Frequently Asked Questions (FAQ)

What are carbapenem-resistant Enterobacteriaceae (CRE)?
- CRE are bacteria of the Enterobacteriaceae family, such as Enterobacter species (spp.), Escherichia coli (E. coli), or Klebsiella spp. that are resistant to one or more carbapenem antibiotics (doripenem, ertapenem, imipenem, and meropenem).

What are carbapenemase-producing CRE (CP-CRE)?
- Some CRE produce an enzyme, carbapenemase, that breaks down beta-lactam antibiotics (penicillins, cephalosporins, monobactams, and carbapenems), making the antibiotics ineffective. CP-CRE have the ability to spread rapidly and can cause infections that are difficult to treat and associated with high mortality rates.

What laboratory tests can detect carbapenemase?
- Phenotypic tests detect carbapenemase production by bacteria. Molecular tests identify the specific type of carbapenemase, such as KPC or NDM. Phenotypic, molecular, or both types of testing may be performed.

Who will report CP-CRE?
- CP-CRE is a laboratory-reportable condition, with no clinical criteria included. Healthcare providers are not required to report CP-CRE cases, but are still responsible for reporting any outbreaks and unusual infectious disease occurrences. Healthcare providers may be contacted by local health department staff during an investigation.

What is reportable?
- CP-CRE, limited to Enterobacter spp., E. coli, and Klebsiella spp., are reportable per the most recently published Centers for Disease Control and Prevention (CDC) case definition. Other Enterobacteriaceae (for example, Citrobacter spp.) and non-Enterobacteriaceae (for example, Pseudomonas aeruginosa and Acinetobacter baumannii) can produce carbapenemases but are not reportable as CP-CRE; however, these need to be reported as unusual infectious disease occurrences.
- Laboratories that perform carbapenemase testing, or use a public health or reference laboratory to obtain carbapenemase testing, will report the following:

Any Enterobacter spp., E. coli, or Klebsiella spp. where the isolate is:
1. Positive for carbapenemase production by a phenotypic method (see Table 1)
-OR-
2. Positive for a known carbapenemase resistance mechanism by a recognized molecular test (see Table 1)

1 https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/LabReportableDiseases.pdf
2 Klebsiella pneumoniae carbapenemase (KPC), New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), imipenemase (IMP) metallo-β-lactamase, OXA-48 carbapenemase, or novel carbapenemase
4 https://wwwn.cdc.gov/nndss/conditions/carbapenemase-producing-carbapenem-resistant-enterobacteriaceae/
### Table 1. Phenotypic and molecular methods for carbapenemase testing

<table>
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<tr>
<th>Phenotypic tests for carbapenemase production</th>
<th>Molecular tests for resistance mechanism</th>
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<td>Carba NP</td>
<td>BioFire</td>
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<td>Carbapenem inactivation method (CIM)</td>
<td>Polymerase chain reaction (PCR)</td>
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<td>Metallo-β-lactamase test (e.g., E-test)</td>
<td>Verigene</td>
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<td>Modified carbapenem inactivation method (mCIM)</td>
<td>Whole-genome sequencing (WGS)</td>
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<td>Modified Hodge test (MHT)⁶</td>
<td>Xpert Carba-R</td>
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</table>

Laboratories that are able to perform carbapenemase testing should wait until all tests (antimicrobial susceptibility, phenotypic and/or molecular carbapenemase) are resulted **before** submitting a report.

- **Laboratories that do **not** perform or obtain carbapenemase testing, will report the following:**

  *Enterobacter* spp., *E. coli*, or *Klebsiella* spp. from any site, resistant to any carbapenem: doripenem, imipenem, or meropenem (minimum inhibitory concentration (MIC) ≥4 µg/ml); or ertapenem (MIC ≥2 µg/ml).

These laboratories can access public health laboratory resources for carbapenemase testing by contacting their local health department.

Regardless of carbapenemase testing capacity, all laboratories should submit all antimicrobial susceptibility testing results (MIC values and interpretation).

### How does this new reporting requirement affect existing local health department CRE reporting requirements?

- The updated Title 17 reporting requirements do not change existing local health department reporting requirements (for example, isolate submission, reporting of all CRE cases, or reporting mechanism). Per California state regulations, CP-CRE is a laboratory-reportable condition. For further clarification, contact the applicable local health department.

### Where can I find additional resources?

- **CDPH Website: CRE for Public Health and Healthcare Providers**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/CRE_InfectionPreventionStrategies.aspx)
- **CDPH Website: CRE for Patients and their Families**
  (www.cdph.ca.gov/Programs/CHCQ/HAI/Pages/Carbapenem-resistantEnterobacteriaceae(CRE).aspx)
- **CDC Website: CRE in Healthcare Settings**
  (www.cdc.gov/hai/organisms/cre/index.html)

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⁵ Validated carbapenemase testing methods developed in the future may be added to this list.

⁶ A positive MHT can be used to confirm CP-CRE for *Klebsiella* spp and *E. coli* but not *Enterobacter* spp. An isolate that tests positive on MHT but negative by PCR for KPC, NDM, OXA-48, VIM, and IMP should have additional characterization performed with another phenotypic test for carbapenemase such as mCIM.