CP-CRE Reporting: New HAI Reporting Requirement

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In January 2018, Carbapenemase Producing – Carbapenem Resistant Enterobactericaeae (CP-CRE), a healthcare-associated "super-bug", became a reportable infection in Michigan. According to the Centers for Disease Control (CDC), CP-CRE are considered urgent pathogens because they are high-consequence antibiotic-resistant threats due to significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and therefore require urgent public health attention to identify infections and to limit transmission. Treatment options are limited for CP-CRE and infections are often associated with high mortality rates. CP-CRE have resistance mechanisms that are highly transmissible between organisms (via plasmids) and between patients (via hands of healthcare workers, contaminated environments or equipment). Other types of healthcare-associated infections, like catheter-associated urinary tract infections or central line-associated bloodstream infections, are not mandated to be reported in Michigan. Therefore, this recent change in CP-CRE reporting requirements has been both confusing and challenging to local health departments, infection preventionists at healthcare facilities, and clinical microbiology laboratories who are not used to reporting healthcare-associated infections (HAI), nor the complex characteristics of CP-CRE infections.

WALKING THROUGH THE REPORTING PROCESS

Cases can be reported to Michigan Department of Health and Human Services (MDHHS) in a couple of ways: **1) Electronic lab reporting** – where the clinical laboratory automatically reports culture results into Michigan Disease Surveillance System (MDSS), or **2) Manual reporting** – where either the healthcare facility, clinical laboratory, or local health department creates the case in MDSS based on the lab report.

WHAT TO LOOK FOR ON THE LAB REPORT

Enterobacteriaceae

Enterobacteriaceae are a family of more than 70 bacteria. Of these, 3 species represent about 90% of CP-CRE infections: ***Klebsiella* species, *Enterobacter* species, and *Escherichia coli*.**

Therefore, only these 3 species are reportable. When reviewing the lab reports, look for the organism isolated. If the organism is not one of these 3, agencies do not have to report it.

Carbapenem antibiotics

Carbapemens are a group of antibiotics that are used as a last resort to treat infections. They are typically reserved for very sick individuals who may have comorbid conditions and who have often been on multiple antimicrobials for a long time. There are four carbapemen antibiotics and any combination of them may be on the lab report. The four carbapenems are **Ertapenem, Doripenem, Imipenem, and Meropenem**. If agencies see any of these carbapenems listed, look at the Minimum Inhibitory Concentrations (MIC). The MIC number has to be 4 micrograms per milliliter or greater for Doripenem, Imipenem or Meropenem. For Ertapenem, the MIC number has to be 2 micrograms per milliliter or greater. If agencies don't see any of these four carbapenems listed, please call the reporting laboratory and find out if they tested for them. Sometimes, laboratories may test additional antibiotics and then suppress the results as a way to help guide treatment therapy. It's always best to call and make sure if they were tested. If they didn't test, the report would be marked as *NOT A CASE* as there is no way to verify the surveillance definition. Additionally, if the lab report only includes an interpretation of carbapenem resistance (e.g., susceptible, intermediate, or resistant), call the reporting laboratory to determine the actual MICs. Many clinical laboratories have not implemented newer Clinical Laboratory Standards Institute guidelines for MIC breakpoints and therefore the interpretations provided in the report may not match the MIC cutoffs above.

Carbapenemases

Carbapenemases are enzymes that bacteria may produce that break down carbapenem antibiotics making them ineffective. Often the genes encoding these carbapenemases are located on mobile genetic elements called plasmids which makes them easier to transfer from one bacteria to another. The most common types of carbapenemases in the US include **KPC** (*Klebsiella pneumoniae* carbapenemase), **NDM** (New Delhi Metallo-beta-lactamase), **OXA-48** (Oxacillinase 48-Type beta-lactamase), **IMP** (Imipenemase Metallo-beta-lactamase), and **VIM** (Verona Integron-Encoded Metallo-beta-lactamase). Testing for the presence of carbapenemases can be done in one of two main ways: 1) a phenotypic that detects whether the organism is actively producing a carbapenemase enzyme. Common phenotypic tests include the Modified Hodge Test (**MHT**), **Carba NP**, Neo-Rapid CARB, Carbapenem Inactivation Method (**CIM**) or modified CIM (**mCIM**); 2) a genetic test (e.g., **PCR**) that detects the presence of a specific gene encoding for a carbapenemase.

To determine case status, agencies will need to determine if a phenotypic or genetic test for carbapenemases has been done. To classify a CP-CRE case as *CONFIRMED*, either a positive

phenotypic test or a PCR positive is needed for a carbapenem resistance mechanism (e.g., KPC, NDM, VIM, IMP, OXA-48). If the case only has the MIC(s) resistant to any of the carbapenems, classify the case as *SUSPECT*. Phenotypic testing for carbapenemase production and genetic testing for resistance mechanisms are available to clinical laboratories for Enterobactericaeae, *Pseudomonas aeruginosa,* and *Acinetobacter* spp. isolates from the Bureau of Laboratories.

CASE ENTRY IN MDSS

Enter all case clinical and laboratory information into the Case Detail Form in MDSS. Documentation of any recent healthcare exposures and international travel is crucially important for all novel resistance mechanisms (e.g., NDM, OXA, VIM, IMP) and for KPC outside of endemic areas in the state (e.g., Southeast Michigan, West Michigan, Saginaw-Bay-Flint, and Alpena geographic areas).

Currently, 391 CP-CRE cases have been reported into MDSS. Of those, 53 cases have been confirmed as CP-CRE, 126 cases are suspect CP-CRE, and 212 cases either do not meet the surveillance definition or do not have enough information reported to be classified as a case.

MDHHS has *Interim CP-CRE Case Reporting and Investigation Guidance* along with *Reporting CP-CRE via Electronic Lab Reporting (ELR)* available at www.michigan.gov/hai. The SHARP Unit is working to update guidance as more is learned about case management of CP-CRE cases in MDSS.