PURPOSE:
CDC’s Epidemiology and Laboratory Capacity Cooperative agreement (ELC) has requested Public Health Laboratories to collect, confirm, and characterize carbapenem-resistant Enterobacteriaceae (CRE) and Pseudomonas aeruginosa (CRPA) isolates. These activities will help to identify isolates that produce a carbapenemase and classify the kind of carbapenemase resistance present. Isolates will be collected from jurisdictional healthcare facilities using a strategy that allows for estimating the burden of CRE and CRPA within the population served by the Public Health Laboratory. The Public Health Laboratory and state Epidemiologists will collaborate with the state HAI/AR prevention programs and with the Antimicrobial Resistance Laboratory Network regional laboratories (ARLN). This Guidance document will identify expectations for testing, submitting, and reporting.

ISOLATE COLLECTION:
1. Isolate collection strategies:
   - CRE species for collection and characterization: It is recommended that isolate collection be targeted to *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, and Enterobacter spp. that are resistant to imipenem, meropenem, doripenem, or ertapenem by standard susceptibility testing methods (i.e., minimum inhibitory concentrations of ≥4 μg/mL for doripenem, imipenem or meropenem or ≥2 μg/mL for ertapenem).
   - CRPA collection and characterization: It is recommended that isolate collection include all *P. aeruginosa* isolates that are resistant to imipenem, meropenem, or doripenem by standard susceptibility testing methods (i.e., minimum inhibitory concentrations of ≥8 μg/mL). Mucoid isolates should be excluded.
2. The goal is to obtain isolates from all types of healthcare facilities within the state, including isolates collected from clinical laboratories that serve short term acute care hospitals and long-term acute care hospitals. If possible, isolate collection should be extended to include other types of healthcare facilities (e.g., long-term care facilities).

**Public Health Laboratory Testing Includes:**

1. Drugs for AST:
   • Isolates will be tested against all drugs listed Table 1.

**Table 1.** Drugs used to confirm and further characterize carbapenem-resistant Enterobacteriaceae (CRE) and carbapenem-resistant *P. aeruginosa* (CRPA)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>CRE</th>
<th>CRPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbapenems</td>
<td>2 carbapenems (ertapenem and either imipenem, doripenem or meropenem)</td>
<td>2 carbapenems (selected from imipenem, doripenem and meropenem)</td>
</tr>
<tr>
<td>Cephems</td>
<td>ceftazidime, ceftriaxone&lt;sup&gt;a&lt;/sup&gt;, and cefepime</td>
<td>ceftazidime and cefepime</td>
</tr>
<tr>
<td>B-lactam/B lactamase inhibitor combinations</td>
<td>N/A</td>
<td>piperacillin-tazobactam</td>
</tr>
<tr>
<td>Monobactams</td>
<td>aztreonam</td>
<td>aztreonam</td>
</tr>
<tr>
<td>Polymyxins</td>
<td>colistin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>colistin&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Other third-generation cephalosporin(s) may be substituted for ceftriaxone

<sup>b</sup> Broth microdilution only

2. Phenotypic methods to detect carbapenemase production:
   • Modified Carbapenem Inactivation Method (mCIM)

3. Molecular Detection Targets for CRE and CRPA:
   • *bla<sub>KPC</sub>*, *bla<sub>NDM</sub>*, OXA-48-like genes, *bla<sub>VM</sub>*<sup>a</sup>, *bla<sub>IMP-1</sub>* group

4. Reporting:
   • The Montana Public Health Laboratory will report any isolates requiring immediate public health action to the State HAI Coordinator, the CDC, and the submitter.
   • These findings include:
   • **Novel resistance mechanism in CRE or CRPA.** This novel resistance includes CRE or CRPA testing positive for carbapenemase production by phenotypic methods and negative by PCR. These isolates will be forwarded to the ARLN regional network
laboratory for additional testing. Further testing may also be performed at the CDC Laboratory if needed.

- **Carbapenemase-producing CRPA.**
- **Non-KPC carbapenemase in Enterobactericeae.**
- **Pan-resistance.** An isolate that is non-susceptible to all drugs tested to date.
- **mcr-type resistance.** Detection of mcr-1 or mcr-2 by PCR or WGS (tested at the ARLN if indicated).

Please refer any questions regarding isolate submissions to the Montana Public Health Laboratory. 1-800-821-7284 or Directly to Carrie Biskupiak at 406-444-5526 or Debbie Gibson at 406-444-5970.