Carbapenemase-Producing Carbapenem Resistant *Enterobacteriaceae* (CP-CRE) Statewide Reporting Webinar

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The SHARP Unit

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Carbapenem-resistant *Enterobacteriaceae*

- *Enterobacteriaceae* – enteric organisms, gram negative bacilli

- **Carbapenems** – class of broad-spectrum, β-lactam antibiotics
  - Agents of last resort – one of the few remaining effective therapies
  - Only 4 carbapenems: Doripenem, Ertapenem, Imipenem, and Meropenem

- **Infections** - responsible for urinary tract infections, bacteremia, pneumonia, wound infections
Mechanisms of Carbapenem Resistance

1. Carbapenemases
2. Acquired resistance
3. Naturally imipenem-resistant *Enterobacteriaceae*

*Not all CRE are carbapenemase producers...*
CRE and Novel Resistance Activity

• Carbapenemases:
  • *Klebsiella pneumonias* carbapenemase (KPC)
  • New Delhi metallo-β-lactamase (NDM)
  • Verona integron encoded metallo-β-lactamase (VIM)
  • Imipenemase metallo-β-lactamase (IMP)
  • Oxacillinase-48 (OXA-48)

• Other resistance elements:
  • Mobile colistin resistance (mcr)
Public Health Threat of CRE Infections

• **Treatment options are more limited**
  – New antibiotics have been slow to develop and come to market
    – Although several new agents are now/soon to be available
    – Pan-resistant strains identified

• **CRE infections associated with high mortality rates**

• **Resistance is highly transmissible**
  – Between organisms – plasmids
  – Between patients – hands, healthcare workers

• **Potential for spread into the community**
  – *E. coli* a common cause of community infection
Carbapenem-resistant *Enterobacteriaceae* (CRE) Surveillance and Prevention Initiative
# CRE Surveillance and Prevention Initiative

## Voluntary Participation

<table>
<thead>
<tr>
<th>Phase</th>
<th>Baseline Period</th>
<th>Intervention Period</th>
<th>Acute Care</th>
<th>LTAC</th>
<th>LTC/SNF</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Sept 2012-Feb 2013</td>
<td>Mar 2013- Aug 2014</td>
<td>17</td>
<td>4</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>Phase 2</td>
<td>Mar 2014-Aug 2014</td>
<td>Sept 2014-Feb 2016</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Sept 2015-Feb 2016</td>
<td>Mar 2016-Aug 2017</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>New facilities</td>
<td>Sept 2017-Feb 2018</td>
<td>Mar 2018-Aug 2019</td>
<td>14</td>
<td>7</td>
<td>0</td>
<td>21</td>
</tr>
</tbody>
</table>
Regional CRE Incidence Rates

CRE Rate per 10,000 Patient Days

<table>
<thead>
<tr>
<th>Year</th>
<th>Quarter</th>
<th>CRE Regions in MI, Sept 2017—Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Q3</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td>Q4</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Q1</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Q2</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Q3</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Q4</td>
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<tr>
<td>2017</td>
<td>Q1</td>
<td></td>
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<tr>
<td>2017</td>
<td>Q2</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>Q3</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>Jul-Aug</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>Sept</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>Q4</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>Q1</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>Q2</td>
<td></td>
</tr>
</tbody>
</table>

Colors represent different regions:
- **East**
- **West**
- **Mid**
- **North**
- **LTAC/LTC**
- **Statewide**
# Regional CRE Incidence Rates

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of Facilities</th>
<th>Number of CRE Cases</th>
<th>Total Patient Days</th>
<th>Overall Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>East</td>
<td>19</td>
<td>17</td>
<td>380,099</td>
<td>0.45</td>
</tr>
<tr>
<td>West</td>
<td>7</td>
<td>3</td>
<td>128,213</td>
<td>0.23</td>
</tr>
<tr>
<td>Mid</td>
<td>9</td>
<td>14</td>
<td>132,127</td>
<td>1.06</td>
</tr>
<tr>
<td>North</td>
<td>7</td>
<td>0</td>
<td>43,235</td>
<td>0.00</td>
</tr>
<tr>
<td>LTAC/LTC</td>
<td>19</td>
<td>2</td>
<td>57,431</td>
<td>0.35</td>
</tr>
<tr>
<td>Statewide</td>
<td>61</td>
<td>36</td>
<td>741,105</td>
<td>0.49</td>
</tr>
</tbody>
</table>
## Prevention Measures Implemented

<table>
<thead>
<tr>
<th>Category</th>
<th>Specific Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure Changes</td>
<td>• Screening and presumptive isolation of all patients admitted from an LTAC  &lt;br&gt;• PICU CHG Bath Audits  &lt;br&gt;• Development of practitioner-specific reports to describe infectious diseases specialist approvals of carbapenem use  &lt;br&gt;• In-house laboratory will be performing phenotypic testing to confirm carbapenemase production  &lt;br&gt;• Flagging of CRE patient in our IC surveillance system (RL systems) so that they can be isolated more quickly on subsequent admissions  &lt;br&gt;• Daily CHG bathing of all ICU patients  &lt;br&gt;• Terminal Clean/Bed exchange for patient who has occupied a room for greater than 45 days  &lt;br&gt;• Prompt discontinuance of unnecessary invasive devices  &lt;br&gt;• CHG bathing in confirmed CRE cases for 3 days  &lt;br&gt;• Sending CRE isolates to MDHHS BOL for lab confirmation</td>
</tr>
<tr>
<td>Education</td>
<td>• Improved physician education on prevention and control of MDRO organisms, infection, and colonization  &lt;br&gt;• MDRO Component in 2013 Annual CHM Infection Prevention (IP) Nursing Intranet Learning (NL) Competency, Education  &lt;br&gt;• Hand Hygiene Impact on MDRO/CRE  &lt;br&gt;• Educating new/transiting staff in the proper process of CHG bathing of patients in ICU  &lt;br&gt;• Educational pamphlet will be developed to educate patients and visitors about CRE  &lt;br&gt;• Educate patient care services (RNs, and PCAs) about preventing transmission of CRE, compliance with signage and supplies for Contact Precautions while screening patients for CRE or for a patient that is positive for CRE  &lt;br&gt;• Education to raise awareness of the resistance mechanisms of emerging pathogens  &lt;br&gt;• Present MDRO (including CRE) education for Medical Residents and reach other healthcare personnel (RNs, support services, MDs, etc.) using forums such as unit huddle</td>
</tr>
<tr>
<td>Compliance</td>
<td>Evaluating compliance with isolation practices (i.e., posting of proper signage, availability of gloves, masks, and gowns as well as proper use of these supplies) for all patients that are in isolation</td>
</tr>
<tr>
<td>Communication</td>
<td>Rapid communication between lab, IP and ID physicians, inter-facility communication, Inter-facility communication for CRE positive patients: When a CRE is identified, communication will occur to any outside transferring facility by communication transfer form and/or phone communication</td>
</tr>
<tr>
<td>Pilot project</td>
<td>Project using Dazo fluorescent marking gel to objectively measure thoroughness of disinfection cleaning on critical surfaces</td>
</tr>
</tbody>
</table>
# CRE Infections Prevented

## 2012-Current

<table>
<thead>
<tr>
<th>Initiative Phase</th>
<th>All Facilities</th>
<th>Acute Care</th>
<th>LTAC/LTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1 Facilities</td>
<td>280</td>
<td>235</td>
<td>45</td>
</tr>
<tr>
<td>Phase 2 Facilities</td>
<td>68</td>
<td>50</td>
<td>18</td>
</tr>
<tr>
<td>Phase 3 Facilities</td>
<td>14</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Combined Cohort (Mar 2018 - current)</td>
<td>3</td>
<td>4</td>
<td>-1</td>
</tr>
<tr>
<td><strong>Total Initiative</strong></td>
<td><strong>365</strong></td>
<td><strong>289</strong></td>
<td><strong>76</strong></td>
</tr>
</tbody>
</table>
CP-CRE Reporting
CRE Surveillance & Prevention Initiative vs. CP-CRE Reporting

• CRE Surveillance and Prevention Initiative
  • *Klebsiella pneumoniae* and *Escherichia coli* that are resistant to ANY carbapenem
  • Voluntary - reported through the CRE S&PI only
  • 61 facilities

• New Communicable Disease Reporting for CP-CRE
  • *Klebsiella spp.*, *Enterobacter spp.*, *Escherichia coli* positive for carbapenemase production by a phenotypic test *or* positive for carbapenem resistance mechanism (KPC, NDM, VIM, OXA-48, IMP or other carbapenemase gene) *and* those resistant to ANY carbapenem
  • Mandatory - reported through ELR or manual entry into MDSS
  • Statewide
CP-CRE Reporting Requirements

• Laboratories, infection prevention and Local Health Departments are required to report all cases of CP-CRE according to the following criterion for Klebsiella spp., E. coli, or Enterobacter spp.:

  • Healthcare record contains a diagnosis of Carbapenemase-producing Carbapenem-resistant Enterobacteriaceae (CP-CRE), KPC, NDM, OXA-48, IMP or VIM or other novel carbapenemase

  • Any isolate of Klebsiella spp., E. coli, or Enterobacter spp. demonstrating carbapenemase production by a phenotypic test (e.g., Carba NP, CIM, mCIM)

  • Any isolate of Klebsiella spp., E. coli, or Enterobacter spp. with a known carbapenemase resistance mechanism (e.g., KPC, NDM, OXA-48, IMP, VIM, or other carbapenemase gene) by a recognized molecular test (e.g., PCR, Expert Carba-R)
CP-CRE Reporting Requirements

• If laboratories are unable to detect CP-CRE, (i.e., cannot test for carbapenemase production (phenotypic) or resistance mechanism (molecular test):
  • Report any isolate of *Klebsiella spp.*, *E. coli*, or *Enterobacter spp.* with a minimum inhibitory concentration (MIC) of any of the following:
    • ≥4 mcg/ml for Meropenem
    • ≥4 mcg/ml Imipenem
    • ≥4 mcg/ml Doripenem
    • ≥ 2 mcg/ml for Ertapenem
Carbapenemase and Resistance Mechanism Testing

• Laboratories are *strongly encouraged to submit CRE isolates* to the MDHHS Bureau of Laboratories
  • Confirm organism identification
  • Perform mCIM testing
  • Perform PCR testing for KPC, NDM, OXA-48, IMP, VIM
    • If mCIM or PCR are positive, antimicrobial susceptibility testing (AST) will be performed
1) Confirm ID

2) mCIM
   - Positive (either) ➔ Confirm AST (Case)

3) PCR
   - Negative (both) ➔ Testing complete (Not a Case)
Antimicrobial Resistance Confirmation (ARC)

Gram Stain
Gram negative bacilli

Culture Results
Confirmed as Klebsiella pneumoniae
Identification Performed by MALDI-TOF.

Antimicrobial Susceptibility Results

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>&lt;=4</td>
<td>S</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>&gt;16</td>
<td>R</td>
</tr>
<tr>
<td>Cefepime</td>
<td>4</td>
<td>SDD</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>32</td>
<td>R</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>&gt;16</td>
<td>R</td>
</tr>
</tbody>
</table>

**Modified Carbapenem Inactivation Method (mCIM)**

Positive

Modified Carbapenem Inactivation Method (mCIM) screen positive - this isolate demonstrates carbapenemase production. The clinical efficacy of the carbapenems has not been established for treating infections caused by Enterobacteriaceae and Pseudomonas aeruginosa that test carbapenem susceptible but demonstrate carbapenemase production in vitro. ISOLATES THAT ARE mCIM POSITIVE SHOULD BE CONSIDERED RESISTANT TO ALL CARBAPENEMS REGARDLESS OF MIC. MIC REPORTED FOR EPIDEMIOLOGIC PURPOSES ONLY.

**PCR Result**

KPC (bla-KPC) gene DNA Detected
NDM-1 (bla-NDM-1) gene DNA Not Detected
OXA-48 (bla-OXA-48 like) gene DNA Not Detected
VIM (bla-VIM) gene DNA Not Detected

KPC, NDM, OXA-48, and VIM are the most common carbapenemases in the United States, however there are other less common carbapenemases and other mechanisms of carbapenemase resistance not detected by this PCR assay.

**IMP PCR Result**

IMP (bla-IMP) gene DNA Not Detected
Tips on How to Report Cases into MDSS
MDSS Reporting

• CP-CRE cases should be reported using the Michigan Disease Surveillance System (MDSS)
  • Web-based communicable disease reporting system for the state of Michigan
  • Cases can be reported by:
    • Electronic laboratory report (ELR)
    • Manual case entry
  • Reporting and ELR Guidance available at www.michigan.gov/hai
Electronic Laboratory Reporting (ELR)

• BOL is now reporting all carbapenemase and resistance mechanism testing into MDSS!
  • Both positive and negative results are now reported into MDSS
  • *Klebsiella* spp., *E. coli*, or *Enterobacter* spp., only
  • Populate into Lab Reports tab for culture results, mCIM, PCRs, and AST
  • Allows local health departments to know if a case is Confirmed or Not a Case
Electronic Laboratory Reporting (ELR)

- ELRs will populate into the Lab Reports tab – positive and negative results
ELR Example
Manual Case Entry

• Select ‘New Case’ on the left side menu
Manual Case Entry

• Select ‘CP-CRE’ from the Reportable Condition drop-down menu
Manual Case Entry

- Select the ‘Detail’ button to launch the case investigation form.
CP-CRE Case Investigation Form

- CRE Investigation Form Sections
  - Patient Information
  - Demographics
  - Laboratory Testing
  - Clinical Information
  - Antimicrobial Therapy
CP-CRE Laboratory Testing

- Laboratory Testing information is required to determine case classification
  - Enter lab data into Case Detail Form (instead of Lab Reports tab) for manual case entry
  - Date collected
  - Specimen source
  - Organism
  - MIC (need actual value)
  - Carbapenemase testing
  - Resistance mechanism testing
**CP-CRE Clinical Information**

- **Clinical Information**
  - Healthcare exposures
  - Travel
    - Particularly important for any confirmed NDM, OXA-48, IMP, or VIM cases
Case Classification

CONFIRMED CP-CRE

- Klebsiella spp., E. coli, Enterobacter spp.
  - Positive phenotypic test OR
  - Positive carbapenem resistance mechanism

SUSPECT CP-CRE

- Klebsiella spp., E. coli, Enterobacter spp.
  - Resistance to at least 1 carbapenem
  - No phenotypic or molecular testing done

NOT a CASE

- BOL report is negative for phenotypic and molecular tests
- All carbapenems are susceptible (MICs don’t match case definition)
- Not Enterobactericeae

CSTE Case definition
Actual CP-CRE Reporting

- **SUSPECT Cases**
  - Only MICs known
  - Carbapenem Resistance

- **CONFIRMED Cases**
  - Phenotypic or molecular mechanism known
  - CP-CRE

*Enterobacteriaceae*
Case Deduplication

• **Local Health Departments**
  • An individual should only be counted once per 12 months for the same organism and resistance mechanism
  • When reviewing newly reported cases/lab results:
    • Search to see if the patient has already been reported
    • Confirm whether the organism identification is the same
    • Confirm whether the resistance mechanism present is the same
    • Choose the new detail form when merging cases
Frequently Asked Questions
FAQs on Reporting

• I can’t find results for all of the antimicrobials listed on the case detail form
  • Just looking for the 4 carbapenems:
    • Doripenem
    • Ertapenem
    • Imipenem
    • Meropenem

• There are no MICs for the carbapenems, just a letter (S, I, R) or there are no carbapenems reported
  • Please call the laboratory and get the actual MICs and specifically ask for carbapenem results
FAQs on Reporting

• A report came in from BOL that was positive for *Citrobacter freundii* KPC. What do I do?
  • While this is a confirmed KPC CP-CRE it is not a *Klebsiella spp.*, *E coli*, or *Enterobacter spp.* and is not required to be reported

• A report came in from BOL that was positive for VIM, but it is not a *Klebsiella spp.*, *E coli*, or *Enterobacter spp.* What do I do?
  • That is a novel resistance case
  • Sara will be contacting you for follow-up
  • Case can be entered as CP-CRE
    • Organism: Other, specify
FAQs on Reporting

- Repeat cultures – should facilities be sending every isolate regardless of if they sent it in the past?
  - BOL policy is that if it’s the same organism from same patient, same lab, they will only do the repeat ARC testing every 6 months, unless specifically requested by the submitting lab (e.g., if the AST profile looks completely different, or more resistant than previously)
  - If it is a new species in the same patient then they will test
  - If it is the same patient, different lab then they will test
  - *Example*: tests with all the same organism within the 12 month time frame then subsequent cases can be merged, (even though we don’t the know the mechanism for the later isolates)
FAQs on Reporting

• Does the Modified Hodge Test (MHT) count as a confirmatory test?
  • Yes, technically. However...
  • MHT often can produce false positive results for *Enterobacter* spp. (can pick up AmpC production or other mechanisms of resistance other than carbapenemase production) and therefore the positive results are not reliable
  • MHT does better job of detecting true carbapenemase production in *Klebsiella* spp. and *E. coli*, which are usually KPC
    • However it can miss the metallo-B-lactamase carbapenemases like NDM, giving false negative results
  • MHT is no longer being recommended for confirmatory testing, and it has been removed from the CLSI M100 guidelines for clinical laboratories
    • mCIM test is recommended instead
FAQs on Reporting

• **How long do we have to complete the case detail form?**
  • As with any CD, please try and get the information as soon as possible
  • If anything, verify patient’s chart is flagged and they are in contact precautions
  • We do have time to investigate, but if a contact investigation is needed, it’s easier to test patients still admitted than discharged

• **SUSPECT cases - How much of the form to complete?**
  • If you know the facility submits isolates to BOL for testing, you can wait to see the lab result.
  • If you know they don’t or are unsure, **investigate the case** (demographics, track down the MICs, check healthcare exposures (are they currently admitted and in contact precautions), if LTC/SNF patient – please document current and previous locations in the Notes
FAQs on Reporting

• **Home address is used for hospital/LTC/SNF patients** - how do we detect clusters?
  • Initiative and non-initiative patients can be linked in MDSS
  • If you know the previous hospital/LTC/SNFs location(s), please document in Notes

• **When should we put their home address versus facility address?**
  • If specimen was collected at the LTC/SNF facility – use facility address
  • If they have been a resident in a LTC/SNF within the past 3 months, please indicate the facility address in the Notes
FAQs on Reporting

• *From the LHD perspective:* How do I know which facilities participate in the CRE Surveillance and Prevention Initiative?
  • Brenda and Sara will be providing the Regional Epidemiologists a list of participating facilities in their jurisdictions/counties to pass along to LHDs

• **Do facilities that participate in the CRE Surveillance and Prevention Initiative report twice?**
  • No
  • Cases that meet the surveillance definition for the initiative are the same as the reporting requirement – no dual reporting
  • Cases are entered into MDSS (unless arrangement with Sara or LTAC)
  • Facilities do report # cases, # of patient-days and # of admissions monthly to Sara
Updated Guidance

• Currently updating the Interim CP-CRE Case Reporting and Investigation Guidance
  • Reporting
  • Case Classification
  • Investigation
  • Prevention
• Planning to release January 2019
Investigation

• KPC Endemic vs. Non-Endemic Areas
  • Patient information, demographics, laboratory data, healthcare exposures, travel
  • Information important for prevention purposes
  • Revise MDSS form for needed vs. optional data in future?

• Novel CP-CRE resistance mechanisms, including NDM-1, OXA-48, VIM, and IMP:
  • Please complete the entire case detail form as best as possible
  • Documentation of healthcare exposures and international travel is crucially important
CP-CRE Prevention

- Hand Hygiene
- Contact precautions
- Environmental Cleaning
- Use of devices
- Antimicrobial stewardship
- Chlorhexidine bathing
- Laboratory notification
- Inter-facility communication
- Screening contacts of CRE Patients
- Active surveillance testing
- HCP, Patient & Family Education

CRE Brochures

WHAT ARE CRE CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE)?

CRE is a family of germs that are hard to treat because they are resistant to many commonly used antibiotics.

There are three main types of Enterobacteriaceae that may be resistant to carbapenems, Enterobacter species, Klebsiella species, and Escherichia coli (E. coli).

HOW DOES CRE SPREAD?

- CRE spreads when someone has an infected or colonized body or body fluids.
- CRE is spread between people by touching wounds or touching dirty objects (like tubes that move liquid from the body or breathing machines).
- CRE can also spread in healthcare settings like hospitals and nursing homes.
- CRE can spread between people who are in contact with the CRE germ.

WHAT ARE YOUR TIPS FOR TAKING CARE OF SOMEONE WITH CRE?

- Wash your hands. It's important to wash your hands after you touch wounds.
- Help the person use the bathroom.
- Clean up feces (poop) and any other body fluids, with soap and water and then a household disinfectant cleaner.
- Wash all used clothes, sheets, and linens using only hot water.
- Keep sick people home and out of school or work until they are no longer sick from CRE.
- Avoid close contact with sick people.

WHAT ARE CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE)?

- CRE are a family of germs that are hard to treat because they are often resistant to many commonly used antibiotics.
- CRE infections happen in healthcare settings like hospitals and nursing homes.
- CRE can spread between people who are in contact with the CRE germ.
- CRE is spread when someone has an infected or colonized body or body fluids.
- CRE is spread between people by touching wounds or touching dirty objects (like tubes that move liquid from the body or breathing machines).
- CRE can also spread in healthcare settings like hospitals and nursing homes.
- CRE can spread between people who are in contact with the CRE germ.

WHAT ARE YOU RISK FOR CRE INFECTION?

- CRE mainly affects people who have acute or long-term care illnesses like hospitals, clinics, and long-term care homes.
- CRE usually affects people with weak immune systems like tubes or breathing machines going into their body.

PREVENTION TIPS FOR PATIENTS AND FAMILIES

- Wash your hands. It's important to wash your hands after you touch wounds.
- Help the person use the bathroom.
- Clean up feces (poop) and any other body fluids, with soap and water and then a household disinfectant cleaner.
- Wash all used clothes, sheets, and linens using only hot water.
- Keep sick people home and out of school or work until they are no longer sick from CRE.
- Avoid close contact with sick people.
We Need Your Input!

• Questions, comments, suggestions...
Updated Guidance

• January 2019
• www.michigan.gov/hai
• www.michigan.gov/cdinfo
• Listserves (Communicable Disease, NHSN Users, clinical micro)
Thank You

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