

## Proposal for Conducting Sentinel Surveillance for Invasive Candidiasis in Hennepin, Ramsey, Anoka, Washington, Dakota, Scott, and Carver Counties under the Minnesota Communicable Disease Rule (4605.7046)

**Section:** Health Care-associated Infections/Antimicrobial Resistance

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Under part 4605.7046 of the Communicable Disease Reporting Rule, the Commissioner may select infectious diseases/syndromes and reporting sites for sentinel surveillance if the specified criteria are met. The law specifically says:

“Subpart 1. Disease Selection. The commissioner may select an infectious disease or syndrome for sentinel surveillance, other than a disease or syndrome for which general reporting is required under this chapter, if the commissioner determines that sentinel surveillance will provide adequate data for epidemiological purposes and the surveillance is necessary for

- A. characterization of the pathogen;
- B. monitoring vaccine effectiveness; or
- C. achieving other significant public health purposes for a disease or syndrome that can cause serious morbidity or mortality.

Subpart 2. Site Selection. The commissioner shall select, after consultation with the sites, sentinel surveillance sites that have epidemiological significance to each disease or syndrome selected under subpart 1. In selecting the sites, the commissioner shall consider:

- A. the potential number of cases at the site;
- B. the geographic distribution of cases or potential cases in Minnesota, if indicated by the epidemiology of the disease or syndrome;
- C. the epidemiology of the disease or syndrome; and
- D. the overall impact of sentinel surveillance on a site and the benefit to public health in conducting sentinel surveillance at the site.”

# PROPOSAL FOR CONDUCTING SENTINEL SURVEILLANCE FOR INVASIVE CANDIDIASIS

## 1. Disease Selection

### A. Will population-based sentinel surveillance provide adequate data for epidemiological purposes, specifically characterization of the pathogen or achieving other significant public health purposes for a disease or syndrome that can cause serious morbidity or mortality?

*Candida* is a type of fungus that is normally found in the gastrointestinal tract and on skin of people and poses little risk of serious infections for healthy individuals. In people with weakened immune systems or other debilitating conditions, such as certain cancers, major abdominal surgeries, and recent long-term systemic antibiotic treatment, *Candida* can cause severe and often fatal invasive infections, called invasive candidiasis (IC). These infections can occur in the blood, heart, brain, eyes, bones, and other deep tissue and organ sites in the body. Most cases of IC are health care-associated infections (HAIs), which are infections that patients acquire while receiving treatment for medical or surgical conditions. In the United States (U.S.), *Candida* cause an estimated 46,000 HAIs annually and are one of the most common causes of health care-associated bloodstream infections (BSIs). In one recent national study, *Candida* were the most common type of health care-associated BSI<sup>1</sup>. This is of major clinical and public health importance because, compared with other common HAIs, invasive *Candida* infections are associated with increased mortality, higher health care costs, and increased patient length of stay.

Prompt treatment with antifungal medication is required to eliminate IC. Even with antifungal treatment, mortality among patients with IC is still estimated as high as 40%. To further complicate treatment, data show that some *Candida* species have become increasingly resistant to antifungal medication in recent years. Fluconazole is the most inexpensive and readily available antifungal for treating IC, but an increasing proportion of infections occur with *Candida* species that are resistant to fluconazole. In their 2013 list of antimicrobial resistance threats in the U.S., the Centers for Disease Control and Prevention (CDC) described fluconazole-resistant *Candida* as a serious hazard, **meaning it is considered a significant threat to public health.**

Due to the threat of fluconazole resistance, other types of antifungals are recommended to treat infections with certain *Candida* species. Echinocandins are a class of antifungals first introduced in the early 2000s, and reports of resistance were initially rare. Echinocandins are now the preferred initial treatment for most IC. However, numerous medical centers have reported increasing rates of echinocandin-resistant *Candida* infections, especially echinocandin-resistant *Candida glabrata*. Echinocandin resistance confers a greater mortality risk among patients with *C. glabrata* infections. Complicating this issue is that testing for echinocandin resistance is not routinely done at most clinical laboratories, and resistance may only be recognized when treatment failure occurs. Infections of multidrug-resistant *Candida* species, defined as resistant to more than one class of antifungal drug, are also rising, and are most commonly due to *C. glabrata*. There is evidence that resistant *C. glabrata* infections can be transmitted in the health care setting, but the mechanisms of transmission are unknown. Very few treatment options exist for multidrug-resistant *Candida* infections, and those available are more toxic and often poorly tolerated.

This year the CDC released a clinical alert to U.S. health care facilities describing the global emergence of a new multidrug-resistant *Candida* species, *Candida auris*, as a cause of invasive health care-associated infections with high mortality. While reports of this pathogen are limited in the U.S., in other countries *C. auris* has caused large outbreaks in health care facilities. CDC advises health care facilities to be on the lookout for *C. auris* in patients and to implement certain infection control and environmental cleaning measures when

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<sup>1</sup> Magill, Shelley S et al. Multistate Point-Prevalence Survey of Health Care-Associated Infections. *New England Journal of Medicine* 2014;370:1198-1208.

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identified. Specialized methods for detecting *C. auris* are required, and many clinical laboratories may misidentify this pathogen as a different type of *Candida*.

Population-based surveillance for IC will help characterize the IC disease burden, determine risk factors for IC, and track antifungal resistance among these important pathogens. Key to this surveillance is the ability of the Minnesota Department of Health (MDH) Public Health Laboratory (PHL) to conduct *Candida* species identification on all submitted isolates and antifungal susceptibility testing on *C. glabrata* isolates. Antifungal susceptibility testing of all other *Candida* isolates (i.e., non-*glabrata* species) will be performed by the CDC. We propose to initiate surveillance for IC by including only *Candida* bloodstream infections, referred to as candidemia, and then to expand our work to include other invasive *Candida* infections in the future. Candidemia addresses the most common type of invasive disease and is feasible for health care facilities that currently implement surveillance for other invasive infections.

*The seven county metro area includes the two most populous counties and accounts for just over 50% of the population in Minnesota. Included among the acute care hospitals in this region are transplant centers, children's hospitals, trauma centers, and a Veteran's Affairs hospital. These varied care levels and patient populations will allow for a surveillance area that is comprehensive, thorough, and will provide sufficient data to monitor IC trends and antifungal resistance in Candida spp.*

### **B. Why is the surveillance necessary?**

MDH lacks a systematic method of collecting and studying the incidence of IC and also lacks a means to track antifungal resistance in *Candida*. This impedes MDH's ability to monitor, prevent, and control IC.

As described above, *Candida* can cause severe and fatal invasive infections in certain susceptible and debilitated populations, and recent data describe increasing resistance to available treatment for IC. Sentinel surveillance will provide adequate data for assessing the incidence of IC and tracking the changing epidemiology of IC, including the distribution of *Candida* species causing infections, antifungal resistance patterns, types of infections, and demographics and clinical characteristics of the patients and their outcomes. The global emergence of a novel multidrug-resistant *Candida* species causing severe infections and health care facility outbreaks underscores the need to monitor IC to detect emerging pathogens requiring prompt infection control response in health care facilities.

Objectives of this sentinel surveillance:

- 1) Estimate the incidence and describe the epidemiologic characteristics of *Candida* organisms identified by clinical laboratories serving residents of the Twin Cities metro area.
- 2) Perform species identification on all submitted *Candida* isolates and antifungal susceptibility testing on *C. glabrata* isolates in the MDH-PHL; susceptibility testing of all other isolates will be tested at CDC.
- 3) Identify risk factors associated with invasive infections caused by *Candida*, including risk factors for disease transmission within health care facilities.
- 4) Assess patient outcomes and how outcomes vary by *Candida* species, resistance patterns, and treatment regimens.

## **2. Site Selection**

### **A. Did you consult with the selected site(s)? Explain**

MDH contacted health care facilities and clinical laboratories in the seven county metro area by e-mail to introduce candidemia surveillance and request feedback about the proposed surveillance program. We described the justification for surveillance and the processes by which cases will be reported to MDH and isolates will be submitted to the PHL. We explained that the surveillance mechanisms will be similar to those already in place for Active Bacterial Core surveillance (ABCs) at MDH and that MDH staff will perform chart

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reviews to complete case report forms. There were no issues or concerns raised by health care facilities or clinical laboratories.

### **B. Does the site(s) have epidemiological significance to the disease or syndrome selected? Explain.**

Hennepin, Ramsey, Anoka, Washington, Dakota, Scott, and Carver Counties make up the seven county metro area in the Twin Cities. In total, they comprise greater than 50 percent of the state's population. Twenty-six acute care facilities providing varied levels of care operate within these seven counties, including children's hospitals, long-term acute care hospitals, transplant centers, an academic facility, trauma centers, and a Veteran's Affairs hospital. Together these facilities care for some of the most critically ill Minnesota residents, and therefore those most at risk for IC.

### **C. Did you consider the following factors? Explain?**

- Potential number of cases at the site  
The incidence of IC in these sites is not known; this is part of what we will learn through this project. Based on the incidence of candidemia in other U.S. metropolitan areas conducting this surveillance, we estimate approximately 350 candidemia cases annually in the seven county metro area.
- Geographic distribution of cases or potential cases in Minnesota, if indicated by the epidemiology of the disease or syndrome  
Invasive *Candida* infections are likely more reflective of greater severity of patient illness than geographic distribution. Several of Minnesota's largest health care facilities, including transplant centers, Level One Trauma centers, and a large academic facility are located within the proposed sentinel surveillance area.
- Epidemiology of the disease or syndrome  
Surveillance data from other U.S. regions demonstrate that IC continues to be a significant cause of HAI morbidity and mortality. There have been indications that the *Candida* species causing invasive infections may be changing, along with associated increases in antifungal drug resistance. Comprehensive data is lacking about population-based epidemiology in various U.S. regions and the influence of demographic risk factors. The global emergence of multidrug-resistant *Candida auris* causing severe invasive infections and health care facility outbreaks is the newest threat posed by *Candida*, and much remains unknown about this novel pathogen, especially in the United States.
- Overall impact of sentinel surveillance on a site and the benefit to public health in conducting sentinel surveillance at the site  
Little is known about the epidemiology of IC in Minnesota, and national data is limited as very few sentinel sites in the U.S. conduct surveillance for IC. Establishing sentinel IC surveillance will allow MDH to estimate the IC burden and risk factors in Twin Cities metropolitan area residents, describe trends in the local epidemiology of IC, as well as provide insight into the epidemiology in Minnesota as a whole. MDH surveillance data will also contribute to more thorough national descriptions and regional comparisons of IC epidemiology. Participating facilities will benefit from understanding the burden and epidemiology of IC and antifungal resistance both in the Twin Cities metro region and in their facility. Species identification by the PHL will enable more rapid detection of *Candida auris* and other emerging *Candida* threats requiring prompt infection control response. In total, the information gained from this surveillance can inform prevention efforts and guide treatment of these life-threatening infections.