How to meet CRE reporting and submission requirements

Bureau of Infectious Disease and Laboratory Sciences
Massachusetts Department of Public Health

October 10, 2017
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Using Control Panel (cont.)

Entering questions and posting them for the presenter.
Please note: This webinar will be recorded and archived. We will send out a link to the recorded webinar and PowerPoint slides for those who could not attend today’s call.

There will be a short survey emailed to all webinar attendees. Thank you in advance for taking the time to complete the survey.

Questions/Comments

• Telephone 617-983-6801
• Email: isishelp@state.ma.us
Objectives

- Introductions to the MDPH MDRO Team
- Reporting requirements
- Mapping of electronic laboratory results from your facility
- Isolate submission to MDPH
MDPH Team

- Kerri Barton, AR Contractor/Epidemiologist
- Melissa Cumming, Antibiotic Resistance Coordinator
- Tracy Stiles, Microbiology Division Director
- Scott Troppy, Antibiotic Resistance Surveillance Epidemiologist
- Samorga Young, Research Analyst
Acronyms

- **CRE**: Carbapenem-resistant Enterobacteriaceae
- **CP-CRE**: Carbapenemase-producing CRE
  - **KPC**: *Klebsiella pneumoniae* carbapenemase
  - **NDM**: New Delhi metallo-beta-lactamase
  - **OXA-48**: Carbapenem-hydrolizing oxacillinase
  - **VIM**: Verona integron-encoded metallo-beta-lactamase
  - **IMP**: Imipenemase metallo-beta-lactamase
- **MCR-1**: Mobilized Colistin Resistance gene
What must be reported?

- Any CRE (isolated from any source), including CP-CRE (reportable since December 2013)
  - Klebsiella pneumoniae
  - Klebsiella oxytoca
  - Enterobacter cloacae
  - Enterobacter aerogenes
  - E. coli

- Any identified novel resistance (isolated from any source) or organism of concern
  - This includes mcr-1 and Candida auris

105 CMR 300.000 Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements. (Latest version from January 2017):
http://www.mass.gov/eohhs/docs/dph/cdc/reporting/rptbldiseases-labs.pdf
Why is reporting important?

- Cases of CRE are difficult to treat due to resistance to most antibiotics
  - Some cases of CP-CRE are resistant to nearly all available antibiotics

- It is vital that these cases are identified quickly in order to implement proper infection control measures to prevent the spread of infection in healthcare facilities
Epidemiologic Investigation

- After a case is reported to MDPH, an Epi may contact the infection preventionist at your facility to discuss infection control measures and collect:
  - Demographics
  - Clinical history
  - History of carbapenem use
  - Whether they attend a supervised care setting*
  - Risk factors in the previous 30 days:
    - Travel out of country
    - Use of reusable medical device/ procedure*

*Cases with these exposures/risk factors will require additional follow-up
Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

November 2015 Update - CRE Toolkit

http://www.cdc.gov/hai/organisms/cre/cre-toolkit/
Carbapenemase testing methods fall into two categories:

- **Phenotypic screening** (general detection of the presence of a carbapenemase):
  - MHT: Modified Hodge Test
  - CIM: Carbapenem Inactivation Method
  - mCIM: Modified Carbapenem Inactivation Method

- **Mechanism detection** (Targeted testing for a specific carbapenemase mechanism):
  - CarbaNP or PCR to detect KPC, NDM, OXA-48, VIM, and/or IMP, if available
Carbapenemases

- Enzymes that degrade carbapenem antibiotics

- 5 plasmid-encoded enzymes of primary public health concern:
  - K. pneumoniae carbapenemase (KPC)
  - New Delhi Metallo-β-lactamase (NDM)
  - Verona Integron Mediated Metallo-β-lactamase (VIM)
  - Imipenemase (IMP)
  - OXA-48-type

- Found in Enterobacteriaceae and glucose non-fermenters (e.g., Pseudomonas aeruginosa and Acinetobacter)
Mapping results from your facility

Using the ELR portal

Go to the Organism tab and look for Multi Drug Resistant Organism in the drop-down list

Here's the description of what to report:

**Clinical Description:** Carbapenem-resistant Enterobacteriaceae (CRE) infections have many different clinical presentations. Colonization with a CRE is sometimes detected through surveillance cultures.

**What to Report:**
- Isolation of *Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Enterobacter aerogenes,* or *Enterobacter cloacae* with resistance to imipenem, meropenem, doripenem, or ertapenem (from any site);
- Any isolate of *Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Enterobacter aerogenes,* or *Enterobacter cloacae* that demonstrates production of a carbapenemase (e.g., KPC, NDM, VIM, IMP, OXA-48) by a recognized test (e.g., polymerase chain reaction, metallo-β-lactamase test, modified Hodge test, Carba NP).
- Include susceptibility result values (MIC) and interpretations (S, I, R).
Mapping results from your facility

- Review of Loinc/Snomed: Once you have completed your mapping, please test your mapping in the staging site first.

- Send one or two test messages through and let us know; we will review them and give you the go-ahead to send them into the LIVE ELR portal.
Loinc and Snomed as of 10/16/2017

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<th>SNOMED Code</th>
<th>SNOMED Name</th>
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<td>Bacteria identified in isolate by MS MALDI-TOF</td>
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<td>Escherichia coli</td>
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<td>Enterobacter cloacae</td>
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<td>Klebsiella pneumonia</td>
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<td>Intermediate</td>
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Isolate Submission and Testing at MA SPHL

- Submission of CRE isolates was added to the 105CMR300.000 reportable conditions list in January 2017
- A memo was sent out to all clinical laboratories on 8/8/17 with detailed isolate submission requirements
- The go-live date at MASPHEL was 10/4/17
CRE Isolate Submission Criteria

- Any of the following *Enterobacteriaceae* (isolated from any source):
  - *Klebsiella pneumoniae*
  - *Klebsiella oxytoca*
  - *Enterobacter cloacae*
  - *Enterobacter aerogenes*
  - *E. coli*

- With resistance to **one or more** of the following THREE carbapenems:
  - **Imipenem** (MIC >=4 µg/ml)
  - **Meropenem** (MIC >=4 µg/ml)
  - **Doripenem** (MIC >=4 µg/ml)

- OR, demonstrate carbapenemase production (CP-CRE)
We will also accept the following isolates for testing (these will not be captured for surveillance purposes and results *do not* need to be reported to us):

- **CRPA**: Carbapenem Resistant *Pseudomonas aeruginosa*: Submit only the first isolate per month
- **CRAB**: Carbapenem Resistant *Acinetobacter baumanii*: Do NOT submit at this time
How to submit your CRE and CRPA

- One isolate per patient per admission, regardless of source
- Please use general state lab requisition found: [http://www.mass.gov/eohhs/docs/dph/laboratory-sciences/general-submission-form.pdf](http://www.mass.gov/eohhs/docs/dph/laboratory-sciences/general-submission-form.pdf)
- Please send to the clinical microbiology lab
- Please include all susceptibility data generated at your facility
  - Your results may help inform our testing
What testing will be done?

- Isolate identification will be confirmed via Maldi-TOF or API 20E
- mCIM to determine carbapenemase production
- AST testing via sensititre*, Kirby Bauer disk diffusion, or both
- PCR to detect resistance genes: $\text{bla}_{kpc}$, $\text{bla}_{ndm}$
  - $\text{bla}_{imp}$, $\text{bla}_{vim}$, $\text{bla}_{oxa-48like}$, $\text{bla}_{mcr}$

* Still undergoing validation
Discordant results

- Testing done at the MA-SPHL & ARLN/CDC is for surveillance purposes
- Treatment decisions should be based on your facility susceptibility results
Antibiotic Resistance Laboratory Network (7 Regional Labs)
## ARLN (Antimicrobial Resistance Laboratory Network)

### Who tests what? (As of June 20, 2017)

<table>
<thead>
<tr>
<th>Location</th>
<th>Carbapenemase gene identification</th>
<th>Carbapenemase gene colonization screening</th>
<th>mcr gene testing</th>
<th>mcr gene colonization screening</th>
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<tbody>
<tr>
<td></td>
<td>KPC</td>
<td>NDM</td>
<td>OXA-48</td>
<td>VIM</td>
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<td>ARLN Regional Lab</td>
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### Additional Table

<table>
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<tr>
<th>Organism ID</th>
<th>AST</th>
<th>Carbapenemase production testing</th>
<th>Carbapenemase gene identification</th>
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</thead>
<tbody>
<tr>
<td>State testing</td>
<td>Most</td>
<td>Most</td>
<td>Most</td>
</tr>
</tbody>
</table>
Global Emergence of mcr-1

- Since initial report, found globally
  - >20 countries and 6 continents
  - Food animals, meat, vegetables, surface water
  - Ill patients, asymptptomatically colonized patients
- Multiple species: *E. coli*, *K. pneumoniae*, *Salmonella enterica*, *Shigella sonnei*
- Earliest isolates identified from 1980s (chickens, *E. coli*, China)
- Earliest human isolate from 2008 (*Shigella sonnei*, Vietnam)
- Highly transmissible among different bacterial strains
- Increases colistin MICs 8 to 16-fold
  - Typical MICs 4 to 8 μg/ml

Liu, Lancet Infet Dis 2016; 16: 16-68
Skov, Euro Surveill 2016; 21(9):pii=30155
Mcr-1 in the U.S.

- 29 reports as of October 3, 2017
  - 27 human isolates (11 E. coli and 3 Salmonella)
  - 2 porcine isolates collected at slaughter (*E. coli*)

- Primarily ESBLs
  - 1 CP-CRE (NDM)
  - Multiple susceptible to most antibiotics, including 3rd generation cephalosporins
Tracking mcr-1 as of Oct. 3, 2017

Massachusetts
- Isolate Type: Human isolate
- Number Reported: 5
In the event that your facility identifies an *Enterobacteriaceae* with colistin resistance, please call the 24/7 Epidemiology line at 617-983-6800 and send the isolate to MASPHL.

- The ARLN conducts mcr-1 detection testing for clinical isolates
Contact Information

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