Clostridium difficile Infection (CDI) Surveillance

Request for OMB Approval of a New Data Collection

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Fernanda Lessa, MD, MPH
Medical Epidemiologist
Surveillance Branch
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention
1600 Clifton Rd NE, MS A-24
Atlanta, GA 30333
Phone: 404-639-7798
Fax: 404-639-2647
flessa@cdc.gov

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The Centers for Disease Control and Prevention (CDC) is requesting a three year OMB approval for a new data collection, the *Clostridium difficile* Infection (CDI).

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Centers for Disease Control and Prevention (CDC), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of Healthcare Quality Promotion (DHQP), in collaboration with state public health authorities, plans to conduct a longitudinal assessment of the impact of *Clostridium difficile* infection (CDI) in the United States through the Emerging Infections Program (EIP).

Steady increases in the rate and severity of CDI indicate a clear need to conduct a longitudinal assessment of the impact of CDI in the United States. *C. difficile* is an anaerobic, spore-forming, gram positive bacillus that produces two pathogenic toxins: A and B. CDI ranges in severity from mild diarrhea to fulminant colitis and death[1]. Transmission of *C. difficile* occurs primarily in healthcare facilities, where environmental contamination by *C. difficile* spores and exposure to antimicrobial drugs are common. More recently, however, reports of severe cases in populations considered to be at low-risk for CDI such as healthy persons in the community and peripartum women[2,3] raised concerns about transmission of this pathogen in the community. No longer limited to healthcare settings, community-associated CDI has been the focus of increasing attention.

The changing epidemiology of CDI is potentially linked to changes in several factors including host susceptibility, practices in prescribing antimicrobials, infection control practices, or the emergence of more virulent strains of *C. difficile*. The growing impact and magnitude of CDI across the continuum of healthcare delivery continues to be a challenge particularly without a systematic mechanism to collect and study the effects and epidemiology of this disease over population segments, time, and geography. Point

source outbreaks in healthcare institutions have been the primary source of CDI public health evaluation but there is no clear precedent to understand the drivers of CDI both in healthcare and community settings with a robust, longitudinal surveillance program. Quantifying the burden of CDI among cases in the United States and identifying populations at increased risk for disease will aid in developing prevention and control strategies. One strategy to achieve this is through the implementation of a population-based CDI surveillance program.

Furthermore, according to the U.S. Department of Health and Human Services (HHS) Action Plan to Prevent Healthcare-Associated Infections (http://www.hhs.gov/ophs/initiatives/hai/draft-hai-plan-01062009.pdf), prevention of CDI is a national priority, and quantification of burden will help set prevention targets for the U.S. population.

To understand the logistics and resources required to initiate and maintain a longitudinal, multi-site CDI surveillance program, a pilot surveillance study was conducted through CDC's Foodborne Diseases Active Surveillance Network (FoodNet). This pilot study aimed to identify strengths and challenges to conducting CDI surveillance in three hospitals located at two EIP sites (New York and Connecticut) over a three month period. The pilot study protocol was deemed to be research by CDC and local institutions. No OMB was required as only three hospitals participated in the pilot phase. The findings from this pilot study have been used to guide the development of this longitudinal assessment of the impact of CDI in the United States through the EIP. Section 301 of the Public Health Service Act (42 U.S.C. 241) shown in Attachment A authorizes the collection of these data.

Privacy Impact Assessment

Overview of the Data Collection System

Data will be collected on paper forms from existing sources of information, including electronic and paper medical records. Data will be entered into a secure web-based data

management system for transmission to CDC. Data collection and data entry partners will be the EIP staff. The EIP is a collaborative project of the CDC and ten state health departments (EIP sites). The EIP staff are employees of the State Health Department or state agents. A second data collection step will require a telephone interview. EIP staff will contact a subset of CDI cases; those classified as putative community-associated CDI based on medical record review for a telephone interview. Data collected through telephone interview will also be entered into a secure web-based data management system by EIP staff for transmission to CDC. EIP sites will have access to data submitted from facilities within their catchment areas. The information in the CDC database will be maintained indefinitely, since this data collection will be repeated at regular intervals for comparison purposes. Personal identifying information will be maintained by EIP sites until completion of all survey activities, but will not be transmitted to CDC.

Items of Information to be Collected

Information transmitted to CDC will include: state, county of residence, age, gender, date of birth, race/ethnicity, date of stool collection positive for C. difficile, location of stool collection (i.e. hospital inpatient, long term acute care hospital, long term care/skilled nursing facility, emergency room, or outpatient setting), hospitalization and date of admission, residency prior to stool collection (i.e. hospital inpatient, long term acute care hospital, long term care/skilled nursing facility, emergency room, or outpatient setting), hospital admission due to CDI, presence of other enteric pathogens in stool tested for CDI, exposures to healthcare (i.e. chronic hemodialysis, surgical procedure in the 12 weeks prior to stool collection, or emergency room visit in the 12 weeks prior to stool collection), patient outcome (i.e. patient survived and date of discharge or patient died and date of death), colectomy and date of procedure, intensive care unit (ICU) admission and date, CDI recurrence, radiographic findings (including toxic megacolon and ilues), presence of pseudomembranous colitis, clinical findings (including diarrhea and white blood cell counts), Charlson co-morbidity index components, and medication used in the 14 days prior to illness onset (including antimicrobial therapy use, immunosuppressive therapy use, and use of proton pump inhibitors or H2 blockers). Healthcare facilities who

participate in the information collection will be identified by facility identification codes. These facility identification codes are assigned codes that EIP sites use currently in the course of their surveillance activities, and although EIP personnel are able to link facility codes with facility names, CDC will not have these linkages. Local data collectors at participating healthcare facilities and EIP personnel will need to collect information in identifiable form (IIF) for patients within their own facility or catchment area, such as patient name, address, telephone number, date of birth, and medical record number. This information will not be transmitted to CDC.

Each patient will be assigned a unique identification code that will not contain identifying information and that will be randomly generated. CDC will not have access to any linking between patient name and patient identification code.

Identification of Website(s) and Website Content Directed at Children Under 13 Years of Age

The information collection will not involve a website with content directed at children less than 13 years of age.

2. Purpose and Use of Information Collection

Preventing *Clostridium difficile* Infection (CDI) is one of HHS priorities in the HHS Action Plan to eliminate healthcare-associated infections. Essential steps in reducing the occurrence of CDI are to estimate accurately the burden of *C. difficile* in U.S. hospitals, describe the epidemiology of these infections and molecular characteristics of the organism. These goals will be accomplished in the proposed EIP CDI Surveillance.

The EIP CDI surveillance is a collaborative project of the CDC and ten state EIP sites; including California, Colorado, Connecticut, Georgia, Minnesota, New York, New Mexico, Maryland, Tennessee, and Oregon. EIP staff, who are state health department employees or agents of the state, will receive monthly laboratory line lists of all *C. difficile* positive toxin stool specimen among persons residing in the surveillance

catchment area. For each case identified, medical record review will be performed using a standardized case report form. For a subset of cases classified as putative community-associated *C. difficile* cases based on the medical record review, EIP sites will administer a telephone interview. It is estimated that on average 50 telephone interviews will be completed by each EIP site per year. The telephone interview component will help CDC to describe more in depth the epidemiology of community-associated CDI, identify factors that put persons in the community in risk of developing *C.difficile*, and to generate hypotheses for future researches. The interview component of this study is expected to last three years, after that only the medical record review component will continue. For this project, the surveillance population will consist of persons residing in the catchment area of the participating EIP sites who are greater than 1 year of age. This surveillance poses no more than minimal risk to the study participants as there will be no interventions or modifications to the care study participants receive.

In order to describe the molecular characteristics of *C.difficile*, a convenience sample of remnant of positive *C. difficile* stool specimens linked to case-patients will be submitted to reference laboratories for culturing, and isolates will be sent to CDC for confirmation and molecular typing. Outcomes of this surveillance project will include an estimated burden of CDI in the United States by measuring population-based incidence of community- and healthcare-associated CDI among participating EIP sites, a description of the molecular characteristics of *C. difficile* strains that are responsible for CDI in the population under surveillance with a focus on strains from community-associated cases, and a better understanding of the epidemiology of community- and healthcare-associated CDI that will help generate hypothesis for future activities using EIP CDI surveillance infrastructure.

The proposed surveillance for CDI through the EIP will expand CDC capacity to monitor incidence of *C. difficile* in community and healthcare settings as well as to monitor and detect antimicrobial resistance. This activity supports the HHS Action Plan for elimination of healthcare-associated infections, specifically CDC's Strategic Goal of "Healthy Healthcare Settings," specifically the objectives to "Promote compliance with

evidence-based guidelines for preventing, identifying, and managing disease in healthcare settings" and "Prevent adverse events in patients and healthcare workers in healthcare settings" (http://www.cdc.gov/osi/goals/places/healthcare.html).

Privacy Impact Assessment Information

The information described in Section 1 is being collected to determine the population-based incidence of community-associated and healthcare-associated CDI among participating EIP sites, to characterize *C. difficile* strains that are responsible for CDI in the population under surveillance with a focus on strains from community-associated cases, to describe the epidemiology of community-associated and healthcare-associated CDI, and to generate hypotheses for future research activities using the EIP CDI surveillance infrastructure. Healthcare-associated infections (HAIs), including CDI, are recognized as a major cause of morbidity and mortality in the United States, as well as a major contributor to excess healthcare costs (see http://www.hhs.gov/ophs/initiatives/hai/). Eliminating HAIs is a priority of the CDC and other federal agencies. Quantifying the burden of CDI among cases with and without established risk factors will aid in developing prevention and control strategies. During this data collection, CDC will neither receive nor share IIF, with the exception of medical information as described above. No names, addresses, medical record numbers, telephone numbers or facility names are being transferred to CDC. Data will be entered into the electronic data management system and retrieved by CDC using identification codes that do not contain patient identifiers. CDC will analyze and report aggregated data obtained during the survey. The results of the surveillance activities will be used by local, state and federal public health authorities to inform the development of CDI prevention and control strategies.

3. Use of Improved Information Technology and Burden Reduction

This surveillance will use paper data collection forms. Personnel collecting data may need to travel to multiple healthcare facilities and will not necessarily have reliable,

timely access to computers or the internet. All data will be entered by personnel into a online enterprise SQL-supported database with secure web and data servers at the CDC. No paper forms will be submitted to CDC. In accordance with the Government Paperwork Elimination Act (GPEA), Public Law 105-277, all means to maintain records electronically have been taken.

4. Efforts to Identify Duplication and Use of Similar Information

In the United States, the rates of hospitalization with CDI demonstrated a 109% increase from 261 cases per 100,000 discharges to 546 cases per 100,000 discharges between 1993 and 2003 using ICD-9 codes from national inpatient sample data [4]. Abdominal colectomies among these patients increased almost 5-fold and total mortality rose from 20.3 per 100,000 discharges to 50.2 per 100,000 discharges. While useful in determining rates of hospitalization with CDI, discharge data does not account for the burden of community-associated disease or disease burden outside of the acute care setting.

Similarly, data reported to the National Nosocomial Infection Surveillance (NNIS) system revealed an overall increase in CDI among intensive care unit patients from 1987-2001 with indications of both seasonal and geographic variation[5]. More recent data from NNIS are non-existent since this surveillance system ended in 2004. The National Healthcare Safety Network (NHSN), the successor of NNIS, does not track community-associated CDI cases nor collects specimen for further molecular characterization.

No longer limited to healthcare environments, community-associated CDI is the focus of increasing attention. Recently, several cases of serious CDI have been reported in what have been considered low-risk populations, including healthy persons living in the community and in peripartum women. At least 25% of these cases had no history of prior healthcare or antimicrobial exposure[2, 3]. After legislation in Connecticut made CDI a reportable disease, passive surveillance for community-associated CDI reported 6.9 cases per 100,000 persons in 2006, similar to findings in the Philadelphia area the year prior (7.6 per 100,000). More recent data from an active population-based surveillance in Durham county demonstrated that incidence of community-associated CDI can be as high

as 46 per 100,000 persons per year[8]. Surveillance in diverse geographic locations is needed to better understand the national burden and epidemiology of CDI.

5. Impact on Small Businesses or Other Small Entities

Small laboratories or critical access hospitals may participate in the CDI surveillance program. Participation is voluntary, but we anticipate that most if not all facilities selected for participation will agree to participate. Elimination of CDI, an important healthcare-associated infection, is a major goal of all U.S. healthcare institutions, large and small, and we expect that facilities will be highly motivated to participate. Likewise, some states already mandate reporting of CDI by laboratories to the state health department. In these cases, the information is already being made available and participation is mandatory. The data collection and management burden for participating healthcare facilities will be minimized as much as possible. This will be accomplished by having EIP personnel perform the data collection, with the exception of generating the laboratory line-lists used to identify cases.

6. Consequences of Collecting the Information Less Frequently

EIP personnel will complete data collection on cases as they are identified from laboratory reports on an ongoing basis. Performing data collection on cases as they are identified (versus a quarterly or annual basis) will allow for rapid classification of cases into epidemiologic categories (e.g. community-associated) and identification of epidemiologic changes, including rates and severity of disease in geographically diverse patient population segments over time. If epidemiologic classification of cases is not performed in a timely manner this will likely result in a recall bias during interview. In addition, linking these epidemiological changes to several important determinants of disease, including host susceptibility, practices in prescribing antimicrobials, infection control practices, or the emergence of more virulent strains of *C. difficile*, requires timely and consistent data collection. The molecular epidemiology is constantly changing as demonstrated by a recent study done over a 10-year period from a single U.S. institution [9]. The non-collection of these data will prevent CDC to monitor the burden and the epidemiologic changes of CDI. There are no legal obstacles to reduce the burden.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances that require the information to be collected in any of the formats identified, and the request fully complies with regulations.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

A. As required by 5 CFR 1320.8(d), a notice of this proposed data collection appeared in the Federal Register, Vol. 75, No. 168 on Tuesday, August 31, 2010 (See Attachment B). No comments were received from the public

B. The following representatives were consulted during the development of the study methods and data collection instruments. Both of the following contacts were contacted several times between January 2008 and April 2009.

Cliff McDonald, MD
Centers for Disease Control and Prevention
Division of Healthcare Quality Promotion/NCPDCID/CCID
1600 Clifton Rd, NE
Atlanta, GA 30333
(404) 639-3833
Email: CMcDonald1@cdc.gov

Brandi Limbago, PhD
Centers for Disease Control and Prevention
Division of Healthcare Quality Promotion/NCPDCID/CCID
1600 Clifton Rd, NE
Atlanta, GA 30333
(404) 639-2162
Email: BLimbago@cdc.gov

9. Explanations of Any Payment or Gift to Respondents

No monetary incentive or gifts are provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

A unique identifier will be assigned to each patient to allow the reporting EIP facility to link reported data back to the individual patient, however this link will not be shared with CDC. Hospital admission date, birth date and race/ethnicity data will be transmitted to CDC; no other patient identifiers will be transmitted to CDC. Each facility will also have an assigned code. Links between facility codes and names will be maintained by EIPs and will not be shared with CDC. Individual facility data will not be reported by CDC, but rather will be aggregated to provide CDI incidence estimates for the population under surveillance. All patient-level data will be kept in a secure manner and will not be disclosed unless otherwise compelled by law. The data management system has a C&A classification of medium and the e-authorization level has been determined to be level 2. Additionally, all personnel will be required to use the Secure Access Management System (SAMS) to access the data management system.

<u>Privacy Impact Assessment Information</u>

A) This information collection request has been reviewed by CDC/ICRO who has determined that the Privacy Act does not apply. Information submitted to CDC will not include names or individually identifying numbers (such as Social Security Numbers). Patients included in the survey will be assigned unique identification codes; these codes will not contain identifying information. With the exception of hospital admission dates and date of birth, personal identifiers will not be transmitted to CDC.

B) Information received by CDC will be stored in a secure, password-protected database (certification and accreditation at level 2). Information received by CDC will be provided only to those individuals at CDC with a need to know.

C) Respondent consent: Verbal consent will be obtained from patients undergoing telephone interview (Attachment C). For persons 18 years of age or older, verbal consent will be obtained from all eligible participants. Because this study requires that participants be interviewed in a timely manner, all participants will be interviewed over the telephone. The consent will be read to participants who agree to health interview. For persons aged 13-17 years, verbal assent will be obtained. Parents or guardians will be interviewed for children 1-12 years of age. A copy of the consent form read to those study participants aged 13-17 and the parent/guardian, with responses noted and signed by the interviewer, will be retained with each completed questionnaire (Attachments C and D). For the medical review component of this study, consent is not applicable as EIP personnel will perform review of existing medical record data in participating facilities and submit these data to CDC without having any interaction with individual patients.

D) Participation by patients in this project is voluntary. Data will be treated in a secure manner, and no patient name, address, telephone number, medical record number, and facility name will be transferred to CDC.

11. Justification for Sensitive Questions

The reporting of adverse events associated with healthcare can be sensitive unless the institution is assured that the data aggregating organization will provide security for the data and maintain the institution's confidentiality. As discussed in item A.10 above, participating individual's and institution's confidentiality will be assured.

12. Estimates of Annualized Burden Hours and Costs

A. Estimate of Annualized Burden Hours

An estimated total of 9,360 CDI cases will be indentified during one year of surveillance based on a population-based *C.difficile* study conducted in North Carolina[8] and based on the data from the CDI pilot study. While 9,360 CDI cases may be identified through this

longitudinal assessment, only 600 will be contacted for a telephone interview. These 600 CDI cases will be screened for eligibility (Attachment E) and those considered to be eligible will complete the telephone interview (Attachment F). We anticipate that 500 of the 600 cases screened will complete the telephone interview across all 10 EIP sites per year. We anticipate the screening questions to take about 5 minutes (Attachment E) and the telephone interview (Attachment F) 40 minutes per respondent. Medical record abstraction will be conducted by EIP staff as a part of the cooperative agreement. There is no additional burden placed on the hospitals staff. Therefore, no burden is attributed to this activity. (See Attachment G for record abstraction)

Type of Respondents	Form Name	Number of Respondents	Number of Responses per Respondent	Average Burden per Respondent (in hours)	Total Burden Hours
Person in the community infected with C.difficile (CDI Cases)	Screening Form	600	1	5/60	50
	Telephone interview	500	1	40/60	333
Total					383

B. The total cost burden for respondents was estimated based on the Occupational Employment and Wage, May 2009 from the Department of Labor (http://www.bls.gov/oes/2009/may/chartbook.pdf - accessed on February 2, 2010). Because the occupation of the respondents is unknown, we used the U.S. hourly mean wage across all occupations. The U.S. hourly mean wage is $20.90.

Table B: Estimated Annualized Burden Cost

Type of Respondents	Total Burden Hours	Hourly Wage Rate	Total Respondent Cost

Persons in the community infected with C.difficile (CDI cases)	383	$20.90	$8,000.47

13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

None.

14. Annualized Cost to the Government

Costs to the government include costs for surveillance officers (epidemiologists) to develop and coordinate study activities at CDC, EIP personnel to perform local study coordination and data collection and entry activities, costs for a database manager, costs for photocopying data collection forms.

EIP personnel will collect data from medical records of CDI cases using a standardized data abstraction form (Attachment G – case report form). Of the anticipated 9,360 CDI cases annually, 50% will have a full case report form (CRF) completed; whereas the other 50% will only have the first 11 questions of the CRF completed (partial CRF). The full case report form is estimated to take approximately 1 hour per patient, while the partial CRF should take 15 minutes per patient. Therefore, the total hours of work for EIP surveillance officers is estimated to be 5850 annually across all 10 EIP sites.

There will also be costs related to photocopying of CRFs. This is estimated to be $702 ($0.05 to copy each page, estimated 14,040 copies made to support study activities in 10 EIP sites).

The total cost for personnel and photocopying of CRFs is therefore estimated to be $643,765+ $702 = $644,167.

The estimated cost to the Federal government is shown in the following table below.

Table C: Annualized Cost to the Government

Government Employee Title	Total Number of Hours Dedicated to Surveillance per Year	Description of Duties	Hourly Rate[a]	Total Burden per Year	Total Burden for Entire Study Period (3 Years)
CDC Surveillance Coordinator/ Epidemiologist	500	Develop the protocol, data collection forms, training, IRB and OMB submissions. Assist with data analysis	$31.31	$15,655	$46,965
Database manager (1)	500	Create and manage data management system	$35.05	$17,525	$52,575
EIP surveillance officers/ epidemiologists (10)[b]	5850	Local coordination, training, data collection, data entry and submission to CDC	$31.01	$181,408	$544,225
Total personnel cost for 3 years of surveillance				214,588	$643,765

[a] Obtained from http://www.bls.gov/oes/2009/may/oes_nat.htm#b19-0000.

[b] One surveillance officer in each of 10 EIP sites.

Total estimated annual cost to the Federal government: $214,588

15. Explanation for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule Tabulation

A patient-level surveillance dataset will be maintained at CDC. This dataset will be used to describe the burden and distribution of healthcare facility-onset and community-onset CDI. Expected analysis includes incidence stratified by age, gender, race and pace of disease acquisition (healthcare vs. community). Rates will be projected to the national level based on the age and gender distribution of the U.S. population. We will also analyze severity of CDI illness and risk factors to identify populations at risk of CDI. Finally, we will analyze the molecular characteristics of *C.difficile* isolates and its distribution among geographically diverse areas of the United States. Analysis will occur in SAS version 9.2 (SAS Institute, Carey, NC). We request clearance for three years.

Results from this surveillance will be presented at national meetings and published in a manuscript format in a peer-reviewed medical science journal. Conference abstracts and manuscripts will be developed as appropriate to disseminate the findings of this surveillance project.

The surveillance will begin as soon as possible following OMB approval. This is a longitudinal study and data collection and transmission will be ongoing. Analysis and presentation of the results will be completed annually.

Activity	Time Schedule
Conduct Health Interview on subset of cases	3 months after OMB approval
Transmission of data to CDC	3 months after OMB approval
Analysis and presentation of results	Annually

17. Reason(s) Display of OMB Expiration Date is Inappropriate

The proposed survey instrument will display the expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

This data collection has been designed in accordance with the requirements specified in Item 19 of the OMB 83-I. No exceptions to certification are requested.

References

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7. Dumyati G, Hannett GE, Thompson AG, Long C, Stevens V. Clinical Features and Molecular Characterization of Community-Acquired *Clostridium difficile* Infections. 47th Infectious Diseases Society of America Annual Meeting, Philadelphia, PA, Oct 29-Nov 1, 2009. Abstract # 994

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9. Belmares J, Johnson S, Parada JP, Olson MM, Clabots CR, Bettin KM, Peterson LR, Gerding DN. Molecular epidemiology of Clostridium difficile over the course of 10 years in a tertiary care hospital. Clin Infect Dis. 2009; 15:1141-7.

List of Attachments

A: United States Code, Title 42, Chapter 6A Part 241

B: 60-day Federal Register Notice

C: Consent for person aged 18 years or older

D: Verbal Assent for persons aged 13-17 years

E: Screening Form for Telephone Interview

F: Health interview form

G. Case Report Form

H: IRB Research Determination