Carbapenemase-producing Organisms: Guidance for Reporting and Containment

September 29th, 2022

Presented via Webinar
Objectives

• Provide background information on carbapenemase-producing organisms (CPO)
• Review new CPO laboratory reporting requirements
• Present carbapenemase testing recommendations
• Describe CPO prevention strategies and activities
• Summarize guidance for public health and facility-based response to reports of CPO
Carbapenemase-producing Organisms
What are carbapenemases?

- Carbapenemases are enzymes (proteins) that make carbapenem and other β-lactam antibiotics ineffective.

- **Examples** of carbapenemases:
  - KPC, NDM, OXA-48, VIM, IMP
  - Other variants include OXA-23, OXA-24/40, OXA-58, OXA-237

- Carbapenemase genes encode for carbapenemase enzymes, e.g., $bla_{KPC}$, $bla_{NDM}$
  - Found on mobile genetic elements that can be transferred within and between bacterial species

KPC=Klebsiella pneumoniae carbapenemase; NDM=New Delhi metallo-β-lactamase; OXA=oxacillinase, VIM=Verona integron metallo-β-lactamase; IMP=imipenemase;
What are carbapenemase-producing organisms (CPO)?

• Bacteria that produce a carbapenemase enzyme are called carbapenemase-producing organisms (CPO), and most commonly include carbapenem-resistant:
  • Enterobacterales (e.g., *E. coli*, *Citrobacter* species) (CRE)
  • *Acinetobacter baumannii* (CRAB)
  • *Pseudomonas aeruginosa* (CRPA)

• Examples include:
  • KPC-producing *Klebsiella pneumoniae*
  • VIM-producing *Pseudomonas aeruginosa*
  • NDM-producing *Acinetobacter baumannii*
Why are we concerned about CPO?

- CPO can be **resistant** to all antibiotic classes (pan-resistant)
  - Difficult and more expensive to treat infections
  - Leads to substantial morbidity and mortality

- CPO cause **outbreaks** in healthcare settings
  - Carbapenemase genes can be **transferred** within and between bacterial species
  - Patients can remain **colonized** for many months (no “clearance” recommendations)
  - CPO can be **persistent** in the healthcare environment
  - **Risk factors** include frequent or extended healthcare exposure, presence of indwelling devices, and antibiotic use
CPO are a concern everywhere

- CPO are urgent and serious **antimicrobial resistance (AR) threats** to human health
  - [CDC 2019 AR Threats Report](www.cdc.gov/drugresistance/biggest-threats.html)

- During the **COVID-19 pandemic**, there has been an **increase in AR healthcare-associated infections**
  - Significant increase in antimicrobial use
  - Lapse in core infection prevention and control practices

[Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.]

- Carbapenem-resistant *Acinetobacter* (+78%)
- Antifungal-resistant *Candida auris* (+60%)*
- Carbapenem-resistant Enterobacteriales (+35%)
- Antifungal-resistant *Candida* (+26%)
- ESBL-producing Enterobacteriales (+32%)
- Vancomycin-resistant Enterococcus (+14%)
- Multidrug-resistant *P. aeruginosa* (+32%)
- Methicillin-resistant *Staphylococcus aureus* (+13%)
CPO Cases Reported in California, January 2019–July 2022

CP=carbapenemase-producing; CRAB=carbapenem-resistant *Acinetobacter baumannii*; CRE=carbapenem-resistant Enterobacterales; CRPA=carbapenem-resistant *Pseudomonas aeruginosa*; Big 3=E. coli, Enterobacter and Klebsiella species
Carbapenemases in California, January 2019–June 2022
Most Common Carbapenemases among CPO Cases

GES=Guiana extended-spectrum β-lactamase; IMP=imipenemase; KPC=Klebsiella pneumoniae carbapenemase; NDM=New Delhi metallo-β-lactamase; OXA=oxacillinase; VIM=Verona integron metallo-β-lactamase
Regional Outbreak of NDM-CRAB

- Detected via targeted surveillance
- Previously rare in US
- Majority NDM+OXA-23, pan-nonsusceptible
- Spread exacerbated by COVID-19 challenges
- Outbreaks in hospitals and skilled nursing facilities (SNF)

For more information, see [CDPH NDM-CRAB CAHAN](https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CAHAN_NDM_OXA23_CRAB_May2021.pdf)
HEALTHCARE-ASSOCIATED INFECTIONS PROGRAM

Novel MDRO among International Travelers

Ongoing Risk of Highly Drug-Resistant Infections in Patients Following Hospitalization or Invasive Procedures in Mexico

February 2021

The California Department of Public Health (CDPH) and local public health partners are alerting healthcare providers of a recent increase in reports of VIM-producing carbapenem-resistant *Pseudomonas aeruginosa* (VIM-CRPA) in patients following hospitalization or invasive medical procedures in Mexico for routine healthcare visits, medical emergencies, and medical tourism. Since our November 2019 Health Advisory describing an initial cluster of five VIM-CRPA cases with similar exposure from August to October 2019, there have been three additional reports of VIM-CRPA identified in California from August to December 2020. These patients reported undergoing invasive procedures in Guadalajara and Tijuana, Mexico. The most recent case was identified in December 2020; the patient reported having plastic surgery at a Tijuana-area healthcare facility in October 2020.

CDPH VIM-CRPA CAHAN (PDF)
(www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CAHAN_VIM-CRPA_Mexico_Feb2021.pdf)
CPO Reporting for Cluster Detection

- **Initial report**
  - Acute care hospital (ACH) reports 2 VIM-CRPA cases to public health lab
  - LAC Department of Public Health investigation identifies outpatient clinic as common source

- **More cases**
  - Clinic reports 2 suspect cases to DPH, but no carbapenemase testing done at ACH
  - LAC Public Health Laboratory tests isolates, and confirms VIM

- **Investigation**
  - DPH & clinic collaborated to improve IPC practices, identify source(s) of transmission
  - Additional case finding did not identify other cases
New CPO Reporting Requirements
Carbapenemase-producing Organisms Added to Title 17

September 6, 2022

Dear Public Health Colleagues,

The California Department of Public Health, in consultation with the California Conference of Local Health Officers, recently updated Title 17 sections 2500, 2502 and 2505 of the California Code of Regulations. This letter is to inform you of these changes and to remind you of the reporting requirements outlined in these sections. These changes, effective immediately, are summarized below.
CPO Reporting

• Labs should report the following results for any specimen:
  • Positive phenotypic test result for carbapenemase production, with or without identification of a specific carbapenemase type
  • Positive molecular test result detecting a carbapenemase gene
  • Detection of a carbapenemase gene by next-generation sequencing (e.g., whole genome sequencing)
  • Specimen positive for a carbapenemase gene without bacterial species identification (e.g., rectal screening swab)
• Labs should wait until all tests (i.e., phenotypic and molecular carbapenemase test) are resulted before submitting a report.
CPO Reporting

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  - Specimen positive for a carbapenemase gene without bacterial species identification (e.g., rectal screening swab)
- Labs should wait until all tests (i.e., phenotypic and molecular carbapenemase test) are resulted before submitting a report.
- Title 17 regulations do not supersede local health department requirements (e.g., provider reporting through NHSN, isolate submission, etc.)
## Replacing CP-CRE with CPO

<table>
<thead>
<tr>
<th>Expand reportable organisms</th>
<th>Reportable organisms</th>
<th>Report antimicrobial susceptibility testing results</th>
<th>Report untested carbapenem-resistant organisms</th>
<th>Lab-reportable within 1 working day</th>
<th>Provider reporting</th>
<th>Submit isolate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Enterobacter</em> spp., <em>E.coli</em>, <em>Klebsiella</em> spp.</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td></td>
<td>All carbapenemase-producing organisms</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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</table>
## Replacing CP-CRE with CPO

<table>
<thead>
<tr>
<th></th>
<th>CP-CRE</th>
<th>CPO</th>
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<td><strong>Reportable organisms</strong></td>
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<td>All carbapenemase-producing organisms</td>
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<td>No</td>
</tr>
<tr>
<td><strong>Submit isolate</strong></td>
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<td>No</td>
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**Expand reportable organisms**

**Simplify reporting**
## Replacing CP-CRE with CPO

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<td>All carbapenemase-producing organisms</td>
</tr>
<tr>
<td>Simplify reporting</td>
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<tr>
<td>Report antimicrobial</td>
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</tr>
<tr>
<td>susceptibility testing results</td>
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<td></td>
</tr>
<tr>
<td>Report untested</td>
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<td>No</td>
</tr>
<tr>
<td>carbapenem-resistant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>organisms</td>
<td></td>
<td></td>
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<tr>
<td>Keep other requirements</td>
<td></td>
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<tr>
<td>Lab-reportable within 1</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>working day</td>
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<tr>
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</tr>
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</table>
California Reportable Disease Information Exchange (CalREDIE)

- For local health departments (LHD) using CalREDIE:
  - Combining *CPO (Excluding Enterobacteriaceae)* and *CP-CRE* conditions
  - Minor changes to the laboratory results and epidemiologic information sections
  - Oct. 19th, 2022 CalREDIE LHD Users Call
- For healthcare providers, reporting laboratories and LHD:
  - Accurate and complete demographic information is increasingly important for public reporting
    - Complete patient race, ethnicity, gender, and address information as much as possible
## Electronic Laboratory Reporting Best Practices

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genus &amp; Species</td>
<td>Each accession number should be associated with at least one organism</td>
<td>✗ “Carbapenem-resistant Enterobacteriaceae”</td>
</tr>
<tr>
<td></td>
<td>(unless no identification performed)</td>
<td>✗ “Isolate”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ “Klebsiella pneumoniae”</td>
</tr>
<tr>
<td>Specimen Source</td>
<td>Each accession number should be associated with single specimen source</td>
<td>✗ “TA”</td>
</tr>
<tr>
<td></td>
<td>that is clearly spelled out</td>
<td>✗ “Culture”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ “Urine”</td>
</tr>
<tr>
<td>Carbapenemase Test Results</td>
<td>If a carbapenemase is detected, clearly indicate the specific type of</td>
<td>✗ “carbapenemase-resistant [insert organism].”</td>
</tr>
<tr>
<td></td>
<td>carbapenemase gene identified (if applicable).</td>
<td>✗ “KPCKP”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ “NDM gene detected”</td>
</tr>
<tr>
<td>Comments and Local Fields</td>
<td>All key information should be indicated using specific LOINC and SNOMED</td>
<td></td>
</tr>
<tr>
<td></td>
<td>codes in the body of the ELR message. The comments field and local fields</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(e.g., Local Test Name) can repeat this information, but should be as clear as possible.</td>
<td></td>
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</tbody>
</table>
Carbapenemase Testing Recommendations
Why Carbapenemase Testing Matters

• Treatment options differ* depending on carbapenemase type
  • An individual’s carbapenemase status can guide effective prescribing decisions
  • Local epidemiology can drive empiric treatment decisions
• Helps prioritize infection prevention and response strategies
  • Screening and cohorting
• General increase in prevalence and diversity of CPO
  • Carbapenemase-producing Acinetobacter
  • Novel or rare carbapenemases (e.g., GES, IMP)
• Recommended for all labs using old carbapenem breakpoints**

**CLSI: When Should Clinical Microbiology Laboratories Perform Carbapenemase Detection Tests? (PDF) (clsi.org/media/2046/burning-question-when-should-clinical-microbiology-laboratories-perform-carbapenemase-detection-tests.pdf)
Accessing Carbapenemase Testing

• Please use CDPH Microbial Diseases Laboratory (MDL) form ‘Antimicrobial Susceptibility Testing-AST’ to submit carbapenem-resistant organism isolates for carbapenem testing
  • For the most updated submission form and instructions on the MDL website, see CDPH MDL FAQ Sheet (www.cdph.ca.gov/Programs/CID/DCDC/Pages/MDLSubmissionInstructionsandForms.aspx)

• Some local public health laboratories and the regional Antimicrobial Resistance Laboratory Network (www.cdc.gov/drugresistance/ar-lab-networks/domestic.html) provide carbapenemase testing services

• To guide testing decisions, use the CDPH Algorithm for Prioritizing Carbapenemase Testing (PDF) (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH Document Library/CPTestingPrioritizationAlgorithm.pdf)
Algorithm for Prioritizing Carbapenemase Testing

Carbapenem-resistant organism ([Enterobacteriaceae (CRE), Acinetobacter baumannii (CRAB), or Pseudomonas aeruginosa (CRPA)])

Does isolate fit any of the following criteria:
- **Pan-non-susceptible** (intermediate or resistant to all antibiotics tested)?
- Identified as CRAB, or CRPA with specific susceptibility profile?
- From sterile site specimen (e.g., blood)?

**YES**

Carbapenemase producing (CP)?

**YES**
- Obtain carbapenemase testing capable of identifying specific carbapenemase (e.g., KPC, NDM); if carbapenemase-producing organism (CPO), report through electronic laboratory reporting (ELR), including specific carbapenemase.

**NO**

Consider obtaining carbapenemase testing (phenotypic or molecular); if CP, report as CPO through ELR.

Report as CPO, including specific carbapenemase, through ELR.

Part of cluster or outbreak?

**YES**
- Report as Outbreak to local public health and CDPH Licensing & Certification (if licensed healthcare facility); submit isolate if requested to public health for further testing.

**NO**
- Do NOT report.

1 CRPA=carbapenem-resistant *Pseudomonas aeruginosa* non-susceptible to cefepime, ceftazidime, or ceftolozane-tazobactam

2 Contact your local health department to access free carbapenemase testing through a public health lab. In order of priority and as resources allow, obtain carbapenemase testing for other epidemiologically relevant patient isolates, including those: epi-linked to a new CPO case (roommate, residing on same unit, or sharing bathroom, healthcare personnel or medical equipment); admitted from facility with known CPO cluster/outbreak; with history of overnight healthcare exposure or invasive procedure outside U.S.; or admitted from long-term acute care hospital or ventilator-equipped skilled nursing facility, especially with indwelling medical devices.

3 CPO Reporting FAQ (PDF) ([www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH Document Library/CPOReportingFAQ.pdf](http://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH Document Library/CPOReportingFAQ.pdf))
Guidance for Public Health and Facility-based Prevention and Response
A Comprehensive Containment Strategy

With public health support...

• Prevention in All Facilities
  • Build strong foundation for lab surveillance, core infection prevention and control (IPC) practices, antimicrobial stewardship and interfacility communication
  • Conduct proactive screening and onsite IPC assessments

• Early Detection and Aggressive Response in Affected Facilities
  • Investigate, reinforce core IPC practices, conduct screening and onsite IPC assessments, ensure communication

• Mitigation and Maintenance to Prevent Further Spread
  • Focus on strengthening all prevention activities
CPO Prevention Strategies & Activities
CPO prevention activities are part of a comprehensive, regional prevention and response strategy

Targeting high-risk facilities (LTACH, vSNF) in jurisdictions adjacent to interconnected with CPO outbreak jurisdictions, public health to provide:

1. Free, proactive CPO screening to understand baseline prevalence and prevent spread

2. Proactive onsite IPC assessments by experienced HAI infection preventionists
Other CPO Prevention Activities

1. **Regional Prevention Collaboratives** in 3 targeted counties
   - Hands-on, multi-week training for participating SNF staff (certified nursing assistant (CNA), environmental services (EVS))
   - Antimicrobial stewardship (AS) consultation (hospitals and SNF)
   - Peer-to-peer learning, interfacility communication (all participating facilities)

2. **Statewide vSNF Project**
   - Focus on strengthening core IPC practices, with quality improvement project

3. **Statewide LTACH AS Project**
   - Focus on improving AS, with targeted intervention and technical consultation
CPO Response Strategies & Activities
Facility-based Actions: Early Detection and Initial Response

• **Enhanced surveillance**
  - Perform or access carbapenemase testing for CRE, CRAB, CRPA
  - Screen high-risk patients (epi-linked, admitted from long-term acute care hospitals (LTACH), ventilator-equipped SNF (vSNF) or outbreak facility, healthcare exposure abroad)

• **Immediate actions**
  - Case report
  - Contact Precautions and single-bed room if possible
  - Interfacility communication
  - Investigation

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1. [CDPH Algorithm for Prioritizing Carbapenemase Testing](https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPTestingPrioritizationAlgorithm.pdf)
2. [CDPH CPO Screening Decision Tree](https://www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/Tier2_Pathogen_Screening_Decision_Tree_Oct2020.pdf)
### Core response and IPC measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>CPO</th>
</tr>
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<tbody>
<tr>
<td>Good hand hygiene – ABHS preferred</td>
<td>X</td>
</tr>
<tr>
<td>Contact Precautions, single room if possible; Enhanced Standard Precautions if no transmission in SNF</td>
<td>X</td>
</tr>
<tr>
<td>Thorough environmental cleaning and disinfection</td>
<td>X</td>
</tr>
<tr>
<td>Routine adherence monitoring</td>
<td>X</td>
</tr>
<tr>
<td>Cohorting of patients and HCP</td>
<td>X</td>
</tr>
<tr>
<td>Lab surveillance</td>
<td>X</td>
</tr>
<tr>
<td>Screening of high-risk contacts</td>
<td>X</td>
</tr>
<tr>
<td>Intra- and inter-facility communication</td>
<td>X</td>
</tr>
</tbody>
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**Public health can support:**
- Investigation
- Screening
- IPC onsite assessments, education, and recommendations
HEALTHCARE-ASSOCIATED INFECTIONS PROGRAM

Core response and IPC measures apply to other organisms

<table>
<thead>
<tr>
<th>CPO</th>
<th>Candida auris</th>
<th>C. diff</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good hand hygiene – ABHS preferred</td>
<td>X</td>
<td>X</td>
<td>Soap &amp; water</td>
</tr>
<tr>
<td>Contact Precautions, single room if possible; Enhanced Standard Precautions if no transmission in SNF</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Thorough environmental cleaning and disinfection</td>
<td>X</td>
<td>Use <a href="www.epa.gov/pesticide-registration/list-p-antimicrobial-products-registered-epa-claims-against-candida-auris">List P agent</a>¹ (List K agent or bleach, OK)</td>
<td>Use <a href="www.epa.gov/pesticide-registration/list-k-epas-registered-antimicrobial-products-effective-against-clostridium">List K agent</a>²</td>
</tr>
<tr>
<td>Routine adherence monitoring</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
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<td>Intra- and inter-facility communication</td>
<td>X</td>
<td>X</td>
<td>X</td>
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ABHS=alcohol-based hand sanitizer; C. diff=Clostridioides difficile; HCP=healthcare personnel; SNF=skilled nursing facility

¹[List P Agent](www.epa.gov/pesticide-registration/list-p-antimicrobial-products-registered-epa-claims-against-candida-auris)
²[List K agent](www.epa.gov/pesticide-registration/list-k-epas-registered-antimicrobial-products-effective-against-clostridium)
³[List N agent](www.epa.gov/coronavirus/about-list-n-disinfectants-coronavirus-covid-19-0)
Communication is key to preventing interfacility spread!

- Actively seek CPO (and other multidrug-resistant organism (MDRO) status of all admissions
- Flag medical record for future admissions
- Inform receiving facility of patient MDRO status and IPC recommendations
- Reach out to high-volume transfer facilities (hospital-SNF), share IP expertise
- Educate patients and family
- Use interfacility transfer form

CDPH Interfacility Transfer Communications Guide (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/InterfacilityCommunication.aspx)

LACDPH Transferring Guidance for MDROs (PDF) (publichealth.lacounty.gov/acd/docs/LACDPH_TransferringGuidanceforMDROs.pdf)

LACDPH Interfacility Transfers Guide (PDF) (publichealth.lacounty.gov/acd/docs/InterfacilityTransfersGuide.pdf)
Resources

- **CDPH Antimicrobial Resistance Resources landing webpage**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/AntimicrobialResistanceLandingPage.aspx)
- **CDPH CPO Webpage**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE_InfectionPreventionStrategies.aspx)
- **CDPH CPO Reporting FAQ (PDF)**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/CPOReportingFAQ.pdf)
- **CDPH Algorithm for Carbapenemase Testing (PDF)**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH Document Library/CPTestingPrioritizationAlgorithm.pdf)
- **CDPH CRE Quicksheet (PDF)**
- **CDPH CRPA and CRAB Quicksheet (PDF)**
- **CDPH CPO Screening Decision Tree (PDF)**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/CDPH%20Document%20Library/Tier2_Pathogen_Screening_Decision_Tree_Oct2020.pdf)
- **CDPH CRE for Families Webpage**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Carbapenem-resistantEnterobacteriaceae(CRE).aspx)
- **CDPH CRAB for Families Webpage**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Carbapenem_resistantAcinetobacter.aspx)
- **CDPH CRPA for Families Webpage**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Carbapenem_resistantPseudomonas.aspx)
- **LACDPH NMDRO webpage** (including lab newsletters)
  (publichealth.lacounty.gov/acd/Diseases/NMDRO.htm)
- **LACDPH Healthcare Outreach Unit webpage**
  (publichealth.lacounty.gov/acd/HOU.htm)
Upcoming Events

• Carbapenemase-producing Organisms: Carbapenemase Testing Strategies - October
• Carbapenemase-producing Organisms: Carbapenemase Testing to Inform Clinical Treatment Decisions – November or December
• CalREDIE Local Health Department Users Call - Wednesday October 19th
• *Candida auris* Reporting and Isolate Submission
Thank you!

Questions?

For more information, contact
HAIProgram@cdph.ca.gov
hai@ph.lacounty.gov