

Proposal for Conducting Statewide Surveillance for Carbapenem-resistant Enterobacteriaceae (CRE) in Minnesota under the Minnesota Communicable Disease Rule (4605.7080)

Division: Infectious Disease Epidemiology, Prevention and Control Division

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Under part 4605.7080 of the Communicable Disease Reporting Rule, the Commissioner may select new diseases/syndromes if certain criteria are met. Specifically, 4605.7080 says:

“Subpart 1. Disease selection. The commissioner shall, by public notice, require reporting of newly recognized or emerging diseases and syndromes suspected to be of infectious origin or previously controlled or eradicated infectious diseases if:

- A. the disease or syndrome can cause serious morbidity or mortality; and
- B. report of the disease or syndrome is necessary to monitor, prevent, or control the disease or syndrome to protect public health.”

“Subp. 2. Surveillance mechanism. The commissioner shall describe a specific, planned mechanism for surveillance of the disease or syndrome including persons and entities required to report, a time frame for reporting, and protocols for the submission of test results and clinical materials from cases and suspected cases to the Minnesota Department of Health, Public Health Laboratory.”

1. DISEASE SELECTION.

The commissioner shall, by public notice, require reporting of newly recognized or emerging diseases and syndromes suspected to be of infectious origin or previously controlled or eradicated infectious diseases if:

A. The disease or syndrome cause serious morbidity or mortality.

Based on the following information, MDH finds that Carbapenem-resistant Enterobacteriaceae (CRE) causes serious morbidity or mortality.

Enterobacteriaceae is a large family of Gram-negative bacteria (GNB) that can cause a wide range of infections in humans. Several species of Enterobacteriaceae (e.g., *Escherichia coli*, *Klebsiella pneumoniae*, etc.) are responsible for both community- and healthcare-associated infections (HAIs). HAIs are infections that patients get while receiving treatment for medical or surgical conditions, while community-associated infections are those acquired outside of a healthcare setting. Enterobacteriaceae are also among the most common disease causing agents identified in clinical microbiology laboratories. Over the past decade extremely drug resistant Enterobacteriaceae, called carbapenem-resistant Enterobacteriaceae (CRE), have emerged in the United States (U.S.). Carbapenems are broad-spectrum antibiotics, often

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considered antibiotics of last resort for treating patients with severe or resistant GNB infections. CRE are resistant to carbapenems and most other available antibiotics, resulting in limited treatment options, poor patient outcomes (e.g., poor functional status, prolonged hospital stays, discharge to long-term care facilities, etc.), and high mortality rates – contributing to death in up to 50% of patients who develop invasive infections according to one report.¹

Data collected through the National Healthcare Safety Network (NHSN) suggest CRE are on the rise among patients in U.S. healthcare facilities. Risk factors for CRE infection include: recent exposure to healthcare, invasive devices (e.g., urinary catheter), and/or antimicrobial therapy. Patients with a recent history of receiving healthcare in countries outside the U.S. with a high prevalence of CRE may also be at increased risk for CRE colonization/infection. Colonization means that the organism can be found on the body but is not causing any symptoms or disease; however, colonized patients are at increased risk for infection if colonizing bacteria gain access to body sites that are usually sterile like the bladder, the lungs, or the bloodstream. CRE-colonized or infected patients can spread the bacteria to other patients either on the hands of healthcare workers or through the environment. Identifying and isolating these patients is a critical measure to control the spread of CRE in healthcare settings.

B. Report of the disease or syndrome is necessary to monitor, prevent, or control the disease or syndrome to protect public health.

Based on the following information, MDH finds that reporting of Carbapenem-resistant Enterobacteriaceae (CRE) is necessary to monitor, prevent, and control the disease to protect the public's health.

In 2013, the Centers for Disease Control and Prevention (CDC) released its first ever report on antibiotic resistance, *Antibiotic resistant threats in the United States, 2013*. It identified CRE as one of three 'urgent' public health threats requiring immediate and aggressive action. If action to control these infections is not taken quickly, CRE can rapidly become an issue not only in individual healthcare facilities but also across an entire community of interconnected healthcare settings, highlighting the important role for public health in CRE prevention and control efforts. Public health actions outlined in the CDC report include new surveillance and prevention efforts to track CRE, prevent infections, and halt further spread of resistance. In August 2015, CDC published a Vital Signs report calling for continued vigilance and a more coordinated, public health-led approach to CRE prevention across the spectrum of healthcare settings.²

Unlike other antibiotic-resistant organisms (e.g., methicillin-resistant *Staphylococcus aureus*), which represent a single species and a single resistance mechanism, CRE are complex and resistance may be due to a variety of mechanisms. CRE that produce an enzyme known as a carbapenemase are able to efficiently break down carbapenem antibiotics rendering them ineffective. In the U.S., the most prevalent and concerning

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carbapenemase is the *Klebsiella pneumoniae* carbapenemase (KPC). These CRE are referred to as carbapenemase-producing CRE (CP-CRE) and include other less commonly reported carbapenemases such as oxacillinase-48 (OXA-48), the New Delhi metallo- β -lactamase (NDM) and Verona integron-encoded metallo- β -lactamase (VIM). The genes that code for many of these carbapenemases are contained on genetic elements that can be transferred between species of Enterobacteriaceae, facilitating the spread of resistance.

In early 2009, the MDH Public Health Laboratory (PHL) confirmed its first CRE isolate with KPC that a clinical laboratory had submitted. As a result, in 2009 the MDH PHL asked laboratories statewide to be on alert for Enterobacteriaceae with reduced susceptibility to carbapenem antibiotics and to submit isolates for further testing. In 2011, MDH initiated active, laboratory- and population-based sentinel surveillance for CRE in Hennepin and Ramsey Counties. Outside of these two counties, healthcare facilities and clinical laboratories have been voluntarily reporting CRE cases and sending CRE isolates to the MDH PHL for further characterization (e.g., polymerase chain reaction [PCR] testing for CP genes such as KPC). Approximately one-third of CRE reported to MDH are identified as KPC-positive. Both NDM and oxacillinase-48 (OXA-48) carbapenemases have been detected among patients in Minnesota healthcare facilities with recent travel to and receipt of medical care outside the U.S. Statewide reporting of CRE to MDH will increase awareness, allow for prompt follow-up regarding infection prevention and control recommendations, and provide data to facilitate coordination across the spectrum of healthcare.

Statewide surveillance for CRE is also critical to more completely describe the epidemiology of CRE in MN, including microbiologic characteristics (e.g., species, resistance mechanisms, etc.), patient demographics, co-morbidities, site(s) of infection, epidemiologic classification (healthcare- vs. community-associated), and patient outcomes. Most clinical laboratories in Minnesota do not have the resources or capacity to identify specific carbapenemase genes, but the MDH PHL does. Information on resistance genes is crucial to detecting outbreaks and understanding local epidemiology. Data collected through surveillance and isolate submission will be used to monitor CRE trends, estimate the incidence and prevalence of CRE statewide and by region to identify healthcare clusters or geographical areas of concern, describe resistance genes (e.g., KPC) present in MN, and drive targeted infection prevention and control measures to protect the health of Minnesotans.

Because CRE can be spread between patients on the hands of healthcare workers or via contaminated medical equipment (e.g., duodenoscopes), statewide reporting is necessary. Guidelines for preventing the spread of CRE in healthcare settings are outlined in the CDC Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE) – November 2015 Update CRE Toolkit (<http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html>) and MDH Recommendations for the Management of CRE in Acute Care, Long-term Acute Care (<http://www.health.state.mn.us/divs/idepc/dtopics/cre/hcp/acuterecs.html>), and MDH Recommendations for the Management of CRE in Long-term Care Facilities (<http://www.health.state.mn.us/divs/idepc/dtopics/cre/hcp/rec.html>).

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Outbreaks of CRE reported in other states and countries have often involved multiple healthcare settings, highlighting the importance of early detection and prompt implementation of enhanced infection prevention and control measures (e.g., screening cultures to identify CRE-colonized patients), as well as communication of a patient's CRE status between facilities upon transfer. Expanding surveillance beyond the existing sentinel surveillance in Hennepin and Ramsey Counties will improve awareness of CRE in Minnesota and drive targeted interventions and outbreak response activities, which are crucial for protecting the public's health against this serious threat.

2. SURVEILLANCE MECHANISM

The commissioner shall describe a specific, planned mechanism for surveillance of the disease or syndrome including persons and entities required to report, a time frame for reporting, and protocols for the submission of test results and clinical materials from cases and suspected cases to the Minnesota Department of Health, Public Health Laboratory.

A. Disease or Syndrome

CRE includes Enterobacteriaceae isolated from any body site that is resistant to any one of the following carbapenem antibiotics, imipenem, meropenem, doripenem, or ertapenem, based on current Clinical and Laboratory Standards Institutes Standards (M100) or that demonstrates production of a carbapenemase.

B. Reporting Entities

The Commissioner requires all mandated reporters to report CRE. (For a listed of mandated reporters see Minn. Rules, Chapter 4605.7030)

C. Reporting Time Frame

Providers and laboratories must report CRE cases to MDH within one working day after the test result is finalized.

D. Protocol for Submission

a. Provider Submissions.

Providers will report using a designated case report form and must be submitted either by direct electronic transmission, phone, or fax. The report must include, at a minimum, the following information:

- 1) Patient data – patient name, birthdate, gender, race, ethnicity (if available), telephone number, residential address, including street, city, county, state, and postal code

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- 2) Culture data – specimen collection date, specimen source, isolate genus and species, antibiotic susceptibility report (medical record), carbapenemase test results (if known/reported in medical record)
- 3) Facility data – patient medical record number, date of report, physician name, address, and telephone number, name of hospital (including date of admission/discharge) or other healthcare facility, and the diagnostic laboratory name.

b. Clinical and Laboratory Submissions.

Clinical and reference laboratories must forward CRE isolates from any body site (e.g., urine, blood, sputum, wound, etc.) along with results of antibiotic susceptibility testing and carbapenemase testing performed on the isolate to the PHL. The submission must include, at a minimum, the following information:

- 1) MDH isolate submission form(s) with project number
- 2) Results of antibiotic susceptibility testing, including automated testing instrument printouts (e.g., Vitek2, Phoenix, etc.), and/or results of other manual susceptibility testing performed (e.g. manual MicroScan, E-test, disk diffusion, etc.), including MIC value and final interpretation result
- 3) Results of additional testing performed on the specimen and/or isolate(s) for carbapenemase production (e.g., E-test, modified Hodge test, Carba NP, PCR, nucleic acid testing [NAAT], etc.)

Upon request from the Commissioner, each reporting facility shall provide access to additional information from all medical, pathological, and other pertinent records related to the CRE diagnosis, treatment, and follow-up for the purposes of surveillance and infection prevention and control. Epidemiologists review select patient medical records using a standardized case report form that is used to collect basic demographic information and risk factors of epidemiologic or infection prevention concern.

References

1. Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant *Klebsiella pneumoniae* infection and the impact of antimicrobial and adjunctive therapies. *Infect Control Hosp Epidemiol* 2008;29:1099-106.
2. CDC. Vital Signs: Carbapenem-Resistant Enterobacteriaceae. *MMWR Morb Moral Wkly Rep.* 2013;62:165-170.