

2008-R-24

**CIO Name:** National Center for Preparedness, Detection and Control of Infectious Diseases, Coordinating Center for Infectious Diseases

**Project Title:** Epidemiology of Carbapenemase-Producing Enterobacteriaceae in a Healthcare Setting

**Project Description and Objectives:**

Carbapenemase-producing Enterobacteriaceae are now frequently isolated in healthcare institutions in the northeastern United States and isolation of these resistant bacteria are increasing in other parts of the country. The carbapenemase, KPC, confers resistance to all  $\beta$ -lactam agents and it is nearly always found in Enterobacteriaceae that are resistant to most other classes of antimicrobial agents. Some KPC-producing isolates have been resistant to all currently available antimicrobial agents. KPC-producing bacteria have demonstrated a remarkable ability to disseminate with interfacility, interstate, and international transmission having been documented. In the United States, the enzyme has been identified in multiple genera of Enterobacteriaceae with *Klebsiella pneumoniae* being the most common and reports of KPC-producing *Escherichia coli* rapidly emerging. Identification and control of KPC-producers is complicated by the occurrence of KPC-producers with low-level carbapenem resistance, which may not be detected in the clinical microbiology laboratory. To date, all KPC producing bacteria reported in this country have been isolated in hospitalized patients, however, no studies have examined whether these organisms are also circulating outside of acute care hospitals. Given that Enterobacteriaceae circulate commonly both in the community and in healthcare facilities, a better understanding of the epidemiology of KPC-producing bacteria will be critical in developing prevention and control efforts.

This is a surveillance study for KPC-producing bacteria with the purpose of identifying: (1) whether there are patient populations that might harbor KPC-producing Enterobacteriaceae prior to admission to healthcare facilities, (2) transmission dynamics within healthcare facilities, and 3) risk factors for colonization with KPC-producing Enterobacteriaceae. The study would have to occur in an acute care and associated long-term care

healthcare facilities located in geographic part of the country where KPC-producing Enterobacteriaceae are endemic and where KPC-producing Enterobacteriaceae are isolated by the clinical microbiology lab on a regular basis. The study would involve obtaining surveillance cultures for potential KPC-producing Enterobacteriaceae on patients at the time of admission, weekly thereafter during the course of the patient's admission and at discharge. Surveillance specimens will be either a rectal swab or swab of a stool specimen from the patient. Specimens will be inoculated to differential selective media to isolate and identify potential KPC-producing bacteria. To increase the sensitivity of detection, the criteria for a potential KPC-producing Enterobacteriaceae will be a *K. pneumoniae* or *E. coli* isolate that is resistant to extended-spectrum cephalosporins (either ceftazidime, ceftriaxone, or cefotaxime) using the hospital's routine susceptibility testing method. In addition, clinical *K. pneumoniae* or *E. coli* isolates from the healthcare institution with these same susceptibility patterns will be collected. Surveillance and clinical isolates will then be tested by PCR for the *bla<sub>KPC</sub>* gene. Isolates that are positive for *bla<sub>KPC</sub>* by PCR will be typed by pulsed-field gel electrophoresis (PFGE) and the KPC subtype determined by sequence analysis. These microbiological analyses will be used to assess potential transmission of KPC-producing isolates in the institution. The PCR and PFGE analyses would be done in partnership with CDC and could be done at CDC. For all patients positive for a KPC-producing Enterobacteriaceae, a chart review will be conducted to document demographic information, underlying illnesses and co-morbidities, the presence of invasive devices and recent surgery, previous inpatient healthcare exposures in the prior year, antimicrobial exposures in the prior month, dates and locations within the facility (to determine if the patient was on a unit where another patient with a KPC producing Enterobacteriaceae was hospitalized), clinical data to establish colonization or infection with the KPC-producer, treatment information on antibiotics and procedures to treat the infection, and clinical outcome of colonization or infection for the duration of the hospitalization. For each case patient enrolled, similar data will be collected on one or more age and admission date matched control patient to determine risk factors for colonization or infection with a KPC-producing Enterobacteriaceae.

**Awardee Activities:**

1. Awardee will provide input in finalizing study design and submission of the study protocol to their IRB.
2. They will also implement the surveillance cultures and process the surveillance culture to identify potential KPC-producing Enterobacteriaceae. If the hospital needs support for PCR, sequencing, and molecular typing then the isolates can be sent to the CDC for this characterization. The hospital is also responsible for chart abstraction.

**CDC Activities:**

1. The CDC staff involved with the study will provide a study design outline, technical expertise, and data analysis support; and
2. CDC will provide laboratory support for PCR confirmation of the blaKPC gene, molecular typing, and sequence analysis. CDC will also provide data analysis support if needed.

**Special Requirements:** None

**Additional Review Criteria:** None

**Funding Preferences:**

1. Demonstrate the ability to enroll the highest number of cases may be funded over those that rank higher but enroll fewer cases.
2. Demonstrate frequent admissions of patients from long term care facilities.
3. Submit a description of the healthcare center and frequency of isolating KPC producing Enterobacteriaceae.

**Other Information:** None

**Project Period Length:** No more than 2 years

**Approximate Total Project Period Funding:** \$500,000 (This amount is an estimate, and is subject to availability of funds and **includes direct and indirect costs, excluding the additional academic partner administrative costs.**)

**Approximate Average Award:** \$223,500 (This amount is for the first 12-month budget period, and **includes both direct and indirect costs, excluding the additional academic partner administrative costs.**)

Approximate Number of Awards: 1

NOTE: Please note that applications must not exceed either the stated Project Period Length or the Approximate Total Budget Period funding per year. Applications in excess of these limits will be considered non-responsive and therefore will not be reviewed.