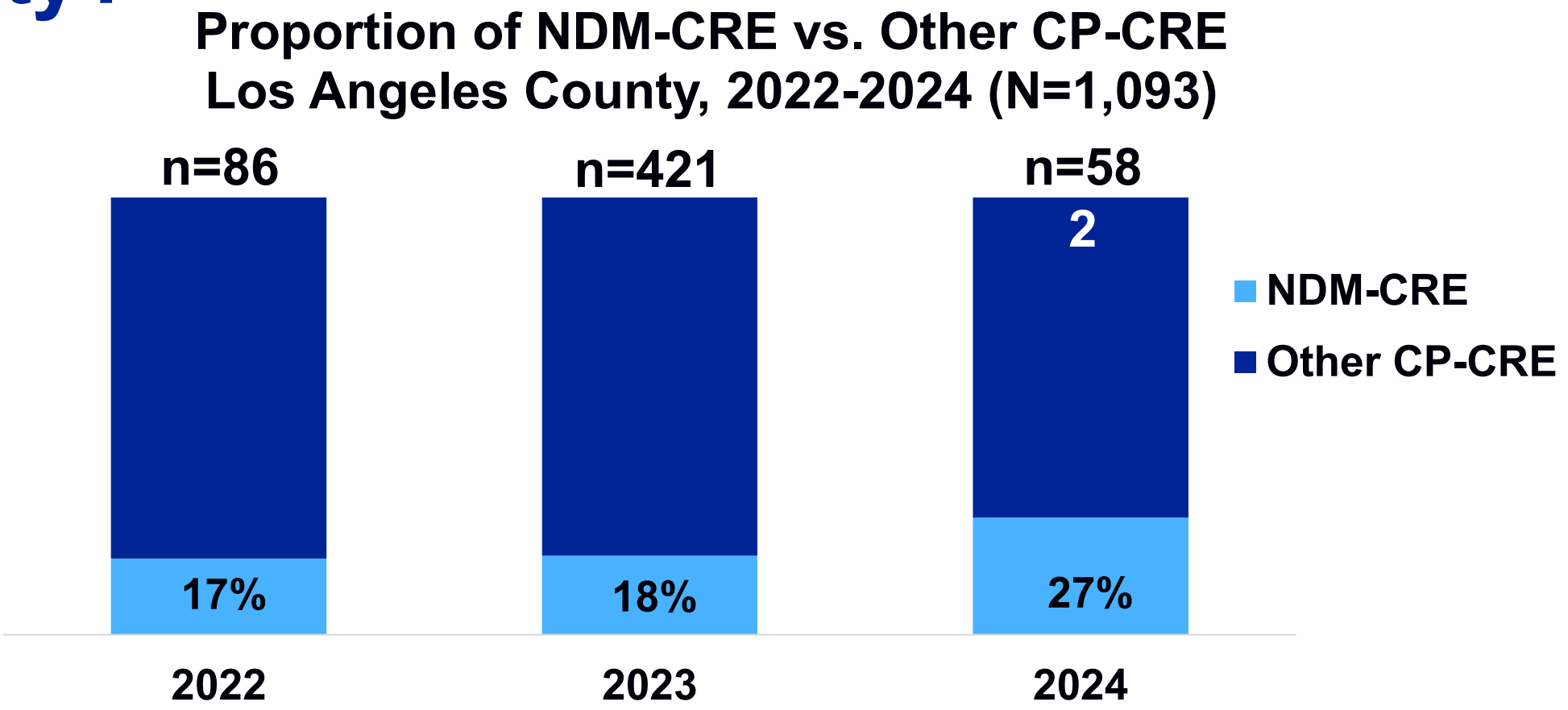
Is the prevalence of CPOs changing in LA County?



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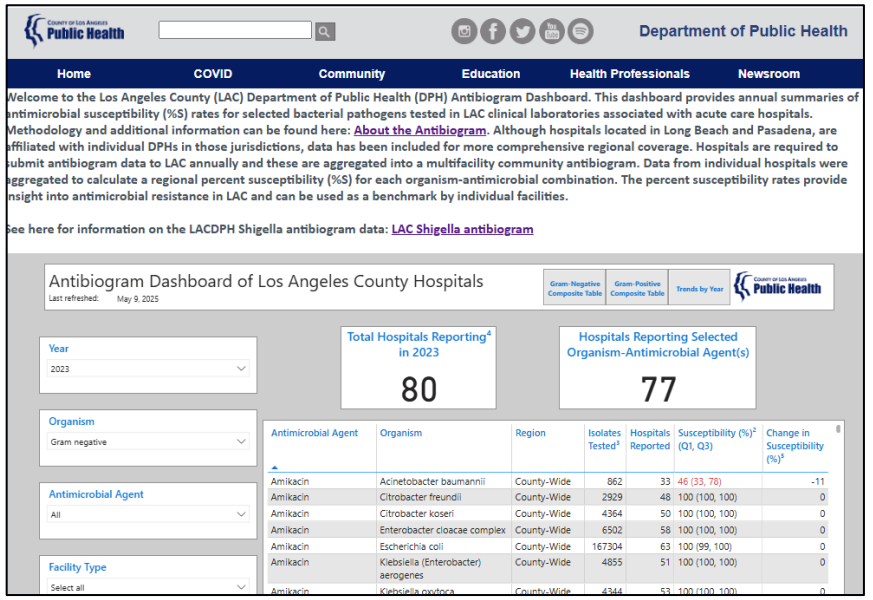
Broader Picture of CRO Data
LACDPH Multifacility Antibiogram Data - 2023

- ≈80 LAC hospitals submit their antibiogram data to LACDPH annually
- Compiled into a multifacility regional antibiogram

Organism	Isolates Tested (N)	Meropenem % S
Acinetobacter baumannii	1,837	43
Enterobacter cloacae complex	8,448	99
Escherichia coli	194,619	99
Klebsiella pneumoniae	37,287	98
Pseudomonas aeruginosa	26,826	90



Antibiogram Dashboard | LACDPH
(publichealth.lacounty.gov/AntibiogramDashboard.htm)

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Clinical and public health labs can work together to identify CPOs for action

Example 1: GES carbapenemases (27 cases reported in California, 2019–June 2025)

- Serine carbapenemase (Ambler Class A like KPC); most common among CRPA
- Not identified with “big 5” test kits
- Facility A voluntarily submits CRPA isolates to LACDPH for testing
  - mCIM positive + “big 5” negative; whole genome sequencing (WGS) identifies GES
  - GES-CRPA identified in 2 patient isolates and Facility A sink

Example 2: Rare VIM-CRPA multistate outbreak associated with artificial tears

- 9 cases identified in California through clinical lab submission and public health lab WGS and colonization testing

Evaluation of a Modified Carbapenem Inactivation Method for Detection of Carbapenemases in *Pseudomonas aeruginosa* | ASM Journals (journals.asm.org/doi/10.1128/jcm.01234-17)

Extensively Drug-Resistant Pseudomonas aeruginosa Outbreak Associated with Artificial Tears | Oxford Academic (academic.oup.com/cid/article/79/1/6/7601234)

CPO Prevention and Response Strategy: a Tiered Approach Based on Local Epidemiology

Tier 1 (novel CPOs)	Tier 2 (e.g., VIM CRE, GES CRPA)	Tiers 3-4 (e.g., KPC CRE, OXA-23 CRAB)

No cases → **Some cases** → **High case burden/ endemicity**

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Carbapenemase Testing Recommendations

Janet Hindler, MCLS MT(ASCP) F(AAM)
Microbiologist, Public Health Laboratory
Los Angeles County Department of Public Health

Carbapenemase Testing for Carbapenem-Resistant Organisms (CRO)
A Primer for Clinical and Public Health Laboratories (Update December 2025)

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AMERICAN SOCIETY FOR MICROBIOLOGY | Clinical Microbiology Reviews

Clinical Microbiology | Review

Laboratory detection of carbapenemases among Gram-negative organisms

Patricia J. Simner,[1,2] Johann D. D. Pitout,[3,4,5] Tanis C. Dingle[3,6]

Will not discuss details of carbapenemase methods… Please check out these resources

CDPH CPO Primer (PDF)
(www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CRO_PrimerTests_for_Carbapenemases.pdf)

Table 1. Tests for Carbapenemases in Gram-Negative Bacteria (Commercial Tests Listed are FDA Cleared)

Method	Routinely performed on [1]			Organisms		
	Isolates	Positive blood cultures	Rectal Swabs	Enterobacterales	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*
Phenotypic – Isolates Only						
Modified Carbapenem Inactivation Method (mCIM) with / without EDTA Carbapenem Inactivation Method (eCIM)	Yes	No	No	Yes	Yes (mCIM only)	No
CarbaNP [2]	Yes	No	No	Yes	Yes	No
BioMerieux Rapidec® Carba NP	Yes	No	No	Yes	Yes	No
BD Phoenix™ CPO Detect	Yes	No	No	Yes	Yes	Yes
Hardy NG-Test® CARBA 5 [3]	Yes	No	no	KPC, NDM, VIM, IMP, OXA-48-like [4]	KPC, NDM, VIM, IMP, OXA-48-like	No
Genotypic - Positive Blood Cultures						

Laboratory detection of carbapenemases among Gram-negative organisms | ASM Journals (journals.asm.org/doi/10.1128/cmr.00054-22)

CPO Primer (PDF) | CDPH (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CRO_PrimerTests_for_Carbapenemases.pdf)

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Case #1: CRO vs. CPO

This is…

- **CRO** (carbapenem-resistant organism)
- Must perform a carbapenemase test to determine if it is…
- **CPO** (carbapenemase-producing organism)

Klebsiella pneumoniae

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	4	S
Ceftriaxone	>32	R
Cefepime	>32	R
Ciprofloxacin	>2	R
Ertapenem	>8	R
Gentamicin	>8	R
Meropenem	>4	R
Piperacillin-tazobactam	>128/4	R
Tobramycin	>8	R
Trimeth-sulfa	>4/76	R

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Case #1: CRO vs. CPO, Continued

- Carbapenem resistance may be due to:
  - Carbapenemase production
  - Other (e.g., impermeability, efflux)
- Carbapenemase genes usually on transmissible plasmids
- CPO pose the greatest threat for carbapenem “R” gene transmission!

Klebsiella pneumoniae

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	4	S
Ceftriaxone	>32	R
Cefepime	>32	R
Ciprofloxacin	>2	R
Ertapenem	>8	R
Gentamicin	>8	R
Meropenem	>4	R
Piperacillin-tazobactam	>128/4	R
Tobramycin	>8	R
Trimeth-sulfa	>4/76	R

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Case #1: Carbapenemase-Producing Enterobacterales (CPE), Continued

Big 5 Carbapenemases:

β-Lactamase Classification (Ambler)		
A (serine)	B (metallo-β-lactamase)	D (serine)
KPC	IMP	OXA-48
	NDM	
	VIM	

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Case #1: Carbapenemase-Producing Enterobacterales (CPE)

Carbapenemase test performed
Optional report comment example:
Carbapenemase-producing *Klebsiella pneumoniae* isolated. Please check Infection Control procedures. Infectious Diseases communication suggested.

***Klebsiella pneumoniae* – Positive for KPC**

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	4	S
Ceftriaxone	>32	R
Cefepime	>32	R
Ciprofloxacin	>2	R
Ertapenem	>8	R
Gentamicin	>8	R
Meropenem	>4	R
Piperacillin-tazobactam	>128/4	R
Tobramycin	>8	R
Trimeth-sulfa	>4/76	R

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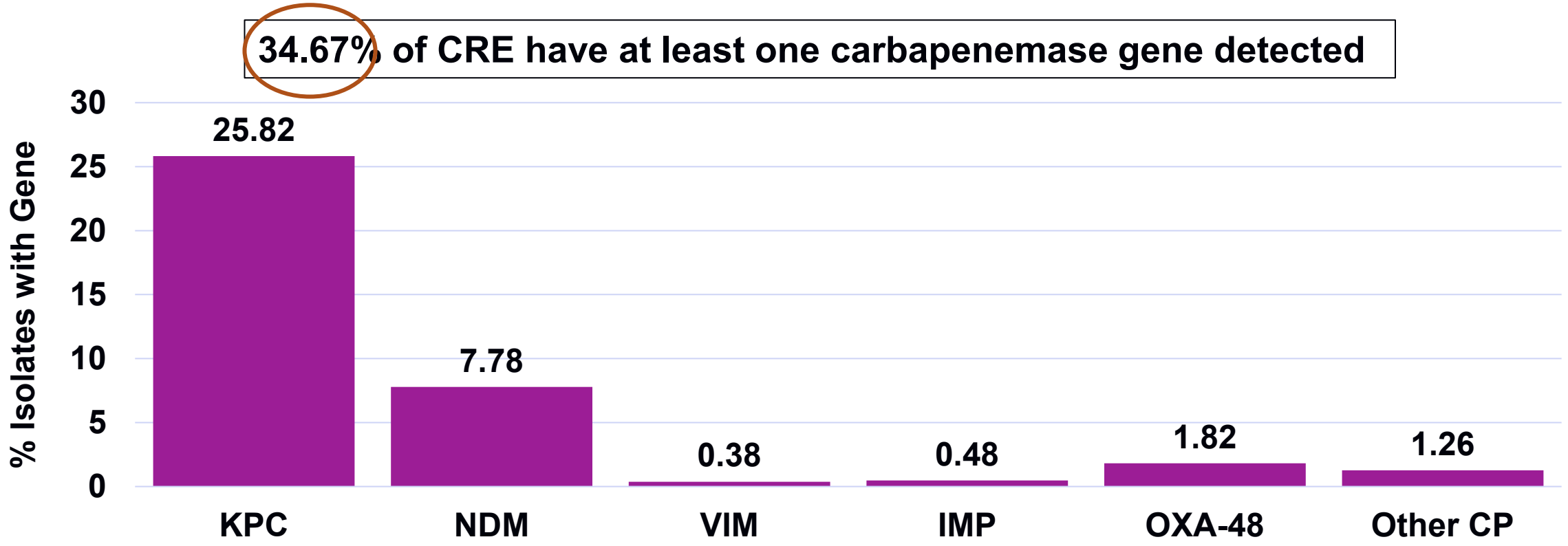
CRE - Carbapenemase Genes Detected by AR Lab Network, 2017-2024 (N=150,915)



AR Patient Safety Portal | CDC
(arpsp.cdc.gov/profile/arln/cre)

Case #2: Cefepime Reporting Rule for CPE

Table 2A-1. Enterobacterales

Comment (18):

"Cefepime S/SDD results should be suppressed or edited and reported as resistant for isolates that demonstrate **carbapenemase production**"

***Citrobacter freundii* – Positive for KPC**

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	8	I
Ceftriaxone	>32	R
Cefepime	~~4~~	~~SDD~~ R
Ciprofloxacin	>2	R
Ertapenem	>4	R
Gentamicin	8	R
Meropenem	4	R
Piperacillin-tazobactam	>128/4	R
Trimeth-sulfa	>4/76	R

M100 35th ed. Table 2A-1; Table G3
(em100.edaptivedocs.net/Login.aspx)

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Case #2: Cefepime Reporting Rule for CPE, Continued

Why?

"Current evidence suggests cefepime therapy may not be effective against carbapenemase-producing strains. Most of these data are based on studies investigating KPC-producing CRE"

M100 35th ed. Table 2A-1; Table G3
(em100.edaptivedocs.net/Login.aspx)

***Citrobacter freundii* – Positive for KPC**

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	8	I
Ceftriaxone	>32	R
Cefepime	~~4~~	~~SDD~~ R
Ciprofloxacin	>2	R
Ertapenem	>4	R
Gentamicin	8	R
Meropenem	4	R
Piperacillin-tazobactam	>128/4	R
Trimeth-sulfa	>4/76	R

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Case #3: Meropenem-vaborbactam Reporting Rule CPE OXA-48

Table 2A-1. Enterobacterales

(13) "Enterobacterales that harbor OXA-48-like enzymes may test susceptible to meropenem-vaborbactam but may not respond to meropenem-vaborbactam in vivo. If an OXA-48-like gene or enzyme is detected, suppress meropenem-vaborbactam or report as resistant."

M100 35h ed. Table 2A-1
(em100.edaptivedocs.net/Login.aspx)

***Escherichia coli* – Positive for OXA-48**

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	8	I
Ceftazidime-avibactam	≤0.5/4	S
Ceftriaxone	>32	R
Cefepime	>32 R	R
Ciprofloxacin	>2	R
Ertapenem	>4	R
Gentamicin	8	R
Meropenem	4	R
Meropenem-vaborbactam	~~4~~	~~S~~ R
Piperacillin-tazobactam	>128/4	R
Trimeth-sulfa	>4/76	R

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Case #3: Meropenem-vaborbactam Reporting Rule CPE OXA-48, Continued

Why?

- Meropenem-vaborbactam "S" breakpoints are higher than meropenem alone due to dosing
- Vaborbactam does not inhibit OXA-48

M100 35h ed. Table 2A-1
(em100.edaptivedocs.net/Login.aspx)

***Escherichia coli* – Positive for OXA-48**

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	8	I
Ceftazidime-avibactam	≤0.5/4	S
Ceftriaxone	>32	R
Cefepime	>32 R	R
Ciprofloxacin	>2	R
Ertapenem	>4	R
Gentamicin	8	R
Meropenem	4	R
Meropenem-vaborbactam	~~4~~	~~S~~ R
Piperacillin-tazobactam	>128/4	R
Trimeth-sulfa	>4/76	R

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Case #4: CRPA

- Carbapenem-resistance generally NOT due to carbapenemase but due to:
  - Impermeability
  - Efflux
- Virtually all carbapenemase-producing *P. aeruginosa* are “I” or “R” to **ceftolozane-tazobactam**

Pseudomonas aeruginosa

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	>32	R
Cefepime	>32	R
Ceftazidime	>32	R
Ceftolozane-tazobactam	≤2/4	S
Ciprofloxacin	>2	R
Meropenem	>4	R
Piperacillin-tazobactam	>128/4	R
Tobramycin	>8	R

Antimicrobial Susceptibility Profiles to Predict the Presence of Carbapenemase Genes among Carbapenem-Resistant Pseudomonas aeruginosa Isolates | ASM Journals (journals.asm.org/doi/10.1128/jcm.02874-20)

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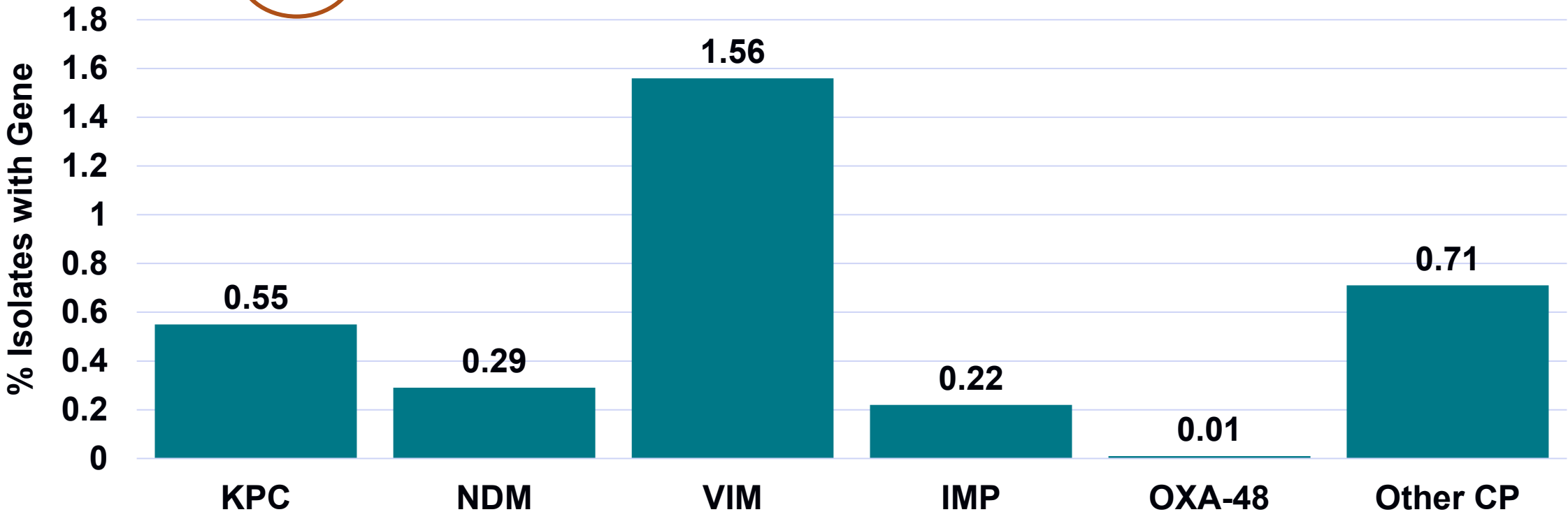
CRPA - Carbapenemase Genes Detected by AR Lab Network, 2017-2024 (N=109,533)

2.6% of CRPA have at least one carbapenemase gene detected



AR Patient Safety Portal | CDC
(arpsp.cdc.gov/profile/arln/cre)

Case #5: CRAB

- Carbapenemase testing in CRAB is complicated
  - No reliable phenotypic test
  - Most CRAB produce “non-OXA-48” OXA carbapenemases
    - Usually OXA-23, a variant not included in most commercial carbapenemase “kits”
    - Significance of these OXA carbapenemases is not clearly defined
- NDM CRAB has been identified in California

Acinetobacter baumannii

Antimicrobial Agent	MIC (µg/mL)	
Amikacin	>32	R
Cefepime	>32	R
Ciprofloxacin	>2	R
Gentamicin	>8	R
Meropenem	>4	R
*Minocycline	1	S
Piperacillin-tazobactam	>128/4	R
Tobramycin	>8	R
Trimeth-sulfa	>4/76	R

*Other tetracyclines (e.g., eravacycline, tigecycline sometimes considered)

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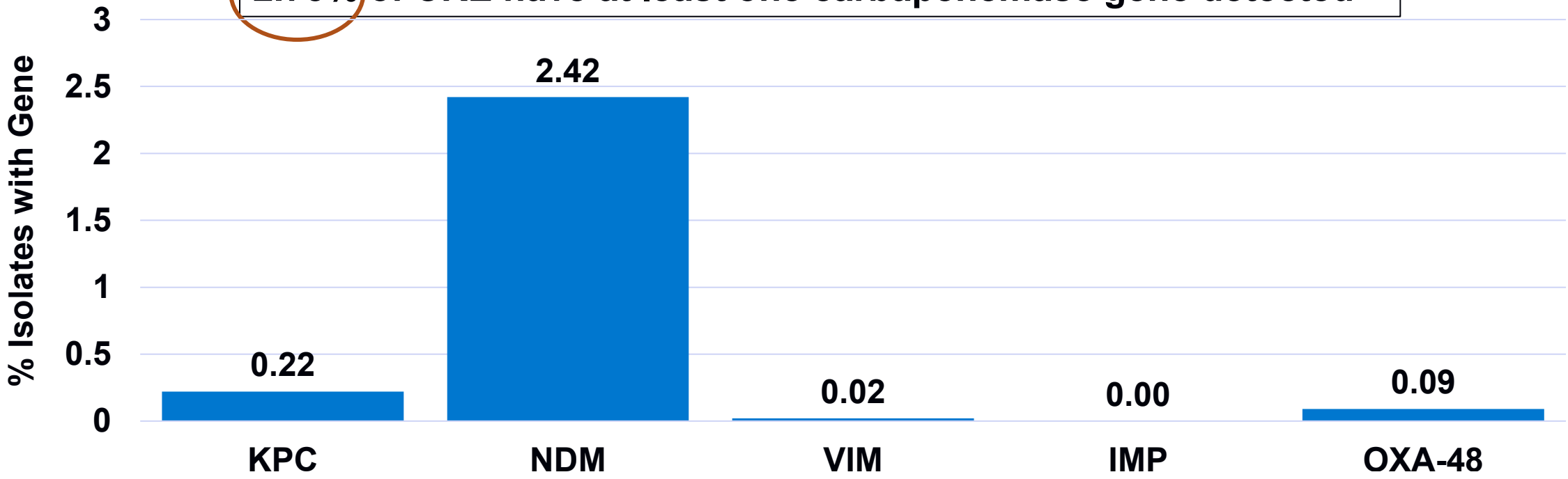
CRAB - Carbapenemase Genes Detected by AR Lab Network, 2017-2024 (N=34,771)

2.75% of CRE have at least one carbapenemase gene detected

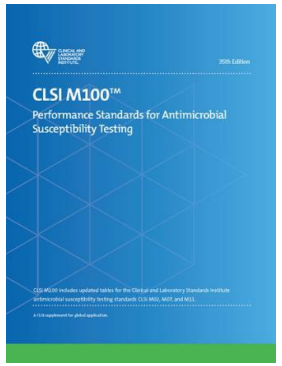


CRAB often harbor non-48 OXA genes including OXA 23, 24/40, 48, 58

AR Patient Safety Portal | CDC
(arpsp.cdc.gov/profile/arln/cre)

CLSI Guidelines for Carbapenemase Testing

- "Should" perform carbapenemase testing of CRE
- **Exception:** *Proteus, Providencia,* and *Morganella* spp. that are only "R" to imipenem
- **Possible exception:** for *E. cloacae* complex and *K. aerogenes* isolates that are only "R" to ertapenem



Enterobacterales
(excluding *Salmonella* and *Shigella* spp.)

Table 2A-1. Enterobacterales (excluding *Salmonella* and *Shigella* spp.) (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
CARBAPENEMS										

(25) Following evaluation of PK/PD properties, limited clinical data, and MIC distributions that include recently described carbapenemase-producing strains, revised breakpoints for carbapenems were first published in June 2010 (CLSI M100-S20-U) and are listed below. Because of limited treatment options for infections caused by organisms with carbapenem MICs or zone diameters in the intermediate range, clinicians may wish to design carbapenem dosage regimens that use maximum recommended doses and possibly prolonged IV infusion regimens, as has been reported in the literature.[5-8] Consultation with an infectious diseases specialist is recommended for isolates for which the carbapenem MICs or zone diameter results from disk diffusion testing are in the intermediate or resistant ranges.

Isolates resistant to any carbapenem tested (eg, ertapenem, imipenem, meropenem) should be tested for a carbapenemase using phenotypic and/or molecular assays. An exception to this recommendation is *Proteus*, *Providencia*, and *Morganella* spp. that are only resistant to imipenem. These assays should identify and ideally differentiate the presence of specific carbapenemase types (eg, KPC, NDM, OXA-48, VIM, IMP).

Decisions related to carbapenemase testing and reporting are best made by each laboratory in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders.

These results do not replace antimicrobial susceptibility testing, but are important for treatment decisions, and to inform infection control and prevention interventions and/or epidemiologic investigations.

Depending on local epidemiology and available resources, carbapenemase testing for *E. cloacae* complex and *K. aerogenes* isolates that are only resistant to ertapenem might not be necessary. Ertapenem resistance in these species is often due to mechanisms other than carbapenemase production and carbapenemases are currently uncommon in such isolates.

See Appendix G, Table G3 regarding suggestions for reporting when mechanism of resistance-based testing (molecular and phenotypic methods) is discordant with phenotypic AST.

The following information is provided as background on carbapenemases in Enterobacterales that are largely responsible for MICs and zone diameters in the intermediate and resistant ranges, and thus the rationale for setting revised carbapenem breakpoints

Goal – Identify and differentiate KPC, NDM, OXA-48, VIM, IMP

CLSI M100 Ed35 (2025). Table 2A-1. Comment 25 | CDPH (em100.edaptivedocs.net/Login.aspx)

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IDSA Guidelines for Carbapenemases and CROs

SECTION 3: CARBAPENEM-RESISTANT ENTEROBACTERALES

- Knowledge of the carbapenemase produced when CRE is identified in clinical isolates is important in guiding treatment decisions as specific newer β-lactam antibiotics have activity against specific carbapenemases.

Clinical Infectious Diseases

IDSA GUIDELINES

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections

Pranita D. Tamma,[1,©] Emily L. Heil,[2] Julie Ann Justo,[3] Amy J. Mathers,[4] Michael J. Satlin,[5] and Robert A. Bonomo[6]

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- **SECTION 4: PSEUDOMONAS AERUGINOSA WITH DIFFICULT-TO-TREAT RESISTANCE**
- **SECTION 5: CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII**

Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections | Oxford Academic (academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae403/7728556)

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Potential Utility of Newer Agents for CPOs[1]

Antimicrobial Agent	Enterobacterales			*Pseudomonas aeruginosa*	*Acinetobacter baumannii*
	KPC	MBLs NDM, VIM, IMP	OXA-48		
Beta-lactam combination agents					
Aztreonam-avibactam	Yes	Yes	Yes	No	No
Ceftazidime-avibactam	Yes	No	Yes	Yes	No
Ceftolozane-tazobactam	No	No	No	Yes	No
Imipenem-relebactam[2]	Yes	No	No	Yes	No
Meropenem-vaborbactam	Yes	No	No	No	No
Sulbactam-durlobactam	No	No	No	No	Yes
Other agents					
Cefiderocol	Yes	Yes	Yes	Yes	Yes

MBL=metallo-beta-lactamase

1 AST must be performed to confirm susceptibility as resistance to these "Yes" agents can occur

2 Does not apply to the members of the family *Morganellaceae*

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The Permanente Medical Group – Northern California

Andrea Kirmaier, PhD

Technical Director of Regional Lab R&D

Where is carbapenemase testing performed?

Kaiser NCAL Regional Laboratory

- 11 service areas
- 77 sites, including 22 hospitals
- ~18 counties

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When is carbapenemase testing performed?

Specimens	Criteria
Direct specimen Surveillance swabs	Orderable only by infectious-disease providers, DPH and CDPH; for high-risk patients (SNF, LTCF, ventilator units, contact of known CP case)
Direct specimen Positive blood cultures	Carbapenemase gene detected via BCID
Isolates	Enterobacterales: ertapenem-R and/or meropenem-I/R from Vitek AST *P. aeruginosa*: meropenem-I/R from Vitek AST *A. baumannii*: meropenem-I/R from Vitek AST

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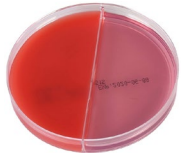
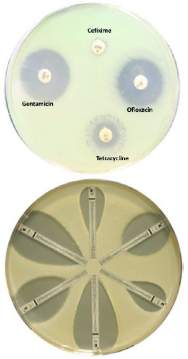
What methods are used for carbapenemase testing?

RECTAL SWAB

BLOOD



NOT BLOOD



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What methods are used for carbapenemase testing? Continued

Specimens	Method(s)	Target(s)
Direct specimen Surveillance swabs (rectal)	Cepheid CARBA-R	blaKPC, blaNDM, blaVIM, blaOXA-48, blaIMP
Direct specimen Positive blood cultures	Roche ePlex BCID-GN	blaIMP, blaKPC, blaNDM, blaOXA-23/48, blaVIM
Isolates	Hardy CARBA 5 (Enterobacterales, Psa)	KPC, NDM, VIM, OXA-48-like, IMP
	Cepheid CARBA-R (*A. baumannii*)	blaKPC, blaNDM, blaVIM, blaOXA-48, blaIMP

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How are results reported?

Pseudomonas aeruginosa **(urine, wound)**

(wound)		VIMS	Organism: PSA	%Prob: 99

(wound)		VIT	Organism:	PSA	Panel:	N804
	MIC Dilutn		MIC Interp			
AMK	%8		%S	Canceled		
A/S	%>32		%R	Canceled		
AZT				Canceled		
CPE	>32		R	Canceled		
CAZ	>32		R	Canceled		
CZA	%>16		%R	Canceled		
C/T	%>32		%R	Canceled		
CIP	>4		R	Canceled		
IMI/REL				Canceled		
LEVO	>8		R	Canceled		
MER	8		R	Canceled		
MIN				Canceled		
TZP	>128		R	Canceled		
TOB	%>16		%R	Canceled		
SXT	>=16/304		R	Canceled		

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How are results reported? (2)

Pseudomonas aeruginosa (urine, wound)

(wound)	VIMS	Organism: PSA	%Prob: 99

(wound)	VIT	Organism: PSA	Panel: N804
	MIC Dilutn	MIC Interp	
AMK	%8	%S	Canceled
A/S	%>32	%R	Canceled
AZT			Canceled
CPE	>32	R	Canceled
CAZ	>32	R	Canceled
CZA	%>16	%R	Canceled
C/T	%>32	%R	Canceled
CIP	>4	R	Canceled
IMI/REL			Canceled
LEVO	>8	R	Canceled
MER	8	R	Canceled
MIN			Canceled
TZP	>128	R	Canceled
TOB	%>16	%R	Canceled
SXT	>=16/304	R	Canceled

(wound)	Comment1	setting up PSA KB to confirm multi R.

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How are results reported? (3)

Pseudomonas aeruginosa (urine, wound)

(wound)	VIMS	Organism: PSA	%Prob: 99

(wound)	VIT	Organism: PSA	Panel: N804
	MIC Dilutn	MIC Interp	
AMK	%8	%S	Canceled
A/S	%>32	%R	Canceled
AZT			Canceled
CPE	>32	R	Canceled
CAZ	>32	R	Canceled
CZA	%>16	%R	Canceled
C/T	%>32	%R	Canceled
CIP	>4	R	Canceled
IMI/REL			Canceled
LEVO	>8	R	Canceled
MER	8	R	Canceled
MIN			Canceled
TZP	>128	R	Canceled
TOB	%>16	%R	Canceled
SXT	>=16/304	R	Canceled

(wound)	Comment1	setting up PSA KB to confirm multi R.

(wound)	KB	Organism: PSA	Panel:	KB Pseudo	Id#:
	Kirby-Bauer Interpretation				
Aztreonam	I Ver				
Ceftazidime	R Ver				
(1)Ciprofloxacin	R Ver				
Cefepime	R Ver				
Ceftolozane/Tazo	R Ver				
(2)Delafloxacin	R Ver				
Cefiderocol	S Ver				
Levofloxacin	R Ver				
Meropenem	R Ver				
(3)Tobramycin	R Ver				
Piperacillin/Taz	R Ver				

Carba5	Group
I (IMP)	
I (IMP)	ND
K (KPC)	
K (KPC)	ND
N (NDM)	
N (NDM)	ND
O (OXA-48)	
O (OXA-48)	ND
V (VIM)	
V (VIM)	Detected
FRZ	iso frzn

Footnotes:
1.Per CLSI guidelines, Amikacin is reported for urine isolates only.
2.Delafloxacin FDA Identified Interpretive Criteria, Injection and Oral Products.
3.Pseudomonas aeruginosa is considered intrinsically resistant to Gentamicin.

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How are results reported? (4)

Pseudomonas aeruginosa (urine, wound)

(wound) VIMS Organism: PSA %Prob: 99

(wound) VIT Organism: PSA Panel: N804

	MIC Dilutn	MIC Interp	
AMK	≤8	≤S	Canceled
A/S	≥32	≥R	Canceled
AZT			Canceled
CPE	>32	R	Canceled
CAZ	>32	R	Canceled
CZA	≥16	≥R	Canceled
C/T	≥32	≥R	Canceled
CIP	>4	R	Canceled
IMI/REL			Canceled
LEVO	>8	R	Canceled
MER	8	R	Canceled
MIN			Canceled
TZP	>128	R	Canceled
TOB	≥16	≥R	Canceled
SXT	>=16/304	R	Canceled

(wound) Comment1 setting up PSA KB to confirm multi R.

(wound) KB Organism: PSA Panel: KB Pseudo Id#:

	Kirby-Bauer Interpretation	
Aztreonam	I	Ver
Ceftazidime	R	Ver
(1)Ciprofloxacin	R	Ver
Cefepime	R	Ver
Ceftolozane/Tazo	R	Ver
(2)Delafloxacin	R	Ver
Cefiderocol	S	Ver
Levofloxacin	R	Ver
Meropenem	R	Ver
(3)Tobramycin	R	Ver
Piperacillin/Taz	R	Ver

Carba5	Group
I (IMP)	
I (IMP)	ND
K (KPC)	
K (KPC)	ND
N (NDM)	
N (NDM)	ND
O (OXA-48)	
O (OXA-48)	ND
V (VIM)	
V (VIM)	Detected
FRZ	iso frzn

Footnotes:
1.Per CLSI guidelines, Amikacin is reported for urine isolates only.
2.Delafloxacin FDA Identified Interpretive Criteria, Injection and Oral Products.
3.Pseudomonas aeruginosa is considered intrinsically resistant to Gentamicin.

ROUTINE CULT RSLT (wound)

!
Final Report
Light growth Pseudomonas aeruginosa ; Carbapenem Resistant Organism
Alert ;
VIM carbapenemase DETECTED.
Rare growth Proteus mirabilis

ORG PSA !

ORG PMIR !

Susceptibility

	Pseudomonas aeruginosa KIRBY BAUER	Proteus mirabilis MBINT	
Ampicillin		<=2	SUSCEPTIBLE
Ampicillin+Sulbactam		<=2	SUSCEPTIBLE
Aztreonam	INTERMEDIATE		
Cefazolin		4	INTERMEDIATE
Cefepime	RESISTANT	<=0.12	SUSCEPTIBLE
Cefiderocol	SUSCEPTIBLE		
Ceftazidime	RESISTANT		
Ceftolozane+tazobactam	RESISTANT		
Ceftriaxone		<=0.25	SUSCEPTIBLE
Ciprofloxacin	RESISTANT [1]	<=0.06	SUSCEPTIBLE
Delafloxacin	RESISTANT [2]		
Ertapenem		<=0.12	SUSCEPTIBLE
Gentamicin		<=1	SUSCEPTIBLE
Levofloxacin	RESISTANT	<=0.12	SUSCEPTIBLE
Meropenem	RESISTANT	<=0.25	SUSCEPTIBLE
Piperacillin+Tazobactam	RESISTANT	<=4	SUSCEPTIBLE
Tobramycin	RESISTANT [3]		
Trimethoprim+Sulfamethoxazole		<=1/19	SUSCEPTIBLE

[1] Per CLSI guidelines, Amikacin is reported for urine isolates only.
[2] Delafloxacin FDA Identified Interpretive Criteria, Injection and Oral Products.
[3] Pseudomonas aeruginosa is considered intrinsically resistant to Gentamicin.

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How Results are Reported: “Hard-wired”

- LIS: abx cascade reporting based on CLSI reporting tiers
- LIS: source-specific reporting
- LIS: intrinsic resistances

How Results are Reported: User Intervention

Blood Isolates

- Enterobacterales, Psa → BCID CP-neg → Vitek meropenem-I/R → Hardy CARBA 5
- *A. baumannii* → BCID CP-neg → Vitek meropenem-R → Cepheid CARBA-R

Proteus mirabilis

- Vitek ertapenem-I → check Vitek ceftazidime/ceftriaxone/cefepime →
  if all S, change ertapenem to S
  if any R, change ertapenem to R and perform Hardy CARBA 5

Enterobacterales

- Vitek cefepime-S/I + meropenem-I/R → Hardy CARBA 5 pos → change cefepime to R

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Testing/Reporting Broader-Spectrum Antimicrobial Agents for CROs/CPOs: Beta-lactam Combination Agents

Antimicrobial Agent	How Test	When Test/Report?	Organism(s)
Beta-lactam combination agents			
Aztreonam-avibactam	Send-out	Upon physician request	Enterobacterales only
Ceftazidime-avibactam	Vitek AST, Kirby-Bauer	Always	Enterobacterales or *P. aeruginosa*
Ceftolozane-tazobactam	Vitek AST, Kirby-Bauer	Always	
Imipenem-relebactam	(Vitek AST)	Send-out upon physician request (not validated in-house)	
Meropenem-vaborbactam	Kirby-Bauer	Always	Enterobacterales only
Sulbactam-durlobactam	Send-out	Upon physician request	*Acinetobacter*

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Testing/Reporting Broader-Spectrum Antimicrobial Agents for CROs/CPOs: Other Agents

Antimicrobial Agent	How Test	When Test/Report?	Organism(s)
Other Agents			
Cefiderocol	Kirby-Bauer	Always	Enterobacterales, *P. aeruginosa, Acinetobacter*
Delafloxacin*	Kirby-Bauer	Always	*E. coli, E. cloacae, K. pneumo* (SSTI, respiratory)
Omadacycline*	Kirby-Bauer	Always	*E. cloacae, K. pneumo* (SSTI, respiratory)
Plazomicin	Kirby-Bauer	Always	Enterobacterales excl. Morg/Prot/Prov

*FDA breakpoints (no CLSI breakpoints available)

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Communication of CRO/CPO Results Beyond the Patient Report: Internal

Bug	Result	Action
Internal		
CRO		Automatic reporting to IPC
CRO		Isolate stored for ~6 months

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Communication of CRO/CPO Results Beyond the Patient Report: External

Bug	Result	Action
External		
Enterobacs, Psa	CRE, CRPA	Report to ACPHD
A. baumannii	CRAB	Report and send to ACPHD
CRO	Carbapenemase-pos (CARBA-5/R)	Report to ACPHD
CRO	XDR	Send isolate to ACPHD
CRO	Resident of Alameda County LTCF or SNF	Send isolate to ACPHD
CPO		Report to CDPH (Title 17)

ACPDH = Alameda County Department of Public Health

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County of Los Angeles Public Health

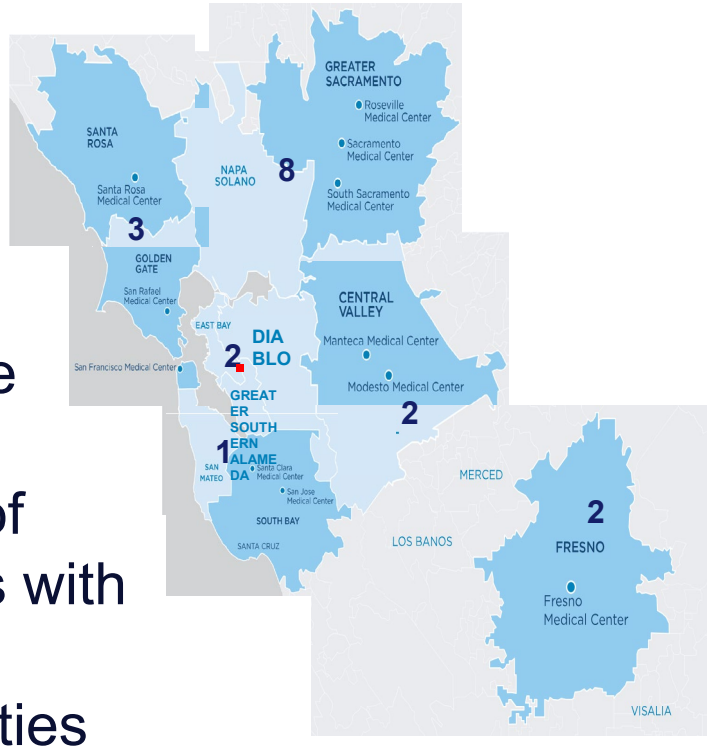
Challenges and Solutions for CRO/CPO Testing and Reporting

Lab Challenges

- Numerous product limitations of the AST cards, requiring alternative testing methods or extensive validations

Reporting Challenges

- FDA vs. CLSI
- Keeping instruments up-to-date
- Keeping the LIS up-to-date
- Due to large geographic area of coverage, different jurisdictions with different rules
  - 11 service areas, ~18 counties
  - County-by-county differences in what is considered a CRO (mero-R vs mero-I/R)



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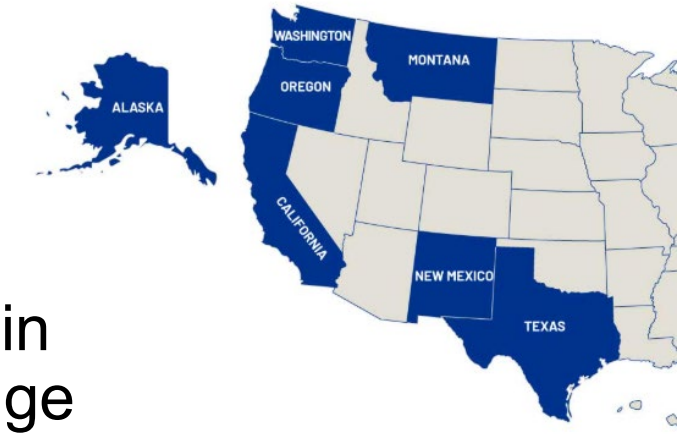
County of Los Angeles Public Health

Providence Saint Joseph Health

Meghan Mikuleky, MHA, MLS(ASCP)^{CM}

Microbiology/Molecular Biology Manager, OC/HD Service Areas

Providence St Joseph Health Orange County/High Desert



- Microbiology Lab located at Providence St Joseph Hospital in Orange, currently serves 4 Ministries (hospitals) in the Orange County/High Desert area:
  - *Providence St Joseph Hospital*-Orange
  - *Providence Mission Hospital*
    - *Laguna Beach*
    - *Mission Viejo*
  - *Providence St Mary Medical Center*

Note: No longer performing outpatient cultures.

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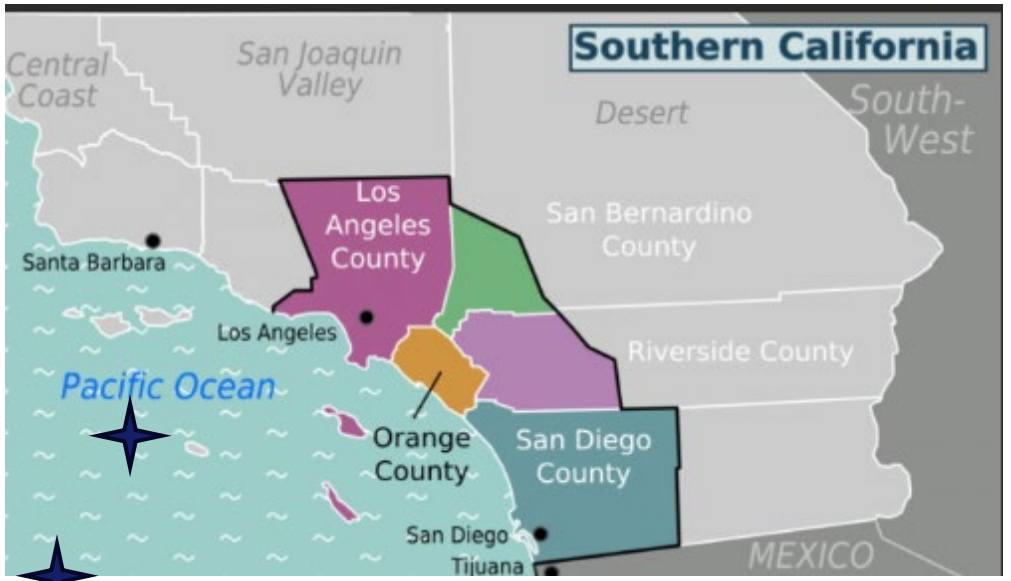
Providence St Joseph Health Orange County/High Desert, Continued

- Predominant patient population:
  - Acute in-patient care
  - Behavior Health- Orange
  - Transplant (kidney, pancreas)-Orange
  - Wound Care- Orange and St Mary
  - Acute In-Patient Rehab- Mission



Note: No longer performing outpatient cultures.

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When is carbapenemase testing performed?

Specimens (Method)	Criteria
Surveillance swab: Rectal Swabs on Admitted Patients HardyCHROM™ CRE Chromogenic Medium	Patient has international travel history, history of carbapenem-resistant organisms, and admission to inpatient acute rehab from outside facility.
Direct specimen **Positive blood cultures** Verigene BC-GN	All gram-negative growth in positive blood culture.
Isolates Cepheid Xpert® Carba-R	First patient isolate showing carbapenem resistance on susceptibility: • Enterobacterales • *Pseudomonas aeruginosa* • *Acinetobacter baumannii*

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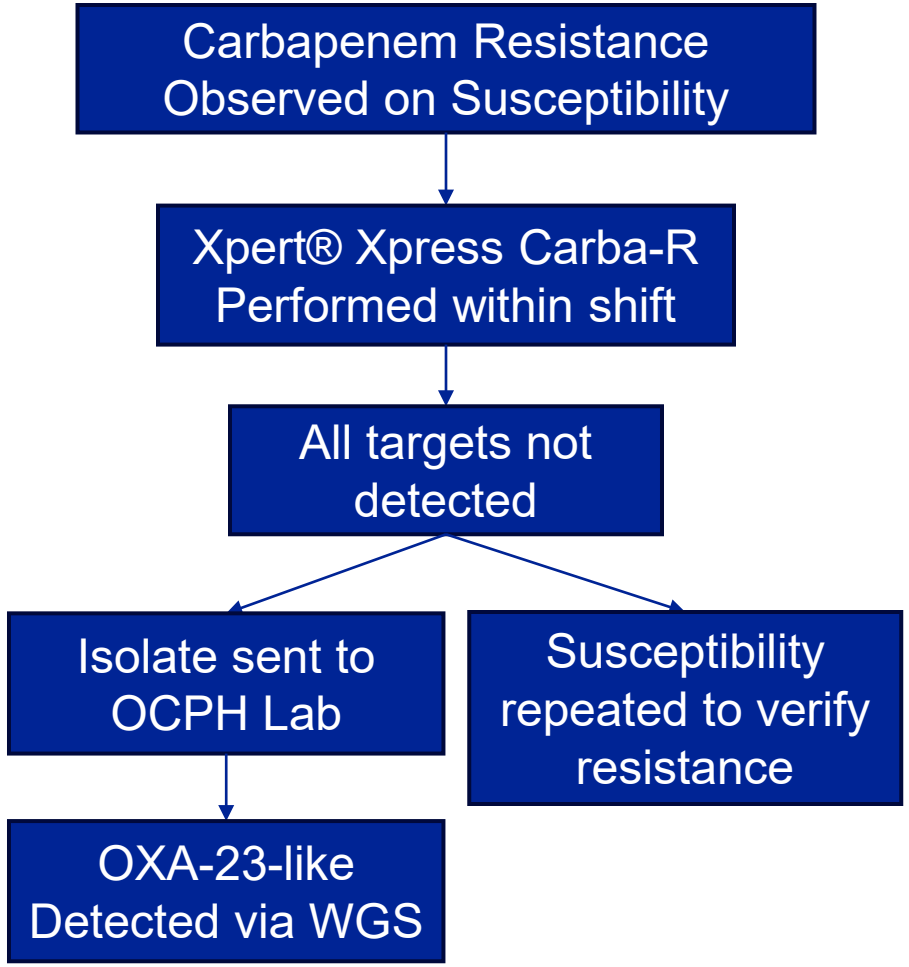
How are results reported? *Acinetobacter baumannii* complex, Carbapenem Resistant CR

Susceptibility

	Acinetobacter baumannii, Carbapenem resistant (CR) Method Not Specified	
Ampicillin + Sulbactam	16/8 ug/mL	**Intermediate**
Cefepime	>16 ug/mL	**Resistant**
Ceftazidime	>16 ug/mL	**Resistant**
Gentamicin	>8 ug/mL	**Resistant**
Meropenem	>8 ug/mL	**Resistant**
Nitrofurantoin		
Oxacillin		
Tetracycline	8 ug/mL	**Intermediate**
Trimethoprim + Sulfamethoxazole	>2/38 ug/mL	**Resistant**
Vancomycin		

Note: Antibiotics with no MIC value were for another organism in culture.



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Testing/Reporting Broader Spectrum Antimicrobial Agents for CRO/CPO: Beta-lactam Combination Agents

Antimicrobial Agent	How Test	When Test/Report?	Organisms
Beta-lactam combination agents			
Aztreonam-avibactam	Send out	ID Physician/Pharmacist Request	Enterobacterales only
Ceftazidime-avibactam	In house, via Microscan NM-56	Always test, cascade report and always reported to ID and pharmacists.	Enterobacterales *P. aeruginosa*
Ceftolozane-tazobactam	In house, via Microscan NM-56		
Imipenem-relebactam	Send out	ID Physician/Pharmacist Request	
Meropenem-vaborbactam	In house, via Microscan NM-56	Always test, cascade report and always reported to ID and pharmacists	Enterobacterales only
Sulbactam-durlobactam	Send out	ID Physician/Pharmacist Request	*Acinetobacter*

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Testing/Reporting Broader Spectrum Antimicrobial Agents for CRO/CPO: Other Agents

Antimicrobial Agent	How Test	When Test/Report?	Organisms
Other Agents			
Cefiderocol	Send out Considering Liofilchem ComASP	ID Physician/Pharmacist Request	Enterobacterales *P. aeruginosa,* *Acinetobacter*

Communication of CRO/CPO Results Beyond the Patient Report

Partner	Reported Via
RN Caring for Patient (If admitted)	Courtesy call to RN to inform and to ensure patient is put in isolation.
MD Overseeing Care of Patient	If admitted-notified by RN If discharged, notified by notification sent to ordering MD
ID Pharmacist	Contacted via Teams to inform M-F. ID Pharmacist also monitors reported organisms.
Infection Prevention	Epic Bugsy Flag and Chart Flag
Local and State Health Department	Epic Beaker is interfaced and reportable flag triggers notification. Isolate is sent to OCPH Lab.
Hospital/Region Infection Prevention Committee and Antibiotic Stewardship	Number of resistant isolates reported in meeting. Trends monitored.

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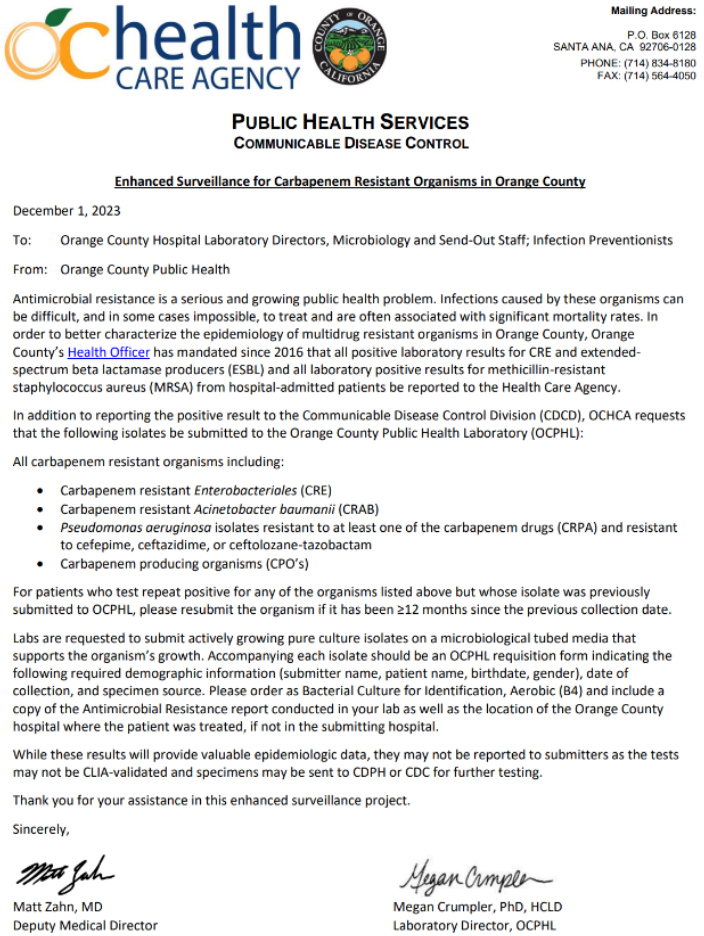
Participation in the AR Lab Network Program

- Due to request from Orange County Public Health in 2023, we submit carbapenem-resistant organisms for epidemiologic data
  - But only Orange County, not San Bernardino County



ochealth CARE AGENCY

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PUBLIC HEALTH SERVICES
COMMUNICABLE DISEASE CONTROL

Enhanced Surveillance for Carbapenem Resistant Organisms in Orange County

December 1, 2023

To: Orange County Hospital Laboratory Directors, Microbiology and Send-Out Staff; Infection Preventionists

From: Orange County Public Health

Antimicrobial resistance is a serious and growing public health problem. Infections caused by these organisms can be difficult, and in some cases impossible, to treat and are often associated with significant mortality rates. In order to better characterize the epidemiology of multidrug resistant organisms in Orange County, Orange County's Health Officer has mandated since 2016 that all positive laboratory results for CRE and extended-spectrum beta lactamase producers (ESBL) and all laboratory positive results for methicillin-resistant staphylococcus aureus (MRSA) from hospital-admitted patients be reported to the Health Care Agency.

In addition to reporting the positive result to the Communicable Disease Control Division (CDCD), OCHCA requests that the following isolates be submitted to the Orange County Public Health Laboratory (OCPHL):

All carbapenem resistant organisms including:

- Carbapenem resistant *Enterobacteriales* (CRE)
- Carbapenem resistant *Acinetobacter baumanii* (CRAB)
- *Pseudomonas aeruginosa* isolates resistant to at least one of the carbapenem drugs (CRPA) and resistant to cefepime, ceftazidime, or ceftolozane-tazobactam
- Carbapenem producing organisms (CPO's)

For patients who test repeat positive for any of the organisms listed above but whose isolate was previously submitted to OCPHL, please resubmit the organism if it has been ≥12 months since the previous collection date.

Labs are requested to submit actively growing pure culture isolates on a microbiological tubed media that supports the organism's growth. Accompanying each isolate should be an OCPHL requisition form indicating the following required demographic information (submitter name, patient name, birthdate, gender), date of collection, and specimen source. Please order as Bacterial Culture for Identification, Aerobic (B4) and include a copy of the Antimicrobial Resistance report conducted in your lab as well as the location of the Orange County hospital where the patient was treated, if not in the submitting hospital.

While these results will provide valuable epidemiologic data, they may not be reported to submitters as the tests may not be CLIA-validated and specimens may be sent to CDPH or CDC for further testing.

Thank you for your assistance in this enhanced surveillance project.

Sincerely,

Matt Zahn, MD
Deputy Medical Director

Megan Crumpler, PhD, HCLD
Laboratory Director, OCPHL

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Challenges and Solutions for CRO/CPO Testing and Reporting

Challenge	Proposed Solution
Understanding of CRO/CPO results by subject experts (ID, ID pharmacist, IPs) but not RNs, hospitalists	Considering adding comments to report, especially when negative, explaining other methods of resistance possible.
Cost of Cepheid test	Reviewing possible other methods, perform on patient's first isolate
Large health system in different states	Advocate/educate decision makers for CA requirements/reporting
Have 2 health departments with different requirements	OC- Requires sending of CR isolates SB- Does not require sending of CR isolates

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Scripps Health

Ian McHardy, PhD, D(ABMM)
Senior Director, Microbiology and Infectious Disease

Scripps Health

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Carbapenemase Testing

Specimens (Method)	Criteria
Rectal Swab Surveillance on Admitted Patients (Cepheid CarbaR)	**Criteria implemented per CAHAN recommendations:** • History of overnight hospitalization and/or invasive procedure outside of the US in the last 12 months • History of LTACH/SNF/subacute residency within the last 12 months • Direct transfer or history of hospitalization in the last 12 months from outside of San Diego County healthcare facility • Known history of CRO or *C. auris* colonization
Positive Blood Cultures (Verigene BCID + BD Phoenix NM311 panels)	All bottles w/ growth (as defined by Gram stain)
Isolates (Cepheid CarbaR)	By request from physician or pharmacist

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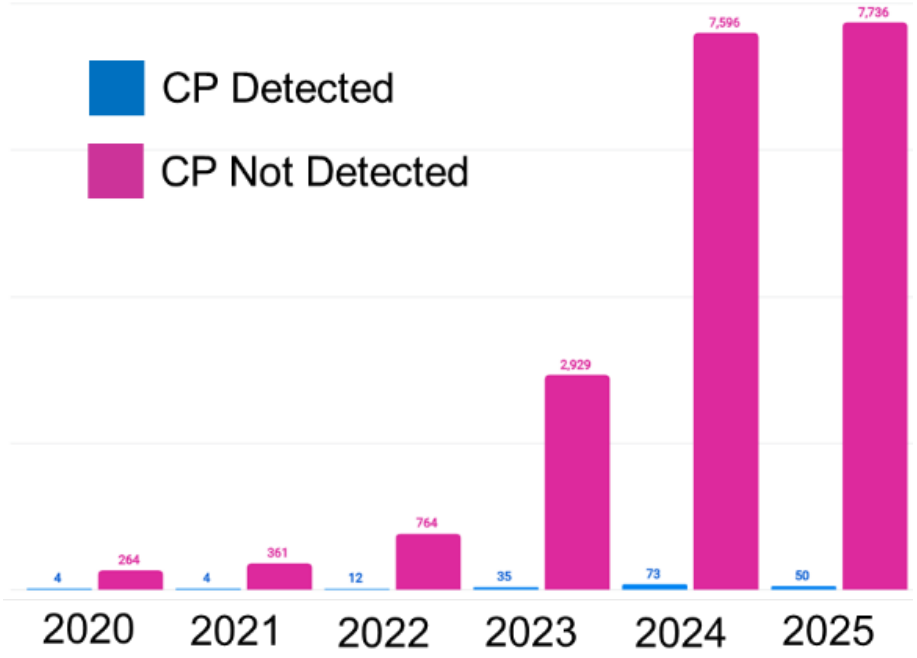
Scripps' Patient Population

Carbapenemase Surveillance



Meropenem Susceptibility

Organisms	Isolates	MER
Klebsiella pneumoniae	2429	99
Escherichia coli	14855	99
Pseudomonas aeruginsoa	2035	91
Enterobacter cloacae complex	544	99
Klebsiella (Enterobacter) aerogenes	415	99
Acinetobacter calcoaceticus-baumannii complex	45	40

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Scripps Case: CPO vs CEO (E=encoding)?

Cepheid Carba-R Surveillance

CRO Screen

Collected 7/24/2025 12:51 Status: Final result

Test Result Released: Yes (seen)

Specimen Information: Rectum; Swab

0 Result Notes

Component Ref Range & Units	
blaIMP Not Detected	Not Detected
blaVIM Not Detected	Not Detected
blaNDM Not Detected	Not Detected
blaKPC Not Detected	Not Detected
blaOXA48 Not Detected	Detected !

Blood Culture + Verigene BCID

Blood Culture

Escherichia coli !!

Lab: SCLABMC

```
2 of 2 sets positive.
The Gram negative Verigene
tests for the following
organisms and resistance
markers: Escherichia coli,
Klebsiella oxytoca, Klebsiella
pneumoniae, Pseudomonas
aeruginosa, Acinetobacter
species, Citrobacter species,
Enterobacter species, Proteus
species, CTX-M, IMP, KPC, NDM,
OXA and VIM.


Reference range: No growth
```

Gram Stain

!!

	Lab
Anaerobic bottle: Gram negative rods	CV
Aerobic Bottle: Gram negative rods	CV
Escherichia coli- DETECTED by Verigene nucleic acid test.	CV
OXACILLINASE Class D beta-lactamases, (OXA) DETECTED by Verigene nucleic acid test.	CV

BD Phoenix – NM311 with Epic cascading rules

Susceptibility

	Escherichia coli MIC	
Amoxicillin + Clavulanate	>16/8	Resistant
Ampicillin	>16	Resistant
Ampicillin + Sulbactam	>16/8	Resistant
Cefazolin	16	Resistant
Cefepime	<=0.5	Susceptible
Cefoxitin	<=4	Susceptible
Ceftazidime	<=2	Susceptible
Ceftriaxone	<=1	Susceptible
Cefuroxime (Oral)	<=4	Susceptible
Cefuroxime (Parenteral)	<=4	Susceptible
Ciprofloxacin	0.5	Intermediate
Gentamicin	<=2	Susceptible
Levofloxacin	0.5	Susceptible
Piperacillin + Tazobactam	64/4	Resistant
Tobramycin	<=2	Susceptible
Trimethoprim + Sulfamethoxazole	>2/38	Resistant

***Carbapenems not automatically reported due to cascading rule challenges in Epic**

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Testing/Reporting Broader-Spectrum Antimicrobial Agents for CROs/CPOs

Antimicrobial Agent	How Test	When Test/Report?	Organism(s)
Beta-lactam combination agents			
Aztreonam-avibactam	Sendout	ID Pharmacist/Physician request	Enterobacterales only
Ceftazidime-avibactam	BD Phoenix NM311/NM312	Gram-negative cascading rules	Enterobacterales or *P. aeruginosa*
Ceftolozane-tazobactam	BD Phoenix NM311/NM312	Gram-negative cascading rules	
Imipenem-relebactam	Disk diffusion	ID Pharmacist/Physician request	
Meropenem-vaborbactam	BD Phoenix NM311/NM312	ID Pharmacist/Physician request	Enterobacterales only
Sulbactam-durlobactam	Sendout	ID Pharmacist/Physician request	*Acinetobacter* sp.
Other Agents			
Cefiderocol	Disk diffusion	ID Pharmacist/Physician request	Enterobacterales or *P. aeruginosa*

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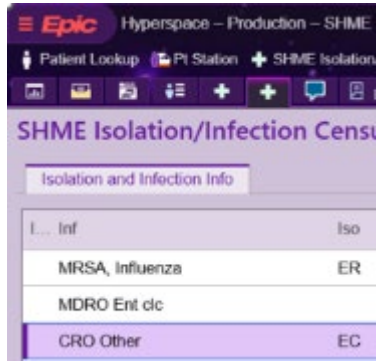
Streamlining CRO/CPO Result Actionability

	Automatic Epic Action(s)	Trigger(s)
Infection control	→ Appropriate Isolation Precautions Ordered → Populates IC Dashboard: Lists all infections and isolations	Culture & Surveillance Result
Antimicrobial Stewardship	→ ID Pharmacist In-basket notifications for Verigene detected CPO → Populates ASP Dashboard: Identifies active drug-bug mismatches and de-escalation opportunities	Culture Result
County/CDPH Reporting	→ Reporting via ELR (on final verify)	Culture & Surveillance Result



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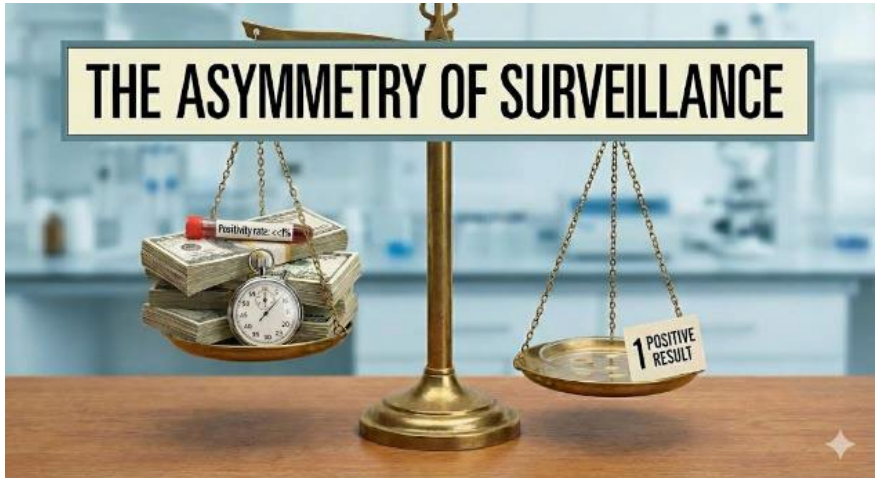
Other Challenges



Journal of Clinical Microbiology

J Clin Microbiol. 2022 Nov 14;60(12):e01181-22. doi: 10.1128/jcm.01181-22

A Pooling Strategy for Detecting Carbapenem Resistance Genes by the Xpert Carba-R Test in Rectal Swab Specimens

Peng Zhang, Qi Wang, Chaoe Zhou, Feifei Zhang, Xinghui Gao, Fred C Tenover, Yi-Wei Tang, Hui Wang

What cost is reasonable to identify each colonized patient?

- Reality can be $5k+
- Cost can be mitigated by pooling (LDT)

A Pooling Strategy for Detecting Carbapenem Resistance Genes by the Xpert Carba-R Test in Rectal Swab Specimens |ASM Journals (journals.asm.org/doi/10.1128/jcm.01181-22)

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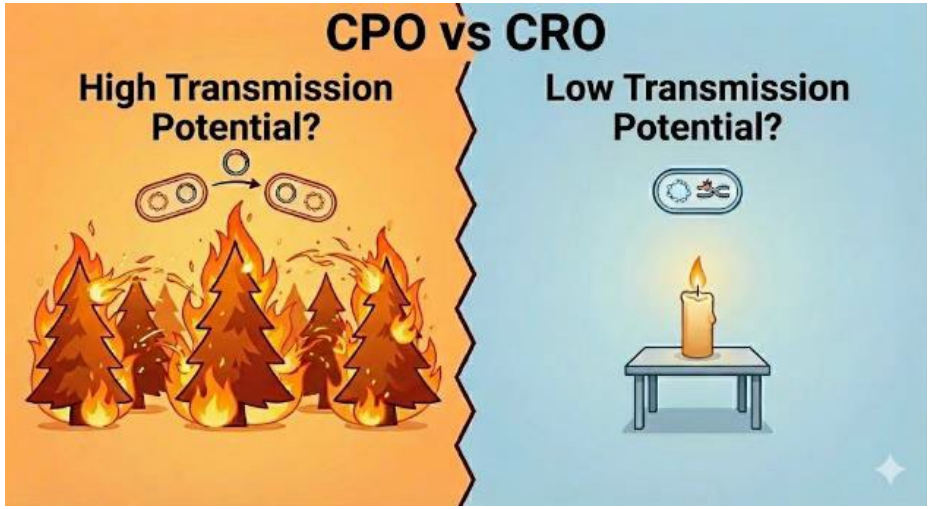
Other Challenges, Continued



Is CPO surveillance the highest leverage intervention in the fight against AMR?

- There is a dearth of evidence to support CPO being more transmissible than non-CP CRO.
- Non-CP CRO are much more common than CPO (here).

Increased focus on improving infection control in common sources: LTACHs, SNFs, vSNFs, etc.?

A Pooling Strategy for Detecting Carbapenem Resistance Genes by the Xpert Carba-R Test in Rectal Swab Specimens |ASM Journals (journals.asm.org/doi/10.1128/jcm.01181-22)

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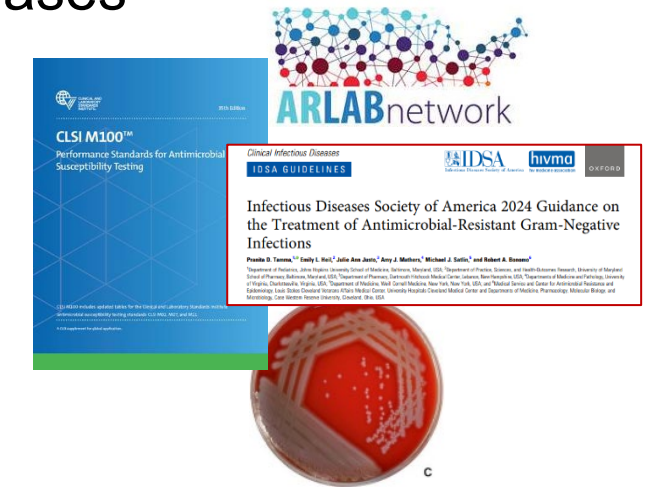
Summary

Practical Strategy for Testing for Addressing the “Case” for Carbapenemase Testing

- Test initial **CRE** isolates from patients for the big 5 carbapenemases
- Follow CLSI reporting rules for CRE:
  - Cefepime
  - Meropenem-vaborbactam in CRE with OXA-48
- Maintain a strategy for testing newer agents for CPOs
  - In house
  - Referral laboratory



Maintain robust communication with infection preventionists, antimicrobial stewardship, and public health!

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Resources

CDPH Resources

#	URL	Description
1	CDPH CPO website (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CarbapenemaseProducingOrganisms.aspx)	Landing page for CPO guidelines and other resources
2	CDPH CPO Quicksheet and Response Phases (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPOQuicksheet.pdf)	Guidance for understanding and managing CPO
3	CDPH CPO Reporting FAQ (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPOReportingFAQ.pdf)	Title 17 CPO reportable condition information
4	CDPH CPO Dashboard (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/ARDataReporting.aspx)	CPO case data reported to CDPH and updated on quarterly

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CDPH Resources, Continued

#	URL	Description
5	CDPH MDL Carbapenemase Testing FAQ (www.cdph.ca.gov/Programs/cls/idld/mdl/Pages/MDL-Expanded-Carbapenemase-Testing-Services-FAQs-2025.aspx)	Q&A about carbapenemase testing services offered at CDPH
6	Carbapenemase Testing for CROs: A Primer for Clinical and Public Health Laboratories (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CRO_PrimerTests_for_Carbapenemases.pdf)	Detailed listing of tests available for CRO/CPO and testing and reporting recommendations. (2025 update available soon)
7	CDPH Prioritizing Carbapenemase Testing Algorithm (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPTestingPrioritizationAlgorithm.pdf)	Guidance for working up CRO isolates

LACDPH Resources

#	URL	Description
8	LACDPH MDRO Website (publichealth.lacounty.gov/acd/mdro/index.htm)	Landing page for LACDPH MDRO guidelines and other resources
9	LACDPH Resource - Labs with Carbapenemase Testing Capacity (PDF) (publichealth.lacounty.gov/acd/docs/LaboratorieswithCPOScreening.pdf)	Referral laboratories that perform carbapenemase testing
10	LACDPH Multifacility Antibiogram Dashboard (publichealth.lacounty.gov/AntibiogramDashboard.htm)	Composite antibiogram data from LAC acute care hospitals

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CLSI Resources

#	URL	Description
11	Current CLSI M100 Standard (em100.edaptivedocs.net/Login.aspx?_ga=2.142608565.1088588701.1681740909-2137643289.1674665502)	Current CLSI M100 document (read only)
12	CLSI M100 Course (clsi.org/shop/education/courses/m100-course/)	Describes how to navigate CLSI M100 - 2025 (M100 35th edition) - 1.5 CE PACE
13	CLSI Biannual News Updates (www.clsi.org/resources/clsi-ast-news-updates/)	Newsletter featuring current AST topics
14	CLSI "Shop" "Education" "Microbiology" (www.clsi.org/shop/education/?page=1&specialtyAreas=microbiology&sortBy=Date:%20Newest%20First)	Access to educational programs beyond those listed above. Many address AST, provide CE credit and are free.

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Other Resources

#	URL	Description
15	Implementation of Carbapenemase-Producing Organism Colonization Screening Protocol (PDF) (www.aphl.org/aboutAPHL/publications/Documents/ID-CPO-Screening-Guide.pdf)	APHL guideline for CPO colonization screening
16	FDA cleared diagnostic tests – search for AST for specific agents (www.fda.gov/medical-devices/tests-used-clinical-care/find-all-in-vitro-diagnostic-products-and-decision-summaries-november-2003)	Allows search for all FDA cleared tests

Complete an evaluation to obtain 1 laboratory continuing education unit (CEU)

What's Happening with CROs in California in 2025? Webinar Evaluation (required for lab CEU)

12/10/25 webinar evaluation
(forms.office.com/g/U85aePHZ1H)

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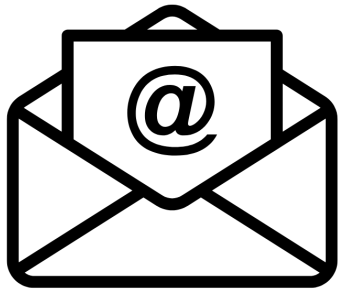
Thank You

Questions?



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hai@ph.lacounty.gov

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