

**FOA# CK17-1701**

**PPHF 2017: Epidemiology and Laboratory Capacity (ELC/EIP) –  
Emerging Infections Programs – Primary  
Financed in Part by 2017 Prevention and Public Health Funds**

**ATTACHMENT 1 – EIP ACTIVITY DESCRIPTIONS**

**Table of Contents:**

<b>Page</b>	<b>Section</b>	<b>Title</b>
2	A	General EIP Function and Structure
6	B	Active Bacterial Core Surveillance (ABCs)
15	C	Foodborne Disease Active Surveillance Network (FoodNet)
23	D	Influenza
31	E	Healthcare-Associated Infections and Antimicrobial Resistance
43	F	Human Papillomavirus (HPV-IMPACT)
48	G	Lyme and Other Tickborne Diseases (TickNET)
50	H	Rotavirus
52	I	Prion Disease
57	J	Arbovirus
60	K	Congenital Cytomegalovirus

**General EIP Function and Structure**

**Background**

EIPs are population-based centers of excellence established through a network of state health departments collaborating with academic institutions; local health departments; public health and clinical laboratories; infection control professionals; and healthcare providers. The state health departments, collaborating institutions/organizations, and CDC together make up the EIP network.

EIPs assist in local, state, and national efforts to prevent, control, and monitor the public health impact of infectious diseases. Activities of the EIPs fall into the following general categories: (1) active surveillance; (2) applied public health epidemiologic and laboratory activities; (3) implementation and evaluation of pilot prevention/intervention projects; and (4) flexible response to public health emergencies and newly emerging issues.

EIP sites must establish and maintain general, crosscutting functions and structures in order to successfully conduct the programmatic surveillance and research activities. These are outlined in detail in Strategies and Activities section, below. This general function and structure includes particularly, scientific, programmatic, and business/administrative oversight and support.

Using the metaphor of a tree with roots, trunk, and branches, (see main FOA Background section and recent Emerging Infectious Diseases article at <http://wwwnc.cdc.gov/eid/article/21/9/15-0619>), the trunk is the capacity and functionality needed to sustain the network and ensure it can adapt (the General EIP Function and Structure activity described in this Appendix), while the branches are disease area-specific activities (described in Appendices II-XI).

**Purpose**

The purpose of this general EIP function and structure activity is to support EIP sites to establish and maintain key crosscutting scientific, programmatic, and business/administrative capacity. This is intended to include staff, activities, and related costs that are essential to assuring general EIP infrastructure that are not supported by the applicant's Indirect Cost Rate Agreement and that are better allocated to General EIP Function & Structure than allocated across one or multiple programmatic activities.

**Note to current EIP grantees under expiring FOA CK12-1201** (applicants that are not current EIP grantees - should disregard this paragraph):

Current EIP grantees under expiring FOA CK12-1201 also receive a portion of their general capacity support via the Affordable Care Act/Prevention and Public Health Fund (PPHF)-specific EIP cooperative agreement FOA CK12-1209. Current EIP grantees can expect to have that PPHF support continue via FOA CK12-1209 at current levels until that cooperative agreement expires on September 29, 2017. On September 30, 2017, all costs/activities funded via CK12-1209 will be transitioned to and supported under this new FOA CK17-xxxx beginning with the 2<sup>nd</sup> budget period of this FOA (that begins January 1, 2018). Therefore, current EIP grantees should include in their budget for this General EIP Function and Structure activity of FOA CK17-xxxx, continuation of CK12-1209 costs/activities only for September 30, 2017 – December 31, 2017.

## **Outcomes**

Robust EIP infrastructure and crosscutting activities that will ensure a highly functional platform/foundation for conducting EIP programmatic activities and achieving the public health outcomes for EIP.

## **Strategies and Activities**

1. Scientific, Programmatic, and Business/Administrative Oversight and Coordination. Ensure effective scientific, programmatic, and business/administrative leadership, management, coordination, execution, and continuity of EIP activities overall. Organize staffing and related support structure to effectively manage crosscutting functions and to adequately support grantee's portfolio of programmatic activities. This includes scientific and programmatic coordination and management of crosscutting fields such as culture-independent diagnostic testing (CIDT), and advanced molecular detection (AMD), and information technology (IT).
2. Populations/Catchment Areas. EIP programmatic activities are conducted in defined populations (as appropriate) that may include an entire state, a geographically defined area within a state, or a population defined by a healthcare delivery system. Assure populations for each EIP activity are appropriately determined and are of adequate/appropriate size and composition necessary for each activity. The population base may vary by activity and may change over time as needs evolve.
3. Flexibility and Efficiency. Organize resources in a manner that allows for flexibility to respond to new public health issues as they arise and for optimal efficiency across multiple projects conducted in one or more facilities within a site. As a manifestation of EIP capacity for flexible response, each EIP will be expected to participate in a workgroup convened on short notice to review newly emerging infectious disease issues. Should that group determine that EIPs could help guide the response to that issue in the short-term, each EIP is expected to contribute to rapid study design and initiate and complete the relevant study in a very short period of time (e.g., within one month of its proposal). In this proposal, describe how applicant will ensure (1) the surge capacity that would be used to participate in workgroups convened on short notice to review newly emerging infectious disease issues and (2) the surge capacity that would be used, if the workgroup determines that EIPs could help guide the response to that issue in the short-term, to contribute to rapid study design and initiate and complete relevant studies in a timely manner.
4. Collaborations and Partnerships. Develop and operate the EIP site to function effectively as a member of the national network. Participate actively in EIP working groups to help establish network priorities, coordinate projects, monitor progress, and, when appropriate, ensure standardized implementation of activities across sites. Establish and maintain working relationships with local partners, including but not limited to, academic centers, health departments, infection control practitioners, hospitals, healthcare providers, public and private laboratories, research organizations, tribal organizations (if Native American/Alaskan Native populations are subject of any EIP activities), and other Federal and state government agencies.
5. Training. Incorporate training such as infectious disease fellowships for clinicians, laboratorians, and researchers, as well as other training opportunities for public health students and local public health professionals. Opportunities can include, but are not limited to, fellowships, educational

conferences or seminars, thesis advising or mentoring, and work study or research assistant positions.

6. **Data Management.** Collect, manage, analyze, and interpret data from EIP projects; publish and disseminate important public health information resulting from EIP projects in collaboration with CDC and other EIP sites as appropriate. Ensure and maintain ability and capacity to conduct medical record reviews, surveys, laboratory audits, and analysis of hospital admissions and discharge data. Work with CDC programs and the network to ensure quality assurance.

Work with CDC programs and the network to assure compliance with CDC's Policy on Public Health Research and Non-research Data Management and Access. The goal of the policy is to ensure public access to federally funded public health data. This specifically requires development of Data Management Plans (DMPs) for each EIP activity that includes collection of public health data. DMPs should be developed jointly by CDC and EIP grantees within the first 6 months after award and updated as appropriate throughout the life cycle of the data. DMPs should include:

- Descriptions of the data to be produced
- How access will be provided to the data (including provisions for protection of privacy, confidentiality, security, intellectual property, or other rights)
- Use of data standards that ensure all released data have appropriate documentation that describes the method of collection, what the data represents, and potential limitations for use
- Plans for archival and long-term preservation of the data, or explanation of why long-term preservation and access cannot be provided.

7. **Information Systems.** Information systems and technology are critical to maintaining and improving the collection, quality, and management of data resulting from EIP activities. Recognizing this, EIPs are adopting an EIP IT Strategy. The EIP IT Strategy focuses broadly on improving and modernizing information systems and adopting and taking advantage of electronic data exchange. As part of this cooperative agreement, grantees should ensure there are adequate resources dedicated to EIP IT projects and focused on implementing the EIP IT Strategy. Grantees should also maintain appropriate attendance and involvement on EIP IT Workgroup web meetings. EIP IT activities could, for one or more projects, work toward interoperability and integration among systems. This could include, for example, transitioning from standalone databases to the state integrated surveillance information systems, and enabling standalone databases to send and receive data from other databases or the integrated system. Electronic data exchange, which includes electronic laboratory reporting (ELR), receiving data from an Immunization Information System (IIS), and electronic case reporting (eCR) from electronic health records, should be a priority. Grantees should make sure EIP projects use existing ELR and work with their state ELR program to prioritize new feeds. Systems used for some EIP projects should be enhanced to receive data from the state IIS. Also, grantees should participate in the national effort to define eCR, including planning for promising pilot projects with one or more partners.

8. **Laboratory Specimens.** As culture-independent diagnostic testing becomes more prevalent, work with CDC and other EIP network sites to develop and implement strategies to 1) sustain the availability of a certain number of clinical isolates and 2) provide for a bank of appropriate specimens for culture-independent testing. In general, provide specimens to CDC or other

appropriate laboratories for evaluation when required by EIP protocols (e.g., for studies, evaluation of diagnostics, etc.).

9. Program Evaluation. Assure capacity for general EIP program evaluation and performance measurement. Metrics/measures of effectiveness for individual EIP activities may be developed in collaboration with CDC and/or independently. Some EIP activities have established performance metrics that must be used. Refer to specific guidance in each of the programmatic appendices.
10. Human Subjects. Ensure appropriate local review of EIP activities and provide local IRB status and/or determination of all research projects undertaken. For activities involving research on human subjects, each institution that participates in human subjects research is required to review each protocol annually and submit current copies of IRB approval letters in the annual non-competitive continuation applications and to PGO as determinations are made during the year. For specific EIP studies that involve human subjects, obtain institutional review board approval prior to the commencement of study activities and assure subjects are recruited according to study protocols.
11. Office of Management and Budget Paperwork Reduction Act (OMB-PRA). Work with CDC scientists to obtain OMB-PRA approvals, as needed.
12. Dual Use Research of Concern (DURC). Comply with the responsibilities for the PI as described in the United States Government Policy for Institutional Oversight of Life Science (DURC). See <http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf>.

**Active Bacterial Core surveillance (ABCs)**

**Background**

Active Bacterial Core surveillance (ABCs) was established through EIP in 1995 to assess the disease burden of invasive bacterial infections in the community that primarily manifest as bloodstream infections and meningitis. ABCs conducts active, laboratory, population-based surveillance for invasive group A *Streptococcus* (GAS), *Haemophilus influenzae*, *Neisseria meningitidis*, group B *Streptococcus* (GBS) and *Streptococcus pneumoniae*. ABCs also serves as a platform to conduct special studies related to all these infections. Despite their importance, not all of the infections captured under ABCs are reportable to CDC. Even for those infections included in CDC's National Notifiable Disease Surveillance System (NNDSS), case counts may be underestimated because they rely on reporting by laboratories and clinicians whereas ABCs tries to actively identify 100% of the cases within the surveillance area. Additionally, epidemiologic data collected by health departments are often incomplete because of the resources required to collect them and the inflexibility of the system to capture variables of interest. Unlike NNDSS, ABCs also collects isolates that are serotyped and tested for antimicrobial susceptibility. These attributes allow ABCs to fulfill two critical objectives: 1) to determine the incidence and epidemiologic characteristics of important invasive diseases and 2) to determine molecular epidemiologic patterns and microbiologic characteristics of these invasive infections.

For routine surveillance, a case of invasive bacterial disease is defined as isolation of *H. influenzae*, *N. meningitidis*, GAS, GBS, or *S. pneumoniae* from a normally sterile body site (e.g., blood, joint, pleural and cerebrospinal fluid) in a resident of the surveillance area. Additionally, cases include ill persons from whom GAS is isolated from a wound or other tissue in the presence of necrotizing fasciitis (NF) or streptococcal toxic shock syndrome (STSS). Maternal cases of GBS are also included if GBS has been isolated from the placenta or amniotic fluid in the setting of fetal death. As stated, the goal is to detect 100% of laboratory-confirmed cases by actively contacting all clinical laboratories that routinely process specimens from residents of the surveillance area. Audits are performed regularly to ensure that all cases are captured. U.S. census data are used to calculate disease incidence rates within the ABCs population.

Through medical record review for each case-patient, demographics, clinical course, outcome, infection type, underlying conditions and vaccination history are collected. An isolate from the first positive culture is collected for most cases. Molecular typing and antimicrobial susceptibility testing are performed on collected isolates either at CDC or other reference laboratories.

In addition to conducting surveillance and special studies for ABCs pathogens, a key feature of ABCs is its flexibility to respond to public health emergencies and conduct surveillance for other emerging threats. After the 2001 anthrax attack, the ABCs infrastructure was used to establish and test a more sensitive and timely system for identifying inhalation anthrax. After SARS was discovered in 2002, the EIP infrastructure assisted with surveillance activities and the investigation of suspected cases. During the 2009 H1N1 influenza pandemic, early recognition of IPD among H1N1 patients increased emphasis on pneumococcal prevention strategies. Due to rising rates of infections, special surveillance and studies related to pertussis and legionellosis were added to ABCs in 2011.

The ABCs Steering Committee is responsible for helping determine the overall scientific direction of ABCs. This includes reviewing priorities, supporting pathogen committees, reviewing protocols or proposals, monitoring the development and implementation of ABCs programs and projects and

identifying and involving key stakeholders in ABCs programs. The Steering Committee includes representatives from CDC and each EIP grantee.

### **Other National Public Health Priorities and Strategies**

Results from ABCs surveillance have been used in the development and pre-licensure evaluation of multiple vaccines. Post-licensure, ABCs data have been used to formulate national policy recommendations developed by the Advisory Committee on Immunization Practices (ACIP) and to determine the real-world impact of vaccines through vaccine effectiveness studies. ABCs has also had an impact on other prevention-related policies and practices, including guidelines for preventing perinatal GBS infections and preventing invasive GAS in household and healthcare settings. ABCs data have also been used to track antimicrobial resistance. ABCs data were used in CDC's "Antibiotic Resistance Threats in the United States, 2013" report and to inform the National Strategy for Combating Antimicrobial Resistant Bacteria. ABCs data are also used to evaluate "Healthy People" goals for disease reduction.

### **Purpose**

While disease rates have declined for many ABCs pathogens, they remain an important cause of severe bacterial infections. ABCs will implement active, laboratory, population-based surveillance and conduct special studies for invasive GAS, *H. influenzae*, *N.meningitidis*, GBS and *S. pneumoniae* in order to monitor their disease burden, track antimicrobial resistance and evaluate prevention strategies. Enhanced pertussis and legionellosis surveillance and special studies will be done to better understand rising disease rates and evaluate prevention strategies to reverse these rising trends.

### **Outcomes**

#### ***Provide new knowledge***

Surveillance and special studies for ABCs pathogens are intended to enhance our understanding of the disease burden, risk factors, molecular epidemiology and antimicrobial resistance of these pathogens and to evaluate prevention measures. The knowledge will be used to inform policy and prioritize prevention programs at the national level. It is also likely to enhance prevention efforts at the site level.

#### ***Develop staff expertise***

ABCs site personnel will develop expertise in the epidemiology of ABCs pathogens and in developing skills to conduct data abstractions, management and analysis. Formal and informal programs will be implemented to train new staff and to continuously educate existing staff since case ascertainment, data abstractions and data management methods are likely to change over the 5 year period.

#### ***Control outbreaks of infectious diseases***

The ABCs infrastructure will assist health departments in their detection and control of outbreaks. The data are often used to understand baseline rates and to help determine when situations require further investigation. Additionally, EIP/ABCs infrastructure has often been used to investigate outbreaks of non-ABCs pathogens, as described above.

#### ***Develop/modify guidelines***

ABCs data will be used to develop and evaluate prevention guidelines. For instance, recommendations for routine use of pneumococcal conjugate vaccine in adults aged  $\geq 65$  years old will be under review in 2018 by ACIP. Data from ABCs surveillance and special studies will likely be used to inform any revisions made to those recommendations. There will also be opportunities to evaluate the effectiveness of serogroup B meningococcal (MenB) and pertussis vaccines.

### ***Develop/modify intervention recommendations***

ABCs will be used to evaluate B. pertussis post-exposure prophylaxis recommendations. ABCs will also be used to evaluate a Clinical Decision Support tool embedded into electronic medical records that incorporates CDC guidelines to prevent perinatal GBS disease.

## **Strategies and Activities**

### **ABCs Core Activities: REQUIRED**

1. Conduct active, laboratory, and population-based surveillance for invasive bacterial disease due to group A *Streptococcus* (GAS), group B *Streptococcus* (GBS), *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae*. The goal of surveillance is to identify 100% of case-patients (i.e. not a sample) that reside in the surveillance catchment area. A case of invasive bacterial disease is defined as isolation of *H. influenzae*, *N. meningitidis*, GAS, GBS, or *S. pneumoniae* from a normally sterile body site. Body sites include, but are not limited to, blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid, bone, joint fluid, muscle/fascia/tendon (group A *Streptococcus* only), lymph node, brain, heart, vascular tissue, liver, spleen, vitreous fluid, kidney, pancreas, and ovary. The definition also includes GAS isolated from a wound or other tissue in the presence of necrotizing fasciitis (NF) or streptococcal toxic shock syndrome (STSS). Maternal cases of GBS are also included if GBS has been isolated from the placenta or amniotic fluid in the setting of fetal death. Surveillance activities include:
  - a. Identify patients who meet the case definition by establishing contact with all laboratories that regularly process specimens from residents of the catchment area (the laboratories may be located within or outside the catchment area). Case identification may occur through multiple means, including electronic laboratory messaging, receiving electronic line lists, phone calls, or paper reports. Audits (at least annual) should be conducted to assure that 100% of cases are being captured. Audits should include review of the primary data source at every reporting site (e.g. computer-generated electronic printouts, log books, etc.). If data are being generated electronically, a review of data queries (i.e. what pathogens and sterile sites are being captured) should be done. In addition to the annual audit, every 2-3 years each site should perform an evaluation of their overall surveillance methodologies to ensure they are capturing all cases of invasive disease in catchment area residents for each pathogen under surveillance. This includes identifying laboratories located both within and outside the ABCs catchment area that process specimens from residents of the catchment area as well as identifying facilities and/or state/local health departments that serve residents of the catchment area. Routine communication with each laboratory and facility/health department that contributes to ABCs cases is needed to ensure that ongoing surveillance is active- and population-based surveillance.
  - b. Complete standardized case report forms through review of medical records that includes information on demographics, clinical course, outcome, infection type, underlying conditions and vaccination history.
  - c. Collect of isolates for all pathogens under surveillance (GAS, GBS, *H. influenzae*, *N. meningitidis* and *S. pneumoniae*) and ship to CDC labs on a monthly or bi-monthly basis.



- d. Conduct periodic (every 1-2 years) laboratory surveys to assess use of culture independent diagnostics on sterile site specimens. If a decision is made by the ABCs Steering Committee to include such cases in the case definition for all or some of the ABCs pathogens, then sites will be required to perform surveillance activities for those cases.
2. On an annual basis, collect vital statistics records to enhance the quality of ABCs data. Submit the data to CDC between October and December of the following year (e.g. October 2017 for the 2016 surveillance year). The vital statistics collected or reviewed include:
  - a. Number of live births to surveillance area residents and within surveillance area counties, stratified by birthweight and gestational age.
  - b. Maternal and paternal race and ethnicity from birth certificates from case-patients <5 years of age for which race or ethnicity is missing from the medical record.
  - c. Review in-state death registries to determine outcomes for patients with unknown outcomes.
3. Geocode all ABCs cases to the census tract level as a means of capturing area-level socioeconomic factors, such as poverty, educational level, household crowding, and access to healthcare. CDC and site regulations will determine what data may be transmitted to CDC.
4. Provide timely responses to reports and requests for information to assist in preliminary & final analyses, reports, and data close-outs.

**Other ABCs Core Activities: REQUIRED**

1. Participate in ABCs Steering Committee (every 2 months), Surveillance Officer (monthly), and Pathogen Committee conference calls (as needed).
2. Participate in annual ABCs Steering Committee and Surveillance Officer in-person meetings.
3. GBS-related activity: Collect additional infant and maternal information on early- and late-onset GBS disease.
4. Pneumococcal-related activities:
  - a. Evaluate the effectiveness of the 13-valent pneumococcal conjugate vaccine for prevention of *S. pneumoniae* infections among adults using a case-control methodology. Collaborate with CDC to evaluate methods for case and control enrollment and enroll cases and controls, which could include collaboration with the Center for Medicare and Medicaid Services as well as geocoding of cases and controls.
  - b. Evaluate trends in hospitalizations for all cause and pneumococcal-specific community-acquired pneumonia using state-based hospital discharge data.
  - c. Perform surveillance for non-invasive pneumococcal pneumonia among adults by identifying cases with a positive urinary antigen test and clinically or radiographically-confirmed pneumonia within the designated surveillance area. Surveillance activities include collection of case report form data. To adjust for testing practices within hospitals and use of pneumococcal urine antigen tests by hospitals: 1) Use ICD-coded discharge data from hospitals that perform urine antigen testing to assess the frequency of such testing among patients hospitalized with pneumonia, and 2) Assess the proportion of pneumonia hospitalizations within the catchment area that are admitted to hospitals where non-invasive pneumococcal surveillance is being conducted.
  - d. Collect additional demographic, medical and vaccination history information on all invasive pneumococcal infections in children aged 3 months through 59 months with an isolate available for serotyping. This includes contacting parents to identify healthcare providers who provide immunizations to their children, contacting all identified providers to ascertain PCV13 vaccination status, and review of state vaccine registries to obtain complete vaccine information for cases of invasive pneumococcal disease.

5. *H. influenzae*-related activity: Contact healthcare providers or state vaccine registries to obtain complete vaccine information for cases of Hib disease age <5 years to monitor impact of new vaccines.
6. *N. meningitidis*-related activity: Evaluate the effectiveness of the serogroup B meningococcal (MenB) vaccines for prevention of serogroup B meningococcal disease among adolescents, likely in the form of a case control study. Collaborate with CDC to develop the protocol and methods for case and control enrollment.
7. Legionellosis surveillance: Perform at least annual audits of laboratories conducting *Legionella* testing within the ABCs legionellosis surveillance catchment area to ensure that all laboratory-confirmed cases of legionellosis are being identified by the state-based reporting systems.
8. Work to integrate ABCs data needs with sites' changing landscape of access to electronic medical records and public health records. Maintain flexibility to rapidly respond to changes in core surveillance. Sites must have the ability to quickly (within three months) modify data collection methods and site databases to respond to changes in ABCs surveillance. Changes may include addition or deletion of variables submitted to CDC.

### **Additional ABCs Activities: OPTIONAL**

*These activities may be restricted to sites that have successfully participated in core activities for at least two years, except as noted.*

1. If culture independent diagnostic tests (CIDTs) are not included in the ABCs case definition, then sites may elect to expand surveillance for invasive bacterial infections for ABCs pathogens to include patients who test positive by nucleic acid tests obtained from sterile site specimens. This would include gathering data on the type of test used and how it was validated. Including these cases will be required if the ABCs case definition is expanded by the ABCs Steering Committee to include CIDTs.
2. GBS-related activities:
  - a. Implement and evaluate a clinical decision support (CDS) tool at 1-2 hospitals. A link to the tool would be embedded within the hospital's electronic medical records and incorporates CDC guidelines for providing intrapartum prophylaxis to mothers in order to prevent early-onset newborn GBS disease. The evaluation piece includes measuring compliance with guidelines before and after implementation of the CDS.
  - b. Participate in discussions on the feasibility of and methods for conducting surveillance for non-invasive GBS disease in order to inform disease burden estimates needed in consideration of vaccine development. Participate in a pilot to conduct surveillance for non-invasive GBS disease if deemed feasible and worthwhile by the ABCs Steering Committee.
  - c. Conduct analyses and studies that provide the evidence base for vaccine development.
  - d. Conduct analyses and studies to assess and update current perinatal prevention guidelines.
3. Pneumococcal-related activities:
  - a. Complete studies of nasopharyngeal colonization with *S. pneumoniae* among children targeted for vaccination with 13-valent pneumococcal conjugate vaccine. Sites with baseline data are encouraged to evaluate the effects of the new pneumococcal conjugate vaccine after it is introduced into the routine infant immunization program.
  - b. Launch studies of nasopharyngeal colonization with *S. pneumoniae* among adults. These studies will assist in evaluating the indirect effects of vaccinating children with PCV13 and the direct effects of vaccinating adults.
  - c. Collect urine specimens that would be used in the development of a serotype-specific pneumococcal urine antigen test. Urine could be collected from invasive cases or non-

invasive pneumococcal cases. Sites may also choose to collect isolates from sputum cultures which would be used to determine the pneumococcal-specific serotype. Collection of specimens would not have to be population-based, but could occur at select facilities.

4. Conduct expanded surveillance for *H. influenzae* neonatal sepsis and *H. influenzae* in pregnant and post-partum women.
5. Participate in special studies evaluating meningococcal disease epidemiology, outcomes (e.g., short- and long-term sequelae), clinical manifestations (including non-invasive disease, such as urethritis) and prevention and control strategies.
6. Legionellosis-related activities:
  - a. Collect urine and respiratory specimens for the evaluation of *Legionella* urine assays under development that 1) Detect non-*Legionella pneumophila* serogroup 1 (Lp1) infections and 2) Detect Lp1 strain types. This would involve collecting paired urine and respiratory specimens from patients at select laboratories (i.e. does not need to be population-based) and would not require additional collection of patient information.
  - b. Conduct a study to understand differences in legionellosis testing practices across hospitals and regions. This would entail measuring the proportion of patients tested for Legionnaires' disease (by urine antigen or respiratory culture) with admitting or discharge diagnoses related to pneumonia at select facilities. Facilities would be selected based on incidence rates in the region (high, medium and low incidence areas would be selected) and hospital characteristics (level of acuity, size, etc.).
  - c. Evaluate novel legionellosis prevention plans (for example cooling tower registration and reporting regulations, introduction of monochloramine into municipal water systems) including the environmental and public health impacts and unintended consequences.
  - d. Conduct a survey of cooling towers or potable water systems to capture information on water safety and legionellosis prevention plans. This may include 1) an evaluation of the presence (or absence) of legionellosis prevention plans, 2) an evaluation of the uptake and costs of recently passed primary prevention guidance: American Society of Heating, Refrigerating, and Air Conditioning Engineers (ASHRAE) 188 Standard - Legionellosis: Risk Management for Water Systems (see: <http://www.cdc.gov/legionella/health-depts/ashrae-faqs.html>), 3) an evaluation of environmental proxies for *Legionella* in water (such as temperature, disinfectant, pH), and/or 4) an evaluation of legionella colonization.
  - e. Explore avenues for incorporation of ASHRAE-188 into local or state licensing/accreditation /inspection of high risk facilities (e.g., hotels, healthcare, longterm care facilities).
  - f. Expand and evaluate a new "toolkit" translating the industry standard (ASHRAE 188) for end users (building owners, operators, local public health, etc.).
  - g. Compare facilities that have had legionellosis outbreaks or colonization to those that have not to identify facility-level environmental and non-environmental risk factors for outbreaks.
  - h. Explore the application of spatial, temporal, or space-time scan statistics to Legionnaires' disease case occurrence to enhance early and rapid detection of clusters, particularly in urban areas affected by high or increasing incidence of Legionnaires' disease.
  - i. Conduct an investigation to identify risk factors for sporadic Legionnaires' disease (i.e. case control study, case series or other study design).
7. GAS-related activities:
  - a. Conduct supplemental surveillance for severe GAS infections. Participating sites will either a) conduct enhanced surveillance for streptococcal toxic shock syndrome (STSS) and necrotizing (NF) using a single page supplemental form; b) conduct enhanced surveillance for NF including collection of special reports (imaging, pathology, or surgical); c) conduct enhanced surveillance for NF using ICD-9/10 codes; or d) combination of options above.

- b. Conduct a study to identify potential human genetic factors associated with severe presentations of GAS such as NF and STSS. After appropriate IRB approvals, participating sites will retrospectively and prospectively contact persons (cases) who have had NF or STSS to obtain consent to enroll them and to mail potential participants saliva collection kits. Genomics work will be completed by external partners.
8. Conduct surveillance for neonatal sepsis in children less than three days old (first 72 hours of life). This would include the optional collection of isolates, with a particular emphasis on gram negative pathogens, such as *E. Coli*.
9. Conduct surveillance and special studies related to antimicrobial resistant infections:
  - a. Establish and implement methods for monitoring potential complications from antibiotic stewardship efforts aimed at reducing unnecessary antibiotic use (e.g., complications from reduced treatment of otitis media).
  - b. Develop and evaluate programs related to appropriate antibiotic prescribing for community-associated invasive and non-invasive infections.
  - c. Participate in developing and conducting risk factor studies related to community-associated antimicrobial-resistant infections.
  - d. Conduct pharyngitis surveillance with associated isolate collection in 1-2 ABCs sites in order to compare GAS *emmtyp*e and resistance profiles between pharyngitis and invasive GAS infections. Where possible, correlation between microbiologic profiles and local antibiotic use patterns will be evaluated.
  - e. Conduct analyses and studies to evaluate the relationship between antibiotic use and resistance.
10. Perform enhanced surveillance for *Bordetella pertussis*:
  - a. Utilize state-based pertussis reporting systems to conduct enhanced surveillance for *Bordetella pertussis* that is characterized by enhanced case ascertainment and augmented data collection.
  - b. Follow-up on all serology-positive pertussis laboratory results in addition to persons PCR and culture positive for *B. pertussis*.
  - c. Collect complete information on clinical course of infection, vaccination history (DTP/DTaP and Tdap), laboratory testing, and other epidemiologic information of interest (e.g., source of infection) as outlined in the case report form instruction sheet. Incorporate new variables as agreed on by CDC, participating sites, and/or the pertussis pathogen committee.
  - d. Collect isolates of *Bordetella pertussis*, when available, and periodically ship to CDC for further laboratory characterization.
  - e. Collect clinical specimens/DNA extracts that are PCR positive for *Bordetella pertussis* (based on specifications provided by CDC) and periodically ship to CDC for further laboratory characterization.
  - f. Utilize state immunization registries and other methods outlined in the case report form instruction sheet to obtain/verify pertussis vaccination history; collect maternal Tdap vaccination history for all infant cases <1 year of age.
  - g. Conduct annual audits of laboratories (commercial, public health and/or hospital laboratories) conducting testing for *B. pertussis* to ensure the identification of all laboratory-confirmed cases of *B. pertussis*.
  - h. Build and strengthen pertussis case finding infrastructure in order to conduct special studies including evaluations of pertussis prevention and control strategies.
  - i. When available, collect epidemiologic information and specimens on other *Bordetella* species (specifically, *B. parapertussis*, *B. bronchiseptica*, and *B. holmesii*).

- j. Participate in routine conference calls with CDC and other participating sites to standardize surveillance methodology and address issues.
11. Prospectively complete expanded medical record review of hospitalized pertussis cases (all ages) identified through Enhanced Pertussis Surveillance to better understand reasons for hospitalization, severity of illness, underlying medical conditions, factors associated with treatment, and outcomes.
  12. Evaluate secondary transmission of *B. pertussis* among household contacts following a 5-day course of Azithromycin post-exposure prophylaxis and duration of pertussis PCR and serology positivity among cases and household contacts.
    - a. Enroll pertussis cases identified through EPS and their household contacts (all ages); household contacts will be recommended PEP based on existing local public health guidelines and as part of routine follow-up and case investigation.
    - b. Conduct study visits at two time points (enrollment and 2-3 weeks post-enrollment) to interview and collect nasopharyngeal and blood samples from consenting, eligible household contacts; conduct an additional telephone interview 2-3 weeks post second visit on a subset of eligible participants.
    - c. Utilize CDC-developed data management systems and routinely transmit study data to CDC.
    - d. Participate in routine conference calls with CDC and other participating sites to discuss progress, monitor enrollment and address methodology-related questions.
    - e. For case-patients and a subset of eligible household contacts, conduct additional specimen collection (nasopharyngeal and blood samples) at up to 7 time points within 1 year post enrollment to assess duration of PCR and serology positivity.
  13. Assess the impact of pertussis vaccines (DTaP and Tdap) as well as other pertussis prevention and control strategies.
    - a. Develop protocol and identify appropriate methodology and sample size in collaboration with CDC and the pertussis pathogen committee.
    - b. Initiate/conduct evaluation as funding permits.
  14. Disseminated gonococcal infection (DGI): Since late 2015, several reports of cases of disseminated gonococcal infection (DGI) in the Atlanta, Georgia metropolitan area suggest that this syndrome may be on the rise in Georgia and possibly elsewhere. While DGI is thought to be a relatively rare condition, a retrospective review of sterile site cultures of *Neisseria gonorrhoeae* from laboratories in a defined surveillance area for DGI would help define the burden of disease and investigate recent trends. Prospectively, collection of sterile site isolates from DGI cases would allow both susceptibility and whole genome sequence testing to better describe DGI epidemiology and molecular epidemiology, and inform prevention and control strategies. Proposals could include a retrospective review of recent DGI cases in a defined population and a plan for prospective surveillance, including collection of isolates, in conjunction with other ABCs activities.
  15. Participate in other activities as determined appropriate and important for the ABCs sites by the ABCs Steering Committee.

## **Evaluation and Performance Measurement**

### **Routine ABCs activities:**

1. Participate in conference calls related to ABCs (i.e.,  $\geq 1$  site participant per call): 90%
2. Identify all labs located within and adjacent to the ABCs surveillance area that test a significant proportion of isolates from surveillance area residents, performed prior to initiating ABCs surveillance and periodically (e.g., every 2-3 years): 100%

3. Complete at least annual audits of all clinical laboratories within the ABCs surveillance area and of labs outside of the surveillance area that test a significant proportion of isolates from residents of the ABCs surveillance area to verify completeness of case ascertainment: 100%
4. Submit surveillance data electronically to CDC (in CDC's secure format) on a monthly basis. Obtain final case counts from the previous year by April of the following year (i.e., April 2017 for 2016 surveillance year). Obtain final case report form data from the previous year by November of the following year (i.e., November 2017 for 2016 surveillance year): 100%
5. Obtain isolates from cases and ship them to CDC laboratories on a specified schedule for serotyping and other laboratory characterization:  $\geq 85\%$
6. Conduct quality checks of case report form data. Sites should select  $\geq 10\%$  of case report forms (stratified by facility and/or region) to be re-abstracted by a second reviewer. An analysis of discrepancies should be used to train staff conducting case report form reviews and recurring issues should be reported to CDC so methods across the network may be improved. These second abstractions may be done throughout the year or batched on a biannual or annual basis. A brief (1-2 page) report of findings should be sent to CDC at the same time final case report data are sent—the November of the following year (i.e., November 2017 for 2016 surveillance year).

Special or optional ABCs studies:

1. Proportion of eligible cases enrolled in special studies, to be determined for each study by ABCs sites and CDC.
2. Proportion of cases and controls enrolled in special studies (e.g., vaccine effectiveness) with provider verified vaccination status reported:  $\geq 95\%$

**Budget Note:** For any/all activities (required and optional) under this appendix, provide one combined budget that incorporates the costs for all activities.

## **ATTACHMENT 1, SECTION C**

### **Foodborne Diseases Active Surveillance Network (FoodNet)**

#### **Background**

The Foodborne Diseases Active Surveillance Network (FoodNet) provides a foundation for food safety policy and illness prevention in the United States. Since 1996, FoodNet has conducted active, population-based surveillance at select US sites for laboratory-confirmed infections of 9 bacterial and parasitic pathogens transmitted commonly through food (*Campylobacter*, *Cyclospora*, *Cryptosporidium*, *Listeria monocytogenes*, *Salmonella*, Shiga toxin-producing *Escherichia coli* (STEC), *Shigella*, *Vibrio*, and *Yersinia*). FoodNet also conducts active surveillance for pediatric cases of Hemolytic Uremic Syndrome (HUS) through a network of nephrologists and infection control practitioners and by hospital discharge data review.

FoodNet is the principal foodborne disease component of the Centers for Disease Control and Prevention's (CDC) Emerging Infections Program (EIP) and is a collaborative project among CDC, state health departments, the United States Department of Agriculture's Food Safety and Inspection Service (USDA-FSIS), and the United States Food and Drug Administration (FDA). FoodNet's activities are guided by four main objectives: 1) Determine the burden of foodborne illness in the United States, 2) Monitor trends in the burden of specific foodborne illness over time, 3) Attribute the burden of foodborne illness to specific foods and settings, and 4) Disseminate information that can lead to improvements in public health practice and the development of interventions to reduce the burden of foodborne illness.

Through FoodNet, state and federal scientists collaborate to monitor trends in enteric illnesses, identify their sources, and implement special studies. FoodNet's major contributions include establishment of reliable, active population-based surveillance of enteric diseases; development and implementation of epidemiologic studies to determine risk and protective factors for sporadic enteric infections; population and laboratory surveys that describe the features of gastrointestinal illnesses, medical care-seeking behavior, frequency of eating various foods, and laboratory practices; and development of a surveillance and research platform that can be adapted to address emerging issues.

#### **Other Nat'l Public Health Priorities and Strategies**

- Healthy People 2020 (<http://www.healthypeople.gov/2020/topics-objectives/topic/healthcare-associated-infections>; EIP FoodNet provides data for measuring progress in reduction in incidence of select infections)
- Department of Health and Human Services Priority Goals (EIP FoodNet provides data for measuring progress in priority goals associated with reducing foodborne illness in the population)
- National Strategy for Combating Antibiotic-Resistant Bacteria ([https://www.whitehouse.gov/sites/default/files/docs/carb\\_national\\_strategy.pdf](https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf))
- CDC Winnable Battles Initiative (Food safety: <http://www.cdc.gov/WinnableBattles/FoodSafety/index.html>)

#### **Purpose**

Conduct active surveillance and research studies aimed at reducing morbidity and mortality due to diseases commonly transmitted by food and understanding sources of these infections.

## **Outcomes**

### ***Provide new knowledge***

Information provided through FoodNet is instrumental in the understanding and control of foodborne illness. Data are used to understand trends in diseases commonly transmitted by food, and monitor those trends over time to assess the impact of food safety control measures. Since many foodborne illness cases go unreported, data from FoodNet help to fill in gap of underreporting and inform estimates of the true burden of foodborne illness in the United States. In an era of changing laboratory diagnostic practices, close contact with clinical laboratories provides information needed to accurately count cases and inform national case definitions. Research studies provide new information on risk factors for foodborne diseases that can inform the development of regulatory and preventive measures aimed at reducing incidence of these infections. Through this EIP activity, grantees will contribute to the estimation of the total number of foodborne illnesses, monitoring of incidence trends, and development of studies to attribute illnesses to specific sources by establishing a system of active surveillance for selected pathogens, and routine, standardized, reporting of data elements. Grantees will contribute information about laboratory testing practices to determine the impact of culture-independent methods on trends in enteric diseases. Grantees will participate in research studies to understand risk factors for selected foodborne diseases, and prevalence of acute gastrointestinal illness in the general population.

### ***Develop staff expertise***

Staff working in FoodNet sites will develop expertise in active surveillance methods, data management, and development of studies to identify risk factors for foodborne illness. In addition, they will establish strong partnerships with clinical laboratories, hospitals, health care practitioners, and academic institutions. Partnerships will provide the foundation of a strong and flexible network upon which to expand surveillance or conduct additional studies.

### ***Control outbreaks of infectious diseases***

Knowledge and skills gained through establishment of an active surveillance system will result in faster and more complete case detection and facilitate faster outbreak detection. Risk factors identified through research studies will facilitate identification of illness sources.

### ***Develop/modify treatment guidelines***

Information gained through active surveillance and research studies will provide knowledge in the control and clinical treatment of infections by pathogens transmitted commonly through food.

### ***Develop/modify intervention recommendations***

Information gained through active surveillance and research studies will be used to inform the development and evaluate the effectiveness of regulations and interventions aimed at reducing the burden of select foodborne illnesses.

## **Strategies and Activities**

### **FoodNet Core Activities: REQUIRED**

1. Conduct active, population-based surveillance for *Salmonella*, *Shigella*, *Campylobacter*, *Listeria*, *Yersinia*, Shiga toxin-producing *E. coli* (STEC), *Vibrio*, *Cryptosporidium*, and *Cyclospora* infections. Obtain complete information on all FoodNet variables for all cases diagnosed by culture or by culture-independent methods. Variables may include (but are not limited to)



demographics, clinical symptoms, hospitalizations, outcome, travel history, and laboratory subtyping information.

- a. Include in the proposal detailed descriptions of the following:
    - i. Process for primary data collection including the number of laboratories that will be included in surveillance, frequency and method of laboratory contact (e.g., electronic, phone, email, or personal visits), approximate percentage of case follow-up conducted at the state and local level, and approximate percentage of cases interviewed for each pathogen.
    - ii. Process for data quality assurance including review and cleaning of data and frequency of data review.
  - b. Submit data electronically to CDC in the format requested monthly by the specified deadline and upon CDC request.
    - i. Have at least two persons trained in process of data transmission to CDC.
    - ii. Perform data quality checks before transmission of data to CDC.
    - iii. Resolve all errors identified through data exception reports or other methods within 3 months.
    - iv. Provide responses to requests for information from CDC within 1 week of receipt of request.
    - v. Adhere to CDC timelines for preliminary and final data closeout.
  - c. Interview all persons with *Listeria*, *Vibrio*, and *Salmonella* serotype Typhi and Paratyphi infections using national case report forms. Interview all STEC cases and obtain the exposure data approved by CSTE position statement 13-ID-01 in 2013.
2. Conduct audits at least annually of every clinical laboratory within the FoodNet surveillance area and of laboratories outside the surveillance area that test a large proportion of isolates from residents of the surveillance area to verify completeness of case ascertainment.
    - a. Include in the proposal detailed descriptions of the following:
      - i. Frequency of audits.
      - ii. Method for audits (e.g., electronic report review, site visit, other).
      - iii. Method and process for revising surveillance procedures to address gaps identified via audits.
  3. Conduct routine standardized surveillance of clinical laboratories in the FoodNet surveillance area and of laboratories outside the surveillance area that test a large proportion of isolates from residents of the surveillance area to ascertain changes in testing practices for FoodNet pathogens. This includes informing CDC of laboratory diagnostic testing changes monthly and submitting information from all labs to CDC once a year and upon request.
    - a. Include in the proposal detailed descriptions of the following:
      - i. Method for capturing changes in diagnostic testing practices.
      - ii. Frequency and mode for laboratory surveys.
      - iii. Process for informing CDC of laboratory diagnostic testing changes.
  4. Conduct active, population-based surveillance for pediatric cases of hemolytic uremic syndrome (HUS). Conduct passive surveillance for adult cases of HUS or thrombotic thrombocytopenic purpura (TTP) that have a history of diarrhea in the three weeks before diagnosis. Surveillance includes the following:
    - a. Complete HUS case report forms A, B, and C.
    - b. Validate pediatric HUS case ascertainment through 1) annual review of hospital discharge data and 2) bi-annual comparison of HUS cases to STEC cases reported through FoodNet active surveillance.
    - c. Submit serum and isolates from HUS patients to CDC, when available.

- d. Submit data electronically to CDC in the format requested by the specified deadline and upon CDC request.
  - i. Have at least two persons trained in process of data transmission to CDC.
  - ii. Perform data quality checks before transmission of data to CDC.
  - iii. Resolve all errors identified through data exception reports or other methods within 3 months.
  - iv. Provide responses to requests for information from CDC within 1 week of receipt of request.
  - v. Adhere to CDC timelines for preliminary and final data closeout.
5. Obtain exposure information on all or a subset of *Campylobacter* and *Salmonella* cases (sample size to be determined by CDC).
  - a. Collect required variables on the case exposure ascertainment (CEA) variable list determined by the FoodNet Steering Committee [[insert weblink to variable list](#)]. Information collected includes food, water, animal, and environmental exposures. Sites may use existing state-based questions if they can be mapped with a high degree of concordance to CEA data elements. However, if states have not been using another questionnaire for several years, they must use the questions as written by the committee. Include in the proposal detailed descriptions of the following:
    - i. Plan for obtaining CEA data.
    - ii. Data collection methods (i.e., interview at local level or state level).
  - b. Place emphasis on interviewing cases for which isolates are available at the state public health laboratory or CDC.
  - c. Store all isolates with CEA information for future characterization.
  - d. Extract and merge CEA data into the routine active surveillance data transmitted to CDC. All available data should be sent monthly.
6. Submit all available isolates or clinical material to a state public health laboratory for confirmation, including speciation or serotyping, when appropriate.
  - a. Provide appropriate identification variables to allow linking of FoodNet data with data from other data systems (e.g., PulseNet, NORS, NARMS).
  - b. For isolates for which whole genome sequence (WGS) information is obtained, the WGS information should be submitted to National Institute of Health's National Center for Biotechnology Information (NCBI) with appropriate metadata so CDC can link isolate information to epidemiologic information. Isolates will also be subtyped by PFGE and patterns uploaded to PulseNet.
  - c. Submit outbreak-associated bacterial isolates and specimens to CDC as specified in the FoodNet surveillance protocol.
  - d. Include in the proposal a plan for reflex culturing of at least a portion of isolates from specimens with a positive culture-independent diagnostic test (CIDT). Reflex culture can occur at a clinical lab, state public health laboratory, or other institution, as resources allow.
7. Maintain flexibility to rapidly respond to changes in core surveillance.
  - a. Be able to quickly (within three months) modify data collection methods and site databases to respond to changes in FoodNet surveillance. Changes may include addition or deletion of variables submitted to CDC.
8. Participate in all FoodNet Steering Committee, Principal Investigator, and Coordinator meetings and conference calls. Participate in working groups, as appropriate. Attend FoodNet Vision Meeting.

### **FoodNet Additional Activities: OPTIONAL**

1. Participate in projects to identify and develop information technology (IT) resources at state and CDC levels to enable transmission of relational data from states to CDC and enable the CDC FoodNet database to capture case-based data.
2. Participate in geospatial analysis projects by geocoding FoodNet cases to census tract and transmitting census tract information to CDC upon request.
3. Participate in projects that examine the relationship between antimicrobial resistance, exposure and clinical features to better characterize infections. For example, this could include participation in a project to obtain data to explain the possible association between certain foods and *E.coli* UTI or the development and implementation of a plan to interview cases to determine risk factors for antimicrobial resistance.
4. Participate in project(s) to assess feasibility of expanding surveillance activities to other pathogens or co-infections.
5. Arrange for whole genome sequencing (WGS) of selected pathogens isolated in 2016 (pathogens to be selected by the FoodNet Steering Committee) in the state public health lab, another public health lab, or CDC. Obtain clinical and epidemiologic data on all patients whose isolates are tested by WGS. Work with CDC to build capacity to link sequence information with clinical and epidemiologic (including exposure) data.
  - a. Submit all sequence data to NCBI with appropriate metadata using identifiers that link the isolate information to PulseNet entries.
  - b. Extract exposure data from site databases and transmit to CDC. (CDC will develop timeframes and a mechanism for transmission.)
  - c. Ask clinical labs in the catchment area to follow procedures outlined by the site so that any specimens that are positive by a culture independent test are cultured and then sequenced.
6. If state laws allow, explore agreements to allow CDC and other sites to assist with workload for surveillance or special studies when existing resources are insufficient to maintain best practices (e.g., during a major outbreak investigation). For example, one site may assist another with interviews while that site is busy with outbreak response, state laboratories may assist others with reflex culturing of positive CIDT reports or performing WGS on selected isolates.
7. Participate in norovirus working group activities including estimation of norovirus community incidence through surveillance in select outpatient clinics with known population catchments, and norovirus testing of callers to foodborne illness complaint hotlines.
8. For states that do not routinely interview all FoodNet cases, develop and implement plan for interviewing all cases to assess international travel, clinical symptoms, outcome, and exposure information in addition to standard variables and sending information to CDC.
9. Participate in projects to help achieve FoodNet's goal of providing data to attribute the burden of foodborne illness to specific foods and settings
10. Participate in other activities as determined to be appropriate for FoodNet sites by the FoodNet Steering Committee.

*NOTE: In addition to core EIP FoodNet activities, FoodNet sites are expected to participate in PulseNet, National Outbreak Reporting System (NORS), and National Antimicrobial Resistance Monitoring System (NARMS) human isolate surveillance activities. However, funding for these activities is provided through non-EIP mechanisms. Sites should request funding for PulseNet, NORS, and NARMS human surveillance activities through the Epidemiology and Laboratory Capacity for Infectious Diseases ELC cooperative agreement.*

## **Evaluation and Performance Measurement**

### **Quantitative measures:**

*Sites are expected to meet performance metrics as outlined below. Baseline values for each metric will be established for each site based on their current FoodNet data (existing FoodNet sites) or passive surveillance data (new FoodNet sites). Metrics will be calculated twice a year and site performance will be assessed based on continued improvements to metrics. Baselines will be re-evaluated each year.*  
**(next page)**

	Active Surveillance	HUS
<b>Surveillance</b>		
<b>Number (%) cases with information for:</b>		
Age	EP	X
Sex	EP	X
Race	EP	
Ethnicity	EP	
Hospitalization	EP	X
Outcome	EP	X
Diarrhea	EP	X
Bloody diarrhea	EP	
Fever	EP	
Interview	EP	
International travel	EP	
Outbreak-association	EP	
BioID (i.e., whether or not case was culture-confirmed)	EBP	
CIDT Test Type	EP	
<b>Number (%) of cases:</b>		
With national case report forms submitted	L, ST, V	
<b>Number (%) of outbreak-associated cases with:</b>		
NORS ID number	EP	
Outbreak type	EP	
<b>Number (%) of CEA-eligible cases:</b>		
With a CEA interview (defined as having any 1 CEA variable)	C, SE	
With 10 representative* exposure variables completed	C, SE	
With any 40 exposure variables completed	C, SE	
<b>Number (%) of HUS cases with:</b>		
Mode of ascertainment		X
Complete information on STEC testing		X
STEC that link to STEC cases in active surveillance		X
Completion of hospital discharge data review <=2 years from onset		X
<b>Number (%) isolates:</b>		
Received at state public health labs	EBP	X
With serotype/species information	EBP	
<b>Number (%) of specimens:</b>		
From positive CIDTs that are received at state public health laboratory	EBP	
<b>Number (%) of:</b>		
Cases with data exceptions (based on quarterly exception reports)	EP	X
<b>Special Studies</b>		
<b>Number (%) of:</b>		
"Eligible" (i.e., not excluded per study protocol) cases enrolled	EP	X
Isolates from eligible cases submitted to CDC (appropriately labeled per study protocol)	EP	X

EP= Each FoodNet pathogen; EBP=Each FoodNet bacterial pathogen; C=*Campylobacter*; L= *Listeria*; SE=*Salmonella* Enteritidis; SO=*Salmonella* serotypes other than SE; ST= *Salmonella* Typhi and *Salmonella* Paratyphi; V=*Vibrio*

**Qualitative Measures:**

*Sites are expected to address how they are complying with the following metrics in their continuing renewal applications every year:*

- Timeliness
  - Adhere to CDC timelines for changes to data elements.
  - Meet deadline(s) for preliminary and final data closeout.
  - Meet deadline(s) for submission of national case report forms.
- Process
  - Have a documented procedure in place for case audit.
  - Have a documented procedure in place for routine review and cleaning of data before transmission to CDC.
  - Have at least two persons trained in process of data transmission to CDC.
- Data Quality
  - Perform data quality checks before transmission of all data to CDC.
  - Resolve all errors identified through data exception reports or other methods within 3 months.
  - Verify data elements from a random subset of cases, as needed. (Number of cases to be determined by CDC based on case volume).
- Leadership
  - Be an active participant in steering committee, principal investigator, coordinator, and working group meetings/calls.
  - Be an active participate at Vision Meeting.

Both quantitative and qualitative measures may be discussed during coordinator or principal investigator calls or meetings, Vision Meetings, and site visits.

**Budget Note:** For any/all activities (required and optional) under this appendix, provide one combined budget that incorporates the costs for all activities.

## Influenza

### Background

Influenza viruses circulate worldwide each year, causing substantial illness and severe complications including hospitalization and death. In addition, novel strains of influenza virus emerge from time to time, leading to global influenza pandemics. Influenza surveillance programs are crucial for monitoring the timing, burden and severity of seasonal influenza, characterizing circulating virus strains, and describing changes in the epidemiology or risk factors associated with influenza virus infection. Surveillance data may also be used to plan for annual influenza virus strain selection, to alert the public about the intensity and magnitude of an epidemic, and to evaluate the effectiveness of intervention programs. In the event of an influenza pandemic, surveillance programs are essential for guiding response efforts and assisting with resource prioritization.

The Emerging Infections Program (EIP) was established in 1995 to provide a national resource for infectious disease surveillance and response, conduct applied epidemiologic and laboratory research, identify measures to prevent and control emerging infectious diseases, and strengthen national public health infrastructure. In response to reports of elevated rates of pediatric influenza hospitalization and deaths during the 2003–04 influenza season, the EIP principal investigators initiated laboratory-confirmed influenza hospitalization surveillance among persons aged  $\leq 17$  years. During the 2005–06 influenza season, in response to the threat of avian influenza and as part of pandemic planning, EIP sites expanded surveillance activities to include adults hospitalized with laboratory-confirmed influenza so that all ages hospitalized with influenza were represented. During the 2009 pandemic, additional states were added as part of the Influenza Population-Based Hospitalization Surveillance Project (IHSP) to enhance existing surveillance through a cooperative agreement with the Council of State and Territorial Epidemiologists (CSTE). Together the EIP and IHSP sites constitute the Influenza Hospitalization Surveillance Network (FluSurv-NET) which conducts population-based surveillance for children and adults hospitalized with influenza.

Influenza hospitalization surveillance uses hospital laboratory data, admissions information, infection control practitioner databases/logs, or review of reportable conditions databases to identify cases. Cases are residents of pre-identified catchment areas with laboratory-confirmed influenza infection who are hospitalized during an influenza season. Laboratory testing for influenza is ordered at the discretion of clinicians providing patient care. Therefore, efforts to understand clinician testing practices are necessary for some FluSurv-NET analyses. Laboratory confirmation is defined by a positive result from viral culture, direct or indirect fluorescent antibody staining, rapid antigen testing, or real-time reverse transcriptase polymerase chain reaction (RT-PCR). Medical chart reviews of all cases are conducted to collect clinical and epidemiologic information including patient demographics, underlying medical conditions, influenza vaccination, antiviral treatment, clinical outcomes during hospitalization, and hospital discharge diagnoses. Influenza vaccination status is obtained through a hierarchical review of sources including medical chart, vaccination registries, provider records, and lastly by interview of patient or proxy.

During each influenza season, core data collected through FluSurv-NET (including surveillance site, hospital admission date, patient date of birth, type of influenza test performed, and type of influenza virus) are reported weekly to the CDC influenza division with a median lag time of 7 days between date of a positive influenza test result and reporting to CDC. FluSurv-NET primarily produces age-specific

rates of laboratory-confirmed hospitalizations in the United States, calculated using population denominators from the most recent census data available for each surveillance county catchment area. These unadjusted rates are made available to the public weekly through a web-based application called Fluview and can be utilized to provide near real-time information about the current influenza season and compare rates across seasons and age groups.

FluSurv-NET data also provides a platform for timely assessments of seasonal influenza severity and national disease burden estimates. Disease burden estimates depend on modeling that accounts for age-specific influenza testing practices and underreporting of cases. Disease burden estimates, in addition to annual vaccine effectiveness and coverage estimates, are critical for annual estimates of vaccine averted hospitalizations. FluSurv-NET data has also been used for special studies to evaluate influenza antiviral use (which is recommended for all patients hospitalized with influenza) and vaccine effectiveness. More recently, as a result of an initiative to geocode all data, FluSurv-NET data has been used to explore the relationship between socioeconomic and other disparities and influenza-associated hospitalization. FluSurv-NET has and will continue to serve as a platform to address various epidemiologic questions of public health relevance as they arise. A key feature of FluSurv-Net is its flexibility to respond to public health emergencies. During the 2009 pandemic, FluSurv-NET data was critical for rapid monitoring of the pandemic.

### **Other Nat'l Public Health Priorities and Strategies**

FluSurv-NET data has been used to formulate national policy recommendations developed by the Advisory Committee on Immunization Practices (ACIP) and to determine the real-world impact of antiviral treatment and vaccination through antiviral and vaccine effectiveness studies. CDC is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2020" (<http://www.healthypeople.gov/2020/topicsobjectives2020/default>) and to measuring program performance as stipulated by the Government Performance and Review Act (GPRA). This EIP Influenza activity is in alignment with the "Healthy People 2020" priority focus area, Immunization and Infectious Diseases and HHS Strategic Plan Goals and Objectives: Goal 3 - Advance the Health, Safety, and Well-Being of the American People: <http://www.hhs.gov/about/strategic-plan/strategic-goal-3/index.html>. FluSurv-NET also serves as an emergency response resource in the event of an influenza pandemic.

### **Purpose**

Implement population-based surveillance to provide near real-time weekly rates of laboratory-confirmed influenza-associated hospitalizations during each influenza season. Data will be collected to 1) describe demographic and clinical characteristics and clinical course and outcomes among patients hospitalized with influenza, 2) allow annual estimation of disease burden, and 3) assess uptake and effectiveness of vaccination and antiviral treatment. Data will be used to determine the timing and severity of influenza seasons and to guide future influenza prevention and control strategies. Special studies will be conducted to better understand laboratory practices and evaluate prevention strategies in high-risk populations.

### **Outcomes**

#### ***Provide new knowledge***

Surveillance for influenza-associated hospitalizations along with special studies are intended to enhance our understanding of the burden and severity of influenza, to assess risk factors and outcomes associated with influenza, and to evaluate prevention strategies. This knowledge will be



used to inform national policy and help guide future prevention and control efforts as well as pandemic planning.

### ***Develop staff expertise***

Site personnel will develop expertise in the epidemiology of influenza as well as clinical disease course and management. Site personnel will also develop and over time, hone skills to conduct case finding, medical record abstraction using varied electronic and paper medical record systems, and data entry and management, such that influenza hospitalization rates and other measures will be produced using complete and accurate data.

### ***Control outbreaks of infectious diseases***

The surveillance infrastructure will assist health departments and CDC in detection and control of outbreaks of influenza. Sites will have the ability to quickly modify data collection tools and site databases, and maintain flexibility to rapidly respond to changes in core surveillance in response to a novel influenza A virus epidemic of pandemic potential.

### ***Develop/modify treatment guidelines***

FluSurv-NET data will be used to help develop and evaluate prevention and treatment guidelines produced by the ACIP, including influenza vaccine recommendations and antiviral treatment guidance.

### ***Develop/modify intervention recommendations***

FluSurv-NET data will be used to estimate the annual influenza vaccine averted burden and to evaluate the impact of guidance on empiric antiviral treatment in high-risk patients with acute respiratory illness. FluSurv-NET data will also be used to evaluate the impact of influenza testing on both antiviral and antibiotic use in patients with acute respiratory illness with and without influenza.

## **Strategies and Activities**

### **Influenza-associated hospitalizations surveillance: REQUIRED**

1. Conduct active, population-based surveillance for laboratory-confirmed influenza-associated hospitalizations among children and adults during the influenza season (typically beginning on October 1, and ending on April 30 of the following year).
  - a. Clearly identify all hospitals in which residents of the catchment areas are hospitalized so that population estimates can be obtained for rate calculations on an annual basis.
    - i. Identify all hospitals within the catchment area. Estimate the number of acute respiratory illness (ARI)-coded hospitalizations that occur at each hospital within the catchment area and calculate the hospital market share by age group (percent of catchment area residents hospitalized with ARI at each hospital within the catchment area). CDC to provide technical assistance as needed.
    - ii. Estimate the proportion of catchment population hospitalizations that occur outside of the catchment area.
  - b. Utilize hospital laboratories, admission/discharge information, infection control practitioner logs/databases, and review of reportable conditions databases to identify influenza cases.
  - c. Conduct periodic (at least annual) audits of all clinical, reference, commercial, and public health laboratories within the FluSurv-NET surveillance area to verify completeness of influenza case ascertainment.
  - d. Complete a standardized case report form for all identified cases using data obtained from laboratory records and medical chart review.

2. Enter case data into a standardized data collection database provided by CDC or send de-identified data extracts that match the format of the standardized database.
  - a. Submit data electronically to CDC (in an agreed upon secure format) by the specified deadline and upon CDC request.
  - b. Provide timely responses to reports and requests for information to assist in preliminary & final analyses, reports, and data close-outs.
3. Monitor influenza testing practices among all, or a majority of hospitals that fall within the catchment area by:
  - a. Determining the number of influenza cases submitted by each hospital each year.
  - b. Determining the number of ARI-coded hospitalizations by age group during each influenza season (same as 1.a.i above).
  - c. Estimate the ratio of influenza testing to ARI hospitalizations each year for each hospital (number of influenza positive cases/number of ARI hospitalizations).
    - i. Influenza testing of patients hospitalized with ARI at participating hospitals should be encouraged.
    - ii. Hospitals with a relatively low ratio of influenza positive cases to ARI hospitalizations can be identified so that corrective steps can be taken to improve surveillance.
  - d. Participate in the influenza disease burden project every 1-3 years as determined by discussions with CDC.
4. Determine influenza A subtype and influenza B lineage on at least 20% of surveillance specimens each year. Although determination of influenza subtype is not required for all cases, it is highly desirable and recommended.
  - a. Methods for obtaining subtype information or for obtaining specimens to send to public health laboratories for subtype/lineage determination should be described in the proposal.
  - b. Description of a sampling method used to obtain subtype/lineage information on specimens should be submitted to CDC in writing at the beginning of each influenza season and updated if any changes are made.
    - i. Sampling only from hospitals with a large market share or hospitals with full influenza subtyping capabilities is acceptable.
    - ii. Convenience samples are discouraged; however, if only convenience samples are available, this should be clearly indicated. In this instance, other methods to estimate subtype-specific rates will be determined in collaboration with CDC.
  - c. Sites should ensure that subtype information is linked to patient clinical records
5. Early in the season, due to poor specificity of rapid influenza diagnostic tests (RIDT), confirmation of RIDT test results with RT-PCR should be encouraged.
6. Perform geocoding and linkage to US Census data using standardized methods for all cases identified as part of surveillance activity.
7. Ascertain influenza-associated deaths that may have been missed during hospitalization and /or occurred within the first 30 days of hospital discharge. Strategies for ascertaining death after hospital discharge should include:
  - a. Matching the dataset of hospitalized patients captured through regular surveillance with that from the U.S. Social Security Death Index (SSDI) online database to identify death-cases missed by surveillance and/or deaths occurring after hospital discharge.
  - b. Based on the local Vital Statistics/Death certificates available, obtain information about place of death and cause-of-death among those identified through SSDI data match.

**Other core activities related to Influenza-associated hospitalization surveillance: REQUIRED**

1. Participate in scheduled influenza-specific Principal Investigator, Surveillance Officer, and influenza working group conference calls.
2. Obtain influenza vaccination status through medical chart review, verification of state vaccination registries, inquiries to primary care providers or long term care facilities where a case resided prior to hospitalization, or telephone interviews with the case or proxy.
3. Participate in data quality assurance activities as follows:
  - a. Correct or address all errors identified in weekly data cleaning reports.
  - b. Validate a subset of cases to ensure that chart reviewers are consistently recording information on case report forms.
4. Conduct laboratory surveys to describe diagnostic tests used at participating laboratories every 1-3 years as needed (these surveys may be coordinated with other surveillance programs).
5. Maintain flexibility to rapidly respond to changes in core surveillance in response to a novel influenza A virus epidemic of pandemic potential.
  - a. Sites must have the ability to quickly modify data collection tools and site databases to respond to changes in surveillance.
  - b. Changes may include extensive clinical data collection to assess severity of the new epidemic/pandemic; identification of sentinel hospitals where prospective, systematic testing for influenza can be performed at the emergency department or elsewhere in the hospital unit to identify patients hospitalized with severe novel influenza; monitoring influenza vaccine adverse events; and timely report a set of demographic and clinical data to CDC in order to inform stake holders' decision making and public health interventions early in the epidemic/pandemic.

**Interested sites may propose one or more of these enhancements to influenza surveillance activities: OPTIONAL**

For all special studies, the protocol, data collection instruments, data dictionary, and data entry software will be developed in collaboration with CDC and participating sites so that they may be standardized. Special studies may require IRB approval.

**Influenza**

1. Use electronic data to evaluate the use of influenza testing, antiviral treatment, and antibiotic treatment among patients hospitalized with acute respiratory illness (ARI).
  - a. Compare antiviral treatment among patients hospitalized with a positive clinician-ordered influenza test (FluSurv-NET) to antiviral treatment among all ARI cases.
  - b. Compare antibiotic use among patients hospitalized with ARI with influenza testing, and with positive influenza testing, compared to those without influenza testing.
  - c. Explore the impact of other laboratory testing (e.g., procalcitonin) on influenza testing, antiviral use and antibiotic use.
  - d. A plan to retrospectively access data on all patients hospitalized with ARI using electronic medical records (clinical, administrative and pharmacy level data) should be described.
  - e. Data elements of interest will include patient's age, date of birth, race, ethnicity, date of hospital admission, date of hospital discharge, presence of CDC defined high risk conditions for influenza complications (specific ICD codes), clinical outcomes during hospitalization, influenza antiviral treatment information, antibiotic treatment information, and laboratory data.

2. Use FluSurv-NET data for estimation of influenza vaccine effectiveness among pregnant women using a test negative design (cases are RT-PCR influenza positive and comparison group is RT-PCR influenza negative).
  - a. Using data from one hospital (or a small number of hospitals), identify influenza PCR test negative cases among pregnant women.
  - b. After appropriate human subjects criteria are met, collect core information (vaccination status, underlying medical conditions, ICD 10 discharge diagnosis codes, and outcomes) on patients with a negative influenza PCR test.
  - c. Estimate vaccine effectiveness among pregnant woman hospitalized with and without influenza based on influenza test results in collaboration with CDC.
  - d. To assess for biases that may be introduced if clinician testing is based on vaccination status, obtain aggregate data to compare the proportion of ARI hospitalizations with self-reported influenza vaccination who did and did not receive influenza testing.
3. Participate in studies to better assess clinical outcomes among patients hospitalized with influenza through enhanced chart review for complications including pneumonia (review of chest radiology, ICU course, need for pressor support, renal dialysis, etc.), cardiac and other non-respiratory complications (acute myocardial infarction, congestive heart failure, stroke).
4. Participate in studies to better assess severity of influenza disease at admission through collection of vital sign data. These data can be used to help account for biases in admission practices related to the presence of underlying conditions.
5. Participate in studies to better understand the sensitivity and specificity of rapid tests through submission of confirmatory testing results (including positive and negative results) to CDC.
6. Participate in studies to assess the association between hospital infection control policies related to influenza test results and the incidence of hospital-acquired influenza.
7. During a season with circulation of oseltamivir-resistant viruses, collect a sample of specimens from patients for antiviral resistance testing (using high through-put assays such as pyrosequencing). Specimens can be sent to CDC, or a CDC identified laboratory, for testing.

### **Respiratory Syncytial Virus (RSV)**

RSV is a major cause of lower respiratory illness. Longitudinal studies have indicated that virtually all children appear to be infected by 2 years of age, and reinfections can occur throughout adulthood. While RSV disease burden in older children and adults is considered lower than in infants and young children, there is a growing body of evidence that the burden of RSV among older adults is substantial. Currently, there are no antivirals or vaccines available; however, there are over 50 vaccine products in development, with an RSV vaccine targeting older adults  $\geq 60$  years in a phase 3 trial with potential FDA licensure as early as 2017. Establishing the pre-vaccine burden of RSV disease among older adults is an essential component for evaluating the evidence for vaccine use in this age group, as well as the vaccine effectiveness and impact post-licensure. In the near future, surveillance activities will need to be expanded to include maternal, infant, and pediatric populations when vaccine use in these groups becomes closer to licensure.

To assess the use of the FluSurv-NET platform for long-term RSV surveillance, potential activities include, but are not limited to, the following:

1. Among laboratories at participating surveillance sites, conduct a laboratory survey to gather information on RSV diagnostic testing, including use of rRT-PCR, antigen detection, rapid diagnostic assays (usually available commercially), viral culture, etc.
2. Examine RSV testing practices among adult and pediatric physicians at participating surveillance hospitals. Data would include which patients are tested, specimen type, and which laboratory tests are ordered (including for other respiratory viruses in addition to influenza and RSV).
3. Use electronic data to evaluate the use of RSV testing among persons hospitalized with acute respiratory illness (ARI) among different age groups and clinical syndromes.
4. Use electronic data to evaluate hospital-associated RSV coded deaths among different age groups.
5. Implement active, laboratory-based RSV surveillance among adults (e.g., elderly, immunocompromised, underlying medical conditions, pregnant women, etc.) and evaluate feasibility of such surveillance to establish burden and evaluate vaccine impact.
6. Implement active, laboratory-based RSV surveillance among children <5 years of age and evaluate feasibility of such surveillance to establish burden and evaluate vaccine impact.

For all RSV special studies, the protocol, data collection instruments, data dictionary, and data entry software will be developed in collaboration with CDC and participating sites so that they may be standardized. Special studies may require IRB approval.

### **Evaluation and Performance Measurement**

1. Principle Investigator (PI) and Surveillance Officer (SO) participation on conference calls related to this activity:  $\geq 1$  site participant per call for  $\geq 90\%$  of calls
2. Participation by at least one site representative on annual webinar training activity
3. Influenza SO attendance at an annual surveillance officer meeting:  $\geq 1$  site participant
4. Influenza PI attendance at an annual program meeting:  $\geq 1$  site participant
5. Weekly Transmission of data to CDC which involves collection and regular reporting of a minimum set of variables for each case (case ID, hospital admission date, evidence of influenza test result, sex, and date of birth or age):  $\geq 95\%$  data transmissions on time (i.e., data posted by weekly deadline)
6. Case data abstraction into a CDC-approved database and data transmission to CDC through established mechanisms and according to established timelines:
  - a. Collection of complete case report forms for influenza cases:  $\geq 95\%$
  - b. Submission of complete influenza case counts and case report form data to CDC according to pre-established timelines: 100%
7. Address all case report form errors (based on weekly error reports) by data close-out deadline, to be determined by CDC in consultation with sites:  $\geq 95\%$
8. Completion of audit to ensure complete resident influenza case ascertainment, according to established protocols, each year: 100%
9. Documented evidence that the site has engaged participating hospitals and their staff (e.g., infection control practitioners, medical records staff) in increasing ascertainment of potential influenza cases and use of RT-PCR testing.
10. Geocoding of  $>90\%$  of influenza hospitalized cases and transfer of census tract data to CDC (or correspondent data on socioeconomic variables).
11. Ascertainment of death should be 100% completed for the previous season and data should be sent to CDC through designated platform.
12. Proportion of influenza cases with subtype or lineage determination:  $\geq 20\%$

13. Participation in all surveys (laboratory, hospital) related to surveillance: 100%

Special or optional FluSurv-NET studies:

Data from special studies submitted to CDC in a timely fashion and 100% of data delivered by set deadlines.

**Budget Note:** For any/all activities (required and optional) under this appendix, provide one combined budget that incorporates the costs for all activities.

**Healthcare-Associated Infections – Community Interface (HAIC)**

**Background**

Healthcare-associated infections (HAIs) and other healthcare-related adverse events continue to cause significant morbidity and mortality among patients treated in U.S. healthcare institutions and add billions of dollars to healthcare costs. Prevention of these infections is a federal government priority, as outlined in the “National Strategy for Combating Antibiotic-Resistant Bacteria” ([https://www.whitehouse.gov/sites/default/files/docs/carb\\_national\\_strategy.pdf](https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf)). Recent advances in the understanding of the burden and epidemiology of certain HAIs in the United States have been gained through surveillance and applied public health research conducted through the EIP’s Healthcare-Associated Infections Community Interface (HAIC) activity. As the epidemiology of HAIs continues to be better understood, more effective prevention measures can be identified and implemented. The mission of the EIP HAIC activity is to promote patient safety and healthcare quality through:

- 1) Evaluation of the epidemiology and public health effects of healthcare-associated infections to provide a better understanding of emerging pathogens and populations at risk; and
- 2) Exploration of innovations to improve national surveillance and evaluation of healthcare-associated infection prevention and control strategies.

See also: [http://wwwnc.cdc.gov/eid/article/21/9/15-0508\\_article](http://wwwnc.cdc.gov/eid/article/21/9/15-0508_article)

**Other Nat’l Public Health Priorities and Strategies**

- Healthy People 2020 (<http://www.healthypeople.gov/2020/topics-objectives/topic/healthcare-associated-infections>; EIP HAIC provides data for measuring progress in achieving HAI reductions)
- Government Performance and Results Act (EIP HAIC provides data for measuring progress in achieving HAI reductions)
- National Strategy for Combating Antibiotic-Resistant Bacteria ([https://www.whitehouse.gov/sites/default/files/docs/carb\\_national\\_strategy.pdf](https://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf), see Objective 2.2)
- CDC Winnable Battles Initiative (Healthcare-associated infections: <http://www.cdc.gov/winnablebattles/healthcareassociatedinfections/index.html>)

**Purpose**

Implement population-based surveillance and special projects to reduce HAI morbidity and mortality. The two HAIC Activity categories of work are: 1) population-based surveillance for specific pathogens or infections; and 2) special projects, including HAI and antimicrobial use prevalence surveys. Population-based surveillance monitors the incidence of infections due to healthcare-associated pathogens at the population level to track changes over time, identify at-risk populations and estimate disease burden. Special projects are limited-duration projects that address specific HAI-related public health questions..

**Outcomes**

***Provide new knowledge***

- Increased understanding of: 1) the national burden of healthcare-associated infections, particularly those occurring outside of acute care hospitals, and antimicrobial use in healthcare; 2) populations impacted by and risk factors for healthcare-associated infections and antimicrobial resistance; and 3)

changes in the epidemiology of healthcare-associated infections or pathogens and antimicrobial use over time.

***Develop capacity***

Increase in the number, size and variety of healthcare facilities and networks engaged with state health departments in conducting surveillance and/or prevention activities focused on reducing healthcare-associated infections and improving antimicrobial use.

***Develop/modify treatment guidelines***

Increase in the proportion of antimicrobial use in healthcare facilities that is considered appropriate.

***Develop/modify intervention recommendations***

Decrease in the incidence of disease due to major healthcare-associated pathogens, particularly antimicrobial-resistant pathogens.

**Strategies and Activities**

For all projects (both required and optional) described below, the applicant must demonstrate in their proposal, infrastructure that is conducive to performing innovative and flexible population-based surveillance activities, strong relationships with multiple types of healthcare facilities (e.g., acute care hospitals, nursing homes, etc.) in the catchment area, as well as excellent relationships with local healthcare-related organizations (e.g., local chapters of the Association of Professionals in Infection Control and Epidemiology). Willingness and ability to change or rotate pathogens under surveillance as frequently as every 2-3 years for pathogen-specific, population-based surveillance activities should be described in the proposal. Because HAIC surveillance projects include an isolate collection component, the applicant should demonstrate strong relationships with clinical laboratories serving the catchment area. Many established HAIC projects require local Information Technology (IT) infrastructure to host applications and close communication with CDC IT staff for application installation and maintenance. The applicant should demonstrate that these relationships are in place or could be easily established. The applicant should also demonstrate the ability to utilize other data sources pertinent to HAI epidemiology within the state health department, such as vital records data. Lastly, the applicant should demonstrate that site leadership (principal investigator[s] and other managerial and scientific leadership) is available and fully accountable for ensuring the success of each HAIC project and assuring satisfactory performance of HAIC staff and collaborations with the organizations and networks mentioned above. The principal investigator should take responsibility for data quality control, analysis and interpretation. In addition, the principal investigator must be prepared to be actively engaged in working with CDC scientists and other awardees to create common protocols and project methods across sites, and actively participate in leadership calls and the annual HAIC Steering Group in-person meeting.

The applicant must apply to participate in both of the “required” projects: 1) population-based surveillance for one or more of the targeted pathogens; and 2) the required special project. The applicant may apply for any of the optional projects.

The applicant should plan for travel of appropriate personnel to a minimum of two meetings per year: the HAIC Steering Group annual meeting and the annual HAIC Surveillance Officers meeting. Depending upon projects for which the applicant is applying, additional meeting attendance (e.g., for training) may be needed. Sites should consider requesting additional support for 2-3 staff members to attend one national healthcare-associated infections meeting annually.



Sites applying to conduct surveillance for multiple pathogens/HAIs may utilize the same surveillance catchment area for each pathogen/HAI, but this is not necessary. When applying for funding for other HAIC activities, particularly optional activities, sites should consider the potential advantages associated with engaging healthcare facilities outside of the usual catchment areas utilized for population-based surveillance projects such as the CDI surveillance project.

## **REQUIRED ACTIVITIES**

### **HAIC Required Activity Project Category #1: Population-based surveillance**

Sites must apply for **at least one** of the population-based surveillance projects below (i.e., each applicant must apply to conduct either 1) *Clostridium difficile* infection surveillance, 2) the Multi-site Gram-negative Surveillance Initiative, or both). Sites currently participating in these projects are encouraged to apply to continue participation.

#### 1. *Clostridium difficile* Infection (CDI) Surveillance:

Conduct active, population-based, laboratory surveillance for *Clostridium difficile*. Multi-site surveillance includes obtaining laboratory reports of all positive *C. difficile* test results from clinical, reference and commercial laboratories serving the surveillance catchment population. Laboratory reports should include the type of the *C. difficile* positive assay (e.g., GDH, EIA, PCR, etc). Surveillance activities also include completion of case report forms for incident CDI cases, ascertainment of community- vs. healthcare-associated cases, collection of stool specimens positive for *C. difficile* based on toxin or molecular assay from selected laboratories, shipment of these stool specimens to a designated CDI surveillance reference laboratory for culture (*C. difficile* isolates are then sent from the reference laboratory to CDC), and collection of treatment information for incident CDI cases.

- Submit a sample of positive *C. difficile* stool specimens to a designated CDI surveillance reference laboratory. Because of the volume of stool samples that are expected, describe in the proposal the capability for selecting a representative sample of stool specimens for shipment to a designated CDI surveillance reference laboratory for culture. Adhere to protocol timelines for collection and shipping of stool specimens for processing.
- Sites with larger surveillance catchment areas (i.e., > 1.0 million population) should consider utilizing a sampling scheme of CDI cases stratified by age and gender developed by CDC in collaboration with the CDI sampling working group.
- Sites may apply for funding to bolster stool specimen collection and submission to the reference laboratory. If so, describe approaches to ensuring adequate support is provided to clinical and other laboratories serving residents of the catchment area to optimize specimen collection. Work may include enhanced stool specimen collection (e.g., more representative of geographic area).
- Geocode a subset of CDI cases as determined by the CDI Pathogen Group, using a standardized methodology developed by the EIP geocoding working group.

Conduct the following activities, according to HAIC CDI protocols, to ensure complete case ascertainment and to validate data collection efforts:

- Conduct an annual laboratory assessment among all clinical, reference and commercial laboratories serving surveillance catchment population to ascertain changes in testing practices for *C. difficile*. This should be conducted annually as determined by the CDI surveillance working group.

- Conduct a long-term care facility (LTCF) assessment every year to ensure that all laboratories serving LTCFs in catchment area are captured in the surveillance.
  - Conduct a physician/outpatient clinic provider assessment as frequently as determined by the CDI Pathogen Group; the purpose is to ensure that all laboratories serving outpatient providers in the catchment area are captured in the surveillance.
  - Conduct periodic (ideally twice a year) audits of all laboratories within the CDI surveillance area and of laboratories outside of the surveillance area that test stool specimens from residents of the CDI surveillance area to verify completeness of case finding.
  - Develop a process to utilize National Healthcare Safety Network (NHSN) CDI LabID event data reported by catchment area healthcare facilities (also see section on MRSA surveillance). Most U.S. hospitals began reporting these data in 2013, and access to CDI LabID event data can be obtained either through the NHSN group user function via rights assigned to the state health department or through other means. Sites should plan to use NHSN CDI LabID event data for comparison purposes with EIP population-based surveillance data.
  - Utilize the common databases developed by CDC for case tracking and reporting.
  - Provide timely responses to CDC CDI staff requests for information to assist in preliminary and final analyses (including for special studies), reports, and data close-outs.
2. Surveillance for carbapenem-resistant *Enterobacteriaceae*, *Acinetobacter* spp. and *Pseudomonas aeruginosa* - the Multi-site Gram-negative Surveillance Initiative (MuGSI):

Conduct active, population-based surveillance for selected carbapenem-resistant Gram-negative bacteria. Applicants may propose to conduct surveillance for one or more of the following: 1) selected carbapenem-resistant *Enterobacteriaceae* (CRE: *Escherichia coli*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca*); 2) carbapenem-resistant *Acinetobacter baumannii* (CRAB); or 3) carbapenem-resistant *Pseudomonas aeruginosa* (CR-PA). The specific MuGSI organisms under surveillance could change over time. Surveillance involves collection of isolates from sterile sites and urine. Collection of isolates from additional specimen types (e.g., sputum) for some organisms (e.g., *P. aeruginosa*) should be considered.

Active surveillance includes:

- Identification of potential cases through review of laboratory reports, using established protocols, for cases meeting project case definitions (see below), with particular focus on community-onset cases.
- Completion of standardized case report forms through review of medical records.
- Demonstration of the ability to link MuGSI cases to state vital records data to describe mortality after hospital discharge for all MuGSI cases identified.
- Systematic collection of a subset of isolates and shipment to CDC laboratories based on an established shipping schedule. Sites may apply for funding to bolster isolate collection, processing, and submission to CDC. Describe in the proposal approaches to ensuring adequate support is provided to laboratories that process specimens from catchment area residents to optimize isolate collection. Work may include enhanced isolate collection (e.g., more representative of geographic area, more representative of colonizing isolates).

- Assurance of complete resident case ascertainment within the defined project catchment area by outreach to all laboratories serving the catchment area. This would include laboratories serving dialysis facilities, outpatient care centers, nursing homes/skilled nursing facilities, private reference laboratories and hospital laboratories. This should be repeated periodically (every 2 to 3 years) to assure that new laboratories are not missed.
- Performance of periodic (at least annual) audits of all clinical laboratories within the defined catchment area and laboratories outside the defined catchment area that are likely to process specimens from catchment area residents.

Proposals should demonstrate current understanding of CRE and CRAB burden and epidemiology in the proposed catchment areas, as well as any knowledge of CR-PA burden and epidemiology. Also demonstrate a complete understanding of the laboratories (within and outside the catchment area) that may process urine, sputum and sterile site specimens obtained from residents of the catchment area, as well as knowledge of the antimicrobial susceptibility testing methods utilized for CRE, CRAB and CR-PA in these laboratories.

Identify a Principal Investigator (PI) or sub-investigator and a coordinator for this MuGSI project. The MuGSI PI may be the EIP HAIC PI or a doctoral-level sub-investigator designated by the HAIC PI to lead the project. Ideally, the project coordinator should possess a laboratory or microbiology background (e.g., certification as a medical laboratory scientist or medical technologist), and must exhibit the ability to coordinate effectively with local healthcare facility and other laboratories included in this surveillance effort. The coordinator should also have training and experience in infectious diseases epidemiology and surveillance activities, including medical record review.

## **HAIC Required Activity Project Category #2: Special projects**

### 1. Healthcare-Associated Infections and Antimicrobial Use Prevalence Surveys:

Prevalence surveys, conducted on a single day or over a short period of time, provide an efficient means of obtaining a “snapshot” of all healthcare-associated infections (HAI) and antimicrobial drug use in a particular healthcare setting. The EIP has conducted hospital HAI and antimicrobial drug use prevalence surveys in 2010, 2011 and 2015 (see publications on the 2011 survey results available at the following links: <http://www.nejm.org/doi/full/10.1056/NEJMoa1306801>, <http://jama.jamanetwork.com/article.aspx?articleid=1911328>). The EIP also conducted a pilot nursing home HAI and antimicrobial use prevalence survey in 2014 (see abstracts available at the following links: <https://cste.confex.com/cste/2015/webprogram/Paper5406.html>, <https://cste.confex.com/cste/2015/webprogram/Paper5405.html>).

Implement Healthcare-Associated Infections (HAI) and Antimicrobial Use Prevalence Surveys in accordance with plans developed collaboratively by EIP sites and CDC. For 2017, apply to participate in a multi-site Nursing Home Prevalence Survey. Surveys will be conducted in accordance with multi-site protocols developed by the Prevalence Survey Working Group with input from the EIP HAIC Steering Group. Activities include (but are not limited to) the following:

- Maintain an EIP site Prevalence Survey Team (or for new applicants, form a Prevalence Survey Team), to include the Team Leader/survey coordinator. This team will complete

nursing home survey activities in 2017 and 2018. The EIP Prevalence Survey Team Leader or Coordinator is preferably an individual with experience as an infection preventionist and active Certification in Infection Control; individuals with clinical experience (e.g., R.N. or M.D.) and/or with substantial experience in infectious diseases surveillance and epidemiology (such as previous experience conducting phases 2, 3 or 4 of the hospital HAI and Antimicrobial Use Prevalence Survey and/or the pilot nursing home survey) may also serve in this role. The Team must maintain a sufficient number of team members to carry out nursing home survey activities, including nursing home support activities and data collection.

- Submit and maintain Institutional Review Board approval for the nursing home survey, as needed.
- Recruit a minimum of 10 and no more than 20 nursing homes to participate in the nursing home survey according to the sampling and recruitment plan to be developed by CDC in collaboration with the EIP sites.
- Ensure development of a Nursing Home Prevalence Survey Team in each facility, to include a Nursing Home Team Leader. The Nursing Home Team Leader is preferably an individual with responsibility for facility infection control activities or the Director of Nursing and have clinical experience (e.g., R.N.). The team leader will be responsible for completing the healthcare facility assessment form and overseeing data collection for the survey date by members of the Nursing Home Team or the EIP Team.
- Participate in EIP Team and Nursing Home Team survey training activities.
- Participate in EIP Team calls with CDC as requested, and at times on at least a weekly basis, to review progress, discuss challenges, and engage in data collection training.
- Collect nursing home survey data as determined by the survey protocol. Collection of HAI and antimicrobial use data for the nursing home, as well as patient outcome and prescribing quality data, is anticipated to continue through June 2018.
- Complete timely nursing home survey data entry into CDC's electronic, prevalence survey data management system.
- Respond in a timely manner to data queries, and complete data cleaning tasks for the nursing home survey in a timely manner.

The HAI and Antimicrobial Use Prevalence Survey may be repeated at regular intervals over the next several years. The types of healthcare facilities that are recruited to participate may vary from survey to survey. Other healthcare settings that could be the focus for future surveys include long-term acute care hospitals, neonatal and pediatric inpatient units or children's hospitals, specialty hospitals, and outpatient settings. The interval for performing multi-site prevalence surveys in a particular healthcare setting (e.g., acute care hospitals), while not definitively determined, is not expected to be more frequent than every 2 years.

## **OPTIONAL ACTIVITIES**

### **HAIC Optional Activity Project Category #1: Population-based surveillance**

Existing EIP grantees currently participating in one or more of these projects are encouraged to apply to continue participation. New applicants may also apply for optional activities.

1. Active, population-based laboratory surveillance for (A) invasive disease due to methicillin-resistant *Staphylococcus aureus* (MRSA) or (B) invasive disease due to all *Staphylococcus aureus* (SA)

Implement and conduct surveillance for all MRSA or SA isolates identified from normally-sterile body sites in residents of the catchment area. This includes blood, cerebrospinal fluid (CSF), bone, joint, pleural fluid, peritoneal fluid, pericardial fluid, muscle, and internal body sites. In some instances, chart review is required beyond review of laboratory-reported specimen sources to determine whether specimens have been collected from normally-sterile body sites (e.g., specimens labeled as coming from “fluid” or “tissue” only).

- Complete standardized case report forms through review of medical records, including ascertainment of community- vs. hospital-onset invasive MRSA/SA infection status. Review all identified MRSA/SA cases or (in the case of MRSA) use the HAIC MRSA sampling scheme already developed (collecting complete case report form information on a 1:10 sample of hospital-onset cases). Clearly indicate in the proposal whether sampling cases or not.
- Conduct the following activities, according to HAIC MRSA/SA protocols, to ensure complete case ascertainment and to validate data collection efforts:
  - Conduct periodic (at least annual) audits of clinical laboratories within the MRSA/SA surveillance area and of labs outside of the surveillance area (this includes annual assessment with point of contacts at large dialysis referral laboratories) that test specimens from residents of the MRSA/SA surveillance area to verify completeness of case ascertainment.
  - Enumerate all inpatient healthcare facilities within the surveillance catchment area (e.g., hospitals, nursing homes/skilled nursing facilities, inpatient rehabilitation facilities).
  - Assess long-term care facilities (LTCFs) serving the catchment area to determine whether all laboratories serving the LTCFs are reporting invasive MRSA/SA cases to EIP surveillance.
  - Form relationships for the purpose of implementing a process to obtain data reported on MRSA bloodstream infections (i.e., MRSA LabID Event reporting) and central line-associated bloodstream infections (CLABSIs) by healthcare facilities in relevant catchment areas to the National Healthcare Safety Network (NHSN), including from acute care hospitals, long-term acute care hospitals (LTACHs), and inpatient rehabilitation facilities (IRFs). Almost all U.S. hospitals have been reporting these data to NHSN since 2013, and access to data can be either through the group user function via rights assigned to the state health department or through a data use agreement with CDC as an agent of the state. If such data are already accessible to the applicant, describe in the proposal how these data have been utilized, if applicable. Plan to use NHSN MRSA LabID event and/or CLABSI data for comparison purposes with EIP population-based surveillance data.
  - Assess feasibility and potential barriers to obtaining access to MRSA data reported by dialysis facilities to the NHSN through the NHSN Dialysis Event (DE) module. Almost all dialysis facilities in the U.S. are now reporting bloodstream infections from MRSA to NHSN DE, although not all state health departments currently have access to these data.
- Submit data electronically to CDC (in agreed upon secure format) by specified deadlines and upon CDC request.
- Geocode MRSA and MSSA cases using a standardized methodology developed by the EIP geocoding working group.

- Provide timely responses to CDC MRSA/SA staff requests for information to assist in preliminary and final analyses, reports, and data close-outs.
- Participate in HAIC Steering Group, MRSA/SA Surveillance Officer, and MRSA/SAPathogen Committee conference calls.
- Participate in annual HAIC Steering Group and Surveillance Officer Meetings.

Applicants may propose to conduct invasive SA infection surveillance in a subset of the region where invasive MRSA infection surveillance is proposed, but invasive SA infection surveillance should also be population-based.

Sites may apply to collect case-patient MRSA and/or MSSA isolates from laboratories serving catchment area residents and submit these isolates to CDC. It is desirable for sites submitting isolates to submit both MRSA and MSSA isolates, although it is not required. Sites may propose an isolate sampling approach to reduce the burden. Describe approaches to ensuring that participating clinical laboratories have adequate support for EIP isolate-related activities.

Sites may also apply to do the following: 1) link MRSA/SA infection cases to state vital records data to assess mortality after hospital discharge; 2) link MRSA/SA surveillance data to healthcare facility, state or other administrative databases (possibly including pharmacy charge data) to conduct risk factor studies.

## 2. Active, population-based laboratory surveillance for candidemia

- Identify potential cases through review of laboratory reports.
- Complete standardized case report forms through review of medical records.
- Systematically collect bloodstream *Candida* isolates from all clinical laboratories within the catchment area and from laboratories outside of the catchment areas which may receive and process specimens from residents of the catchment areas. Isolates should be shipped to CDC on a monthly or bi-monthly basis.
- Conduct regular (minimum annually for all, ideally more for catchment area labs) audits of clinical laboratories within the catchment area and of labs outside of the catchment area that test a large proportion of isolates from residents of the catchment area to verify completeness of case ascertainment.
- Conduct a regular (ideally every 2-3 years) laboratory survey among all labs serving the catchment area population to ascertain changes in testing practices for *Candida* isolates.
- Securely submit data electronically to CDC monthly and upon CDC request.
- Provide timely responses to reports and requests for information to assist in preliminary and final analyses, reports, and data close-outs.
- Disseminate antifungal susceptibility testing results and isolate reports back to reporting laboratories or hospitals as appropriate.
- Geocode candidemia cases using a standardized methodology developed by the EIP geocoding working group.
- Enumerate all inpatient healthcare facilities within the surveillance catchment area (e.g., hospitals, nursing homes/skilled nursing facilities, inpatient rehabilitation facilities) along with data on facility setting, bed size, ICU size, number of discharges, patient days, etc.
- Collaborate with CDC and other EIP sites on developing special studies to better determine risk factors for echinocandin or multi-drug resistant *Candida glabrata*.

3. Perform active, population-based and laboratory-based surveillance for other selected organisms, particularly antimicrobial-resistant organisms, and/or for specific infection types, with a focus on community-onset and community-associated cases.
  - Acceptable activities include assessing the feasibility of surveillance/piloting a surveillance approach as well as conducting population-based surveillance in a defined catchment area.
  - Infection types of interest include (but are not limited to) community-associated (CA) and community-associated (CO) urinary tract infections. Apply to conduct sentinel surveillance for CA/CO UTIs in a limited number of healthcare facilities (2-5). Surveillance should ideally be conducted in areas where retail meat sampling for pathogens such as *E. coli* and *Enterococcus* species is already occurring. Consider including healthcare facilities that process urine specimens from healthy outpatients (e.g., college health clinics, obstetrics clinics, etc.). Apply to collect isolates from clinical laboratories to submit to CDC for characterization, and to collect demographic and clinical data from case patients, including information pertaining to healthcare exposures antimicrobial drug exposures, and dietary habits.
  - Organisms of interest include (but are not limited to) extended-spectrum beta lactamase (ESBL)-producing Gram-negative bacilli and vancomycin-resistant *Enterococcus*. Conduct surveillance in accordance with protocols developed by CDC in collaboration with EIP sites; surveillance methods are expected to be similar to those described for CDI surveillance, MRSA/SA surveillance, or MuGSI. Apply to conduct population-based surveillance, including active, laboratory-based case identification from all residents of the surveillance catchment area, completion of case reports forms and collection and submission of isolates to CDC.

### **HAIC Optional Activity Project Category #2: Special projects**

1. Epidemiology of sepsis project:
  - Describe the epidemiology of sepsis. Conduct the project in accordance with a protocol developed by participating sites and by CDC staff, which is anticipated to focus on hospitalized patients with a discharge diagnosis (based on billing codes) of severe sepsis or septic shock. Although the project may be focused on community-onset sepsis, data may also be collected on patients identified as having healthcare facility-onset sepsis. An objective of the project will be to describe the epidemiological classifications of sepsis cases; for example, the proportion of sepsis cases that are community-associated, healthcare-associated but community-onset, and healthcare facility-onset.
  - Recruit a convenience sample of 1-5 acute care hospitals. It is desirable to include a variety of hospitals: for example, community hospitals and academic centers, and/or hospitals of varying size.
  - Collect data from patient medical records using standardized data collection forms, including information on pre-hospital factors (including demographic information and health care exposures), underlying illnesses, presenting signs and symptoms, hemodynamic and respiratory status, laboratory testing, treatment, and outcomes. Additional objectives of the project include determining infection sources leading to sepsis and the distribution of pathogens causing sepsis.
  - Enter data (without identifiers) into a CDC-developed sepsis database.

- An additional goal of the project may be to determine how well cases are identified by sepsis surveillance definitions.
2. Other time-limited projects aimed at reducing the burden of HAI surveillance data collection and reporting and/or projects aimed at developing or evaluating innovative surveillance methods may also be proposed. Examples of possible projects include: 1) validation of 2015 hospital HAI and antimicrobial use prevalence survey data, particularly the use of an antimicrobial drug treatment screening criterion to identify patients with HAIs, and HAI determinations using 2011 and 2015 NHSN HAI definitions; 2) assessments of post-discharge mortality among patients included in the 2015 hospital prevalence survey through linkages to vital records data; 3) evaluations of new surveillance definitions or denominators; 4) development and evaluation of approaches to assessing the burden of HAIs, antimicrobial use and antimicrobial resistance and mortality due to HAIs; and 5) projects to define the epidemiology of antimicrobial use in different healthcare settings, and develop and assess approaches to benchmarking and risk adjusting measures of antimicrobial use, including measures pertaining to the quality of antimicrobial prescribing.

### **Evaluation and Performance Measurement**

HAIC activity evaluation and performance measurement is accomplished primarily through site visits and assessments of sites' success in meeting annual performance goals. EIP sites participating in HAIC projects will collaborate closely and communicate regularly (including possible site visits) with CDC HAIC personnel re: site-specific issues and to assure surveillance and other project standard operational procedures are being applied in accordance with established protocols.

#### **HAIC Performance Measures:**

For all projects:

1. Participation by at least one site representative on every project coordinator- and/or surveillance officer-oriented working call and/or webinar related to the activity (participation  $\geq 90\%$ ).
2. Site and/or project Principal Investigator participation on every Principal Investigator call (to include HAIC Steering Group as well as project working group calls) and/or webinar related to the activity.
3. Participation in the annual in-person HAIC Steering Group Meeting by at least one site member.
4. Participation in all necessary in-person annual HAIC Surveillance Officer meetings or Special Project meetings by at least one site member.

For all pathogen-specific population-based surveillance projects:

1. Assurance of data quality activities, adhering to best practices as determined by the HAIC Data Validation Working Group.
  - Performance of activities to ensure complete resident case ascertainment (audits) yearly, with submission of results to CDC and a plan for addressing case ascertainment deficiencies. Auditing should be completed according to the individual pathogen surveillance protocol.
  - Identification of all laboratories that serve residents of the surveillance catchment area, by assessing/auditing healthcare facilities and providers that serve residents of the catchment area according to the individual pathogen protocols and timelines set by those protocols. Programs should work together to complete this task to avoid duplication of effort at the EIP site or healthcare facility level. Methods used and date of task completion should be communicated to CDC on a yearly basis to ensure fulfillment of this performance measure.



- Re-abstraction of a percentage of case report forms (to be determined collaboratively by CDC and EIP site project staff) for each pathogen surveillance project, to ensure data quality.

For CDI surveillance:

1. Collection of *C. difficile* stool specimens according to the protocol; sampling scheme by epidemiologic category should be applied to all saved specimens.
2. Adherence (100%) to standard procedures described in the CDI laboratory manual for shipping stool specimens to EIP reference laboratories.
3. Collection of full case report forms for CDI cases (community- and healthcare-associated cases) based on CDI protocol for at least 95% of cases.
4. Entry of complete data abstraction forms into the CDC web-based application according to timelines to be determined by the CDI Pathogen Group (100%).
5. Participation by surveillance officer or lead project officer (for special projects) in trainings related to CDI activities.
6. Participation in all the audits and assessments (i.e., laboratory, LTCF and physician/outpatient provider) related to the CDI surveillance. Sites that previously participated in surveillance should provide a summary of findings from the most recent LTCF assessment and physician/provider assessments in their applications.

For MuGSI surveillance:

1. Submission of at least 85% of isolates requested by CDC, according to the established isolate protocol.
2. Shipment of 100% of collected isolates to CDC, according to established isolate shipping schedules (including proper packaging requirements).
3. Submission of complete data abstraction forms to CDC (criteria of “completeness” to be established with PI working group) within 4 months of MuGSI case identification; at least 85% of submitted forms should comply with the established criteria for a complete form.
4. Data entry and transfer to CDC through established mechanisms in accordance with project timelines for 100% of case records.
5. Participation by surveillance officer or lead project officer (for special projects) in trainings related to MuGSI activities.
6. Demonstrations of local data usefulness. Examples of how data is used locally should be communicated annually. Examples can include abstracts submitted to national conferences about local data, local feedback reports to participating healthcare facilities, thesis projects or local presentations. At least two different examples should be communicated to CDC annually in order to meet this performance measure.

For MRSA/SA surveillance:

1. Case data abstraction and data transmission to CDC:
  - Collection of complete data abstraction forms for invasive MRSA/SA cases:  $\geq 95\%$
  - Submission to CDC of complete MRSA/SA case counts and data abstraction forms according to pre-established timelines: 100%
  - Correction of all case report form edits by the deadline for data close-out determined by CDC in consultation with EIP sites.
2. Demonstration of access to NHSN MRSA LabID event data from  $>80\%$  of acute care hospitals in the catchment area.
3. Special MRSA/SA studies:
  - Participation in trainings and conference calls related to the study: 100%

For the HAI and Antimicrobial Use Prevalence Surveys:

1. Participation by at least one site representative on all conference calls.
2. Identification of personnel with the appropriate expertise and training to act as the EIP Team survey coordinator and team members.
3. Participation of all EIP team members in all CDC-led survey training activities.
4. Completion of survey data collection, entry, and responses to data queries and requests for corrections in accordance with established project timelines.
5. Participation in data quality assessments developed collaboratively by EIP sites and CDC.

**Budget Note:** Provide one combined budget that incorporates the costs for all activities proposed under this activity EXCEPT candidemia surveillance (Optional Category 1, Project 2, above). Provide a separate candidemia surveillance budget if addressing that optional project.

**HPV Vaccine Impact Monitoring Project (HPV-IMPACT)**

**Background**

Three highly effective human papillomavirus (HPV) vaccines are available in the United States: the quadrivalent, licensed in 2006; the bivalent, licensed in 2009; and the 9-valent, licensed in 2014. All vaccines target oncogenic types HPV 16 and HPV 18, types that cause about 66% of cervical cancers and most other HPV-associated cancers in the United States. The 9-valent vaccine targets 5 additional oncogenic types. Since June 2006, the Advisory Committee on Immunization Practices (ACIP) has recommended routine HPV vaccination of girls 11 or 12 years and catchup vaccination for those age 13 through 26 if not previously vaccinated. In 2011, ACIP recommended routine vaccination of boys age 11 or 12 and for those age 13 through 21 if not previously vaccinated. In February 2015, ACIP included the 9-valent vaccine as one of 3 recommended HPV vaccines for girls/women and boys/men.

While prelicensure trials showed high efficacy against targeted vaccine types for all of these HPV vaccines, post-licensure monitoring is important to characterize vaccine effectiveness and the impact of vaccination on important public health outcomes. Post-licensure surveillance activities include evaluation of a range of early, mid, and late HPV-associated biological outcomes for the timely monitoring of the effects of vaccination. Because of the slow natural history of HPV oncogenesis, the effect of vaccination on invasive cancers will not be evident for decades. Preinvasive cervical intraepithelial neoplasia 2 and 3 and adenocarcinoma in situ (together referred to as CIN2+), which are detected through routine screening, take less time to develop and were used as a surrogate for cervical cancer in vaccine trials. Monitoring impact on these outcomes can provide information on expected future vaccine impact on cervical cancers.

In the United States, interpretation of population-level CIN2+ changes attributable to vaccination is challenging because of a lack of national screening registries and because CIN2+ diagnosis is affected by changes in screening recommendations that have been implemented since vaccine introduction. Determination of screening rates in the population is critical to interpret trends in CIN2+. Trends in CIN2+ are also affected by changes in nomenclature used for histologic diagnosis. Determination of HPV types in CIN2+ lesions allows more specific analysis of vaccine impact CIN2+ and exploration of type replacement or cross protection of vaccines against non-vaccine HPV types.

HPV-IMPACT is an active population- and laboratory-based surveillance of CIN2+ diagnoses, as this allows both monitoring of CIN2+ diagnoses and determination of HPV types.

**Other Nat'l Public Health Priorities and Strategies**

The HPV-IMPACT guidance addresses the following objectives found in the HHS National Vaccine Plan:

- Objective 4.5: Enhance tracking of vaccine-preventable diseases (VPDs) and monitoring of the effectiveness of licensed vaccines.
- Strategy 4.5.1: Strengthen epidemiologic and laboratory methods and tools to diagnose VPDs, assess population susceptibility, and characterize vaccine effectiveness and the impact of vaccination coverage on clinical and public health outcomes.

- Strategy 4.5.2: Monitor circulating strains of relevant vaccine-preventable and potentially vaccine-preventable pathogens, including emerging and re-emerging diseases.
- Strategy 4.5.3: Improve monitoring of disease burden and determine epidemiologic and clinical characteristics of cases of VPDs and potential VPDs by supporting traditional surveillance and use of health information technology, interoperable data standards, and new data resources.
- Strategy 4.5.6: Assure timely evaluation to assess vaccine effectiveness, duration of protection, and indirect (community and herd) protection by current and newly recommended vaccines.

### **Purpose**

Evaluate the impact of the HPV vaccination program and evaluate vaccine effectiveness through a population-based surveillance system that could, in addition to monitoring overall CIN2+ trends, enable monitoring trends in HPV type distribution in CIN2+ lesions among vaccinated and unvaccinated women. Optional projects could also address other HPV-associated outcomes.

### **Outcomes**

#### ***Provide new knowledge***

- Enumerate the CIN2+ cases in the catchment areas.
- Understand HPV types in CIN2+ lesions.
- Increase knowledge of screening rates in light of changes in screening recommendations.
- Increase data on vaccine effectiveness available to inform vaccine policy.

#### ***Develop staff expertise***

- Increase expertise in HPV monitoring.
- Increase epidemiology skills.
- Increase the understanding of local data sources.
- Create and maintain collaborations with laboratories, healthcare providers, immunization programs, large insurers, and other groups as needed to meet project objectives.

### **Strategies and Activities**

#### **Required HPV IMPACT Activities – All 6 activities below are to be addressed:**

1. Conduct surveillance on histologically-confirmed high grade cervical dysplasia, currently called cervical intraepithelial neoplasia grades 2 and 3 and adenocarcinoma in situ (CIN2+).
  - a. Identify pathology labs that process and read cervical biopsy specimens on cases residing in the catchment area, including all local, in-state, and out-of-state labs that serve the catchment area.
  - b. Establish CIN2+ case reporting from identified pathology labs.
  - c. Maintain close working relationships with reporting pathology labs to ensure accurate and complete case reporting.
  - d. Conduct routine case and system audits of reporting pathology labs to evaluate quality, accuracy, and completeness of reporting and to identify limitations of data. At a minimum, participating labs that collectively report 80% of cases each year should be audited.
  - e. Biennially, conduct provider surveys to ensure all pathology labs serving the catchment area are identified and participating in case surveillance.
  - f. Ensure completeness of standardized common data elements on the Case Report Form (CRF), including patient demographics and health insurance information.

2. Obtain archived diagnostic biopsy specimens on CIN2, CIN2/3, CIN3, and AIS in females 18-39 years residing in catchment area. At a minimum, specimens should be provided from all participating labs that collectively report 80% of cases each year. Specimens from at least 250 representative cases must be collected per year, but ideally all adequate specimens should be collected. The HPV vaccination program is ultimately expected to lower the incidence of CIN2+, which might eventually preclude the collection of 250 specimens annually. Sites should continue to submit all adequate specimens from participating labs that collectively report 80% of cases.
  - Retrieve one archived block representative of cervical histology for each specimen from reporting pathology laboratories for processing to permit HPV genotyping at CDC.
    - Specimens should be selected by a designated lab pathologist or other expert laboratory personnel to ensure selected specimen is adequate for typing.
  
3. Obtain the following additional information on reported cases of CIN2, CIN2/3, CIN3, and AIS in females 18-39 years residing in catchment. Priority should be given to cases for which specimens have been or will be obtained for typing. Sources of information may include pathology reports, patient medical records, immunization registries, patient interviews, and billing and administrative data.
  - a. HPV vaccination status and history
    - Collect complete vaccine history on cases aged 18-39 years. Sites should utilize any and all available resources to obtain the information, including vaccine provider records, other medical charts, insurance and other administrative databases, vaccine registries, and patient interviews.
  - b. Missing demographic information
    - Collect race, ethnicity, and insurance status on cases aged 18-39 years. Sites should utilize any and all available resources including medical charts, insurance and other administrative databases, vaccine registries, and patient interviews.
  - c. Cervical cancer screening history and other data elements on case report form
    - Collect date of last cervical cancer screening that led to the reported diagnosis. Sources of information may include medical charts, administrative databases, and patient interviews.
  
4. Estimate cervical cancer screening utilization among all women residing in the catchment area.
  - a. Estimate total number or percentage of 18-39 year-old females residing in the catchment area who received cervical cancer screening within the given analytic time periods, stratified by the following age groups: 18-20, 21-24, 25-29, 30-34, 35-39.
  - b. Sites must provide a detailed description of method(s) used to estimate screening rates. Complete enumeration of females screened in the catchment is preferred but other methods could include use of multiple administrative, laboratory, and other non-patient reported data to estimate rates. To the extent possible, estimates should not rely on patient reported data.
  
5. Data management
  - a. Establish and maintain the flow of information and data linkages from reporting sources to appropriate recipients. Identify method of reporting (e.g., electronic, mail, etc.) by each source.
  - b. Encourage and assist reporting labs to adopt standard histopathologic terminology to identify cases, and standard information systems and data-exchange formats by laboratories to ensure accurate data extraction and reporting.
  - c. Use a standardized algorithm to de-duplicate cases reported to the database over time.

- d. Electronically transmit data, stripped of personal identifiers, to CDC on a routine basis using an agreed upon standard format and secure data transfer protocol.
6. Other activities
- a. Provide the resources necessary for collection, analysis, interpretation, and dissemination of data.
  - b. Participate in quarterly conference calls with CDC and other participating sites for updates and discussion of relevant issues.
  - c. Provide quarterly narrative updates of site specific progress and resolutions to any encountered issues.
  - d. Participate in annual/biennial collaboration meetings to provide updates on results and the status of ongoing activities; work with other sites to develop or revise common enhanced surveillance activity guidelines.
  - e. Provide documentation for any locally developed method(s) related to the monitoring project (e.g., data source enumeration, obtaining vaccination history and other required data elements not available from the primary data source, subset sampling, aggregate data collection, and determination of denominator data) to permit evaluation of comparability and share documents with CDC and other collaborators.

**Optional HPV-IMPACT Activities – Applicants may choose to address 1 or more of the following activities:**

For Optional HPV-IMPACT Activities, once funded, protocols, data collection instruments, data dictionary, and data entry software will be developed in collaboration with CDC and participating sites so that they may be standardized across sites. Special studies may require IRB approval.

1. Evaluate vaccine effectiveness and other vaccine- related research questions through case-control studies, indirect cohort studies, or other designs.
2. Expand laboratory- based surveillance to other HPV-associated outcomes.
3. Use local administrative databases for monitoring cervical cancer screening, detection of CIN2+ lesions and treatment as well as other HPV-associated outcomes.
4. Geocode cases of CIN2+ cases detected as part of the surveillance for CIN2+ (required HPV-IMPACT activity 1) for use in local and combined site analyses.

**Evaluation and Performance Measurement**

*Sites are expected to report performance metrics as outlined below. For current HPV-IMPACT sites, baseline values for each metric will be established for each site based on their current HPV-IMPACT data. For new sites, baseline data will be available after their first year. Baselines will be re-evaluated each year and annual data will be submitted over the funding period.*

**Table 1. Performance measures pertaining to CIN2+ case surveillance**

Performance measure	Relevant sub-populations
Complete race and/or ethnicity	A, B
Complete insurance status	A, B
Known vaccination status (vacc or not vacc) of vaccine age-eligible women <sup>a</sup>	A
At least one date of vaccination among vaccinated women <sup>a</sup>	A

Attempts to obtain vaccine status <sup>b</sup>	A
Trigger test (pap or HPV test)	A

A report percent for cases in women aged 18-39

B report for cases in women aged  $\geq 40$

<sup>a</sup> CDC acknowledges the difficulty of obtaining vaccination status and confirming vaccination date.

<sup>b</sup> Document the process of searching for vaccination status. For example,  
 xx% of vaccine age-eligible women were checked in the vaccine registry for vaccination status  
 xx% of vaccine age-eligible women had their medical records checked for vaccination status

**Table 2. Performance measures pertaining to overall program participation**

Performance measure	Measure
Participate in quarterly PI calls	% of calls
Quarterly data submission	% of quarters
Quarterly update reports	% of quarters
Specimens sent (%) <sup>a</sup>	% of cases
Specimens sent (n) <sup>a</sup>	Number of specimens
Document sampling strategy, if employed	Present/absent
Laboratory audits	Number of labs audited
Biannual provider audit	% of providers audited
% of large laboratories (>10 cases/yr) reporting cases	% of labs
% of laboratories providing specimens, among the laboratories that collectively process 80% of cases	% of labs
Annual population screening data and methodology	Present/absent
Complete lab table annually (Table 3)	Present/absent

<sup>a</sup> If a site can only meet only one minimum of either 80% of enhanced cases with a specimen submitted or 250 specimens sent, provide the rationale for the number of specimens submitted.

**Table 3. Information on participating pathology laboratories**

Lab name /ID	Lab type <sup>a</sup>	Report type <sup>b</sup>	Reporting frequency	Case ascertainment methods <sup>c</sup>	Number of specimens submitted
<b>A</b>					
<b>B</b>					
<b>C</b>					
<b>D</b>					
<b>Etc.</b>					

<sup>a</sup> Lab type: e.g. commercial, hospital, private

<sup>b</sup> Report type: paper, electronic, HL7

<sup>c</sup> ICD-9, SNO-MED, natural language search, diagnostic code/classification: e.g. Bethesda, CIN, dysplasia, immunohistochemistry test, etc.

## Lyme and Other Tickborne Diseases (TickNET)

### Background

Through their bite, ticks expose humans to a remarkable array of pathologic agents, including neurotoxins, allergens, bacteria, parasites, and viruses. The clinical features of tickborne illness range from mild to life-threatening, and collectively tickborne diseases constitute a substantial and growing public health problem in the United States. New agents of tickborne disease are described regularly, and known agents are spreading to new areas.

The most common tickborne disease in the United States is Lyme disease, caused by the spirochete *Borrelia burgdorferi*. With over 37,000 cases reported to CDC during 2013, Lyme disease ranks 5th among all nationally notifiable conditions. Less common but potentially serious tickborne infections include anaplasmosis, babesiosis, ehrlichiosis, and spotted fever group rickettsioses. Recent reports of U.S. patients infected with *Borrelia miyamotoi*, *Ehrlichia muris*-like agent, a novel bunyavirus, and a putative new genospecies within the *Borrelia burgdorferi* sensu lato species complex all serve to highlight the potential for discovery of novel tickborne pathogens.

Tickborne diseases pose special challenges for clinicians and public health agencies alike. Although tickborne diseases occur throughout the United States, the distribution of any given disease can be highly focal, and this information must be known and considered by health care providers when assessing patients. In addition, laboratory testing is often limited to serologic assays that require paired samples drawn several weeks apart to confirm recent infection. This complicates the use of laboratory testing for both patient management and public health surveillance. With regard to prevention, tick checks, repellent use, and other personal protective measures -- while generally benign and inexpensive -- have not been shown to significantly reduce tickborne disease incidence. Despite decades of education about these measures, case reports for the more common tickborne diseases continue to rise.

### Purpose

Better define the public health and economic burden of tickborne diseases in the United States, identify new risk factors, and develop and evaluate effective public health prevention and control strategies.

### Outcomes

#### *Provide new knowledge*

- Better understanding of the economic burden of tickborne diseases.
- Definition of the clinical spectrum and public health importance of newly-identified tickborne pathogens (e.g., *Candidatus Borrelia mayonii*).
- Better understanding of the incidence, epidemiology, clinical features, and risk factors for previously-recognized tickborne diseases.
- New diagnostic assays or assays with simpler interpretation for improved diagnosis of new and previously recognized tickborne diseases.
- Better understanding of the changing distribution of ticks and tick-borne pathogens such that interventions can be effectively targeted.

#### *Control outbreaks of infectious diseases*

- Effective primary prevention or control measures to reduce the burden of tickborne diseases (esp. Lyme disease).



## **Strategies and Activities**

Sites proposing to participate in the activities outlined below should plan for travel of appropriate personnel to one organizational TickNET meeting in Fort Collins, CO, in 2017.

1. Evaluate the economic burden of Lyme disease to patients and society.
2. Foster pathogen discovery and evaluate the incidence, epidemiology, clinical features, and risk factors of newly-identified tickborne pathogens.
3. Define the incidence, epidemiology, clinical features, and risk factors of previously-recognized tickborne diseases.
4. Evaluate the utility and application of new or improved diagnostic assays.
5. Perform studies to evaluate the feasibility, acceptability or effectiveness of personal, household, or community-based interventions to reduce the incidence of tickborne disease.
6. Update and evaluate tick and/or tickborne pathogen distribution data or conduct studies to understand how tickborne pathogens are maintained in local enzootic cycles.

## **Evaluation and Performance Measurement**

1. For all chosen activities:
  - a. Number of staff participating in study conference calls.
  - b. Proportion of calls attended by staff.
2. For economic burden evaluation:
  - a. Number and proportion of participants with complete patient cost data (Phase 1).
  - b. Number and proportion of participants with complete total medical care cost data (Phase 2).
3. For evaluations of the incidence, epidemiology, clinical features, and risk factors of newly-identified and/or previously recognized tickborne pathogens:
  - a. Number of participants enrolled.
  - b. Number of surveys and/or medical record reviews conducted.
  - c. Number of environmental/entomologic assessments conducted.
4. For evaluation of new or improved diagnostic assays:
  - a. Number of patients enrolled.
  - b. Number and type of specimens collected.
5. For intervention studies:
  - a. Number of potential participants contacted for recruitment and proportion enrolled.
  - b. Number and proportion of surveys completed.
  - c. Number and proportion of participants receiving intervention.
6. For entomologic studies:
  - a. Number and type of specimens collected.

## Rotavirus

### Background

Certain histo-blood group antigens (HBGA) expressed on enterocytes have been proposed as receptors or ligands for the protease-cleaved (designated “P”) protein of rotaviruses. Additionally, associations between a population’s frequency of particular HBGA types and disease (or lack of disease) from particular rotavirus P genotypes have been made. There is a need to determine if those infants who shed rotavirus vaccine or who developed anti-rotavirus antibodies after vaccine are more likely to have specific polymorphisms in the secretor (FUT2, fucosyltransferase 2) and Lewis (FUT3) genes, assessed in saliva samples, compared to those infants who did not shed rotavirus vaccine or did not develop anti-rotavirus antibodies.

In the U.S. population, approximately 20% of whites and blacks have the null FUT2 phenotype (“non-secretors”), whereby H antigens are not expressed on mucosal surfaces, in saliva, or in other secretions. This phenotype has been hypothesized to be associated with a lower risk of P[8] rotavirus infection. Both rotavirus vaccines available worldwide consist of genotype P[8] strains. It is therefore possible that the response to a P[8] vaccine is at least in part determined by an individual’s FUT2 phenotype.

### Purpose

Study the vaccine take of oral rotavirus vaccine in U.S. infants and assess for correlation of the vaccine response with the secretor phenotype and genotype status of the infants. If the results indicate that lack of vaccine take is statistically associated with having the FUT2 non-secretor genotype in U.S. infants, it would provide important information and indicate that larger evaluations of vaccine protection by secretor status and specific P genotype of wild-type strains should be further examined. This information will inform how vaccines can be optimized to reduce morbidity and mortality from rotavirus.

### Outcomes

#### *Provide new knowledge*

If our results indicate that lack of vaccine take is statistically associated with having the FUT2 non-secretor genotype in U.S. infants, it would provide important information and indicate that larger evaluations of vaccine protection by secretor status and specific P genotype of wild-type strains should be further examined. It is possible that infants who do not “take” an oral, attenuated vaccine strain of P8 genotype are also not susceptible to disease from wild-type strains of P8 genotype, which have been the most common genotypes circulating in the U.S. most years. It may also suggest that the infant may remain susceptible to strains of other P genotypes because heterotypic antibody may not have developed following vaccination (but could have developed in the secretors). Further, these data could also suggest that U.S. infants that are genotypic non-secretors are at a lower risk than secretors for intussusception caused by oral rotavirus vaccine, which would inform our overall estimate of this adverse event in the U.S. and provide insight into possible mechanisms by which the vaccine causes intussusception. The results would contribute to the understanding of the role of secretor genotype in vaccine protection and susceptibility to rotavirus disease (and possibly to vaccine-associated intussusception), which could have substantial implications for development of more effective vaccines in developing countries where the burden of severe disease is great.

### Strategies and Activities

1. Perform the study among healthy, full term infants who are receiving their rotavirus vaccine through their healthcare provider at ages 2 and 4 months. Informed consent for participation in the evaluation would be obtained.
  - a. Preferred subjects are non-Hispanic infants receiving the monovalent rotavirus vaccine RV1 (Rotarix) (non-secretor phenotypes are uncommon in Hispanic populations).
  - b. Ideally the evaluation should be performed among children born approximately June through September, so that all samples are collected during periods when wild-type rotavirus does not usually circulate.
  - c. With an estimated drop-out rate of 30% between rotavirus vaccine dose #1 and dose #2, and between dose #2 and blood draw, an estimated 176 infants will be initially enrolled from the one site performing the study.
2. Administer a short survey (developed with CDC) regarding feeding type (breast or not) and demographics that includes information on the rotavirus vaccine manufacturer and lot will be obtained.
3. Obtain:
  - a. A saliva sample for HBGA phenotype and genotype assessment at age 2 months.
  - b. Stool samples to determine wild-type rotavirus and rotavirus-vaccine shedding pre-dose #1 and at days 3 and 5 following dose #1 and #2.
  - c. A serum sample for anti-rotavirus IgA antibody 1 month after dose #2. (It is also possible a serum sample would be collected pre-dose #1).
4. Compare the odds of responding to the P[8] vaccine (or being infected through background exposure to wild-type P[8] rotaviruses) as determined by viral shedding or serum antibody in infants with the secretor phenotype/genotype to the odds of vaccine response among infants with the null phenotype/genotype. If variation in Lewis phenotype/genotype is also detected among the enrolled infants, similar analyses will be performed to assess for association between vaccine response and Lewis antigen expression.
5. All laboratory testing will be performed at CDC or a CDC-designated laboratory.

#### **Evaluation and Performance Measurement**

1. Participation on monthly conference calls related to this activity.
2. Number of infants successfully enrolled each week.
3. Number of infants for whom all specimens are collected and stored following established procedures.

## Prion Diseases

### Background

Prion diseases are a family of rare progressive neurodegenerative disorders that affect both humans and animals. These diseases are characterized by unusually long incubation periods often measured in years. They are 100% fatal and are caused by unconventional transmissible agents that are highly resistant to usual inactivation methods. Animal prion diseases include bovine spongiform encephalopathy (BSE), a prion disease of cattle, and chronic wasting disease (CWD), a prion disease of deer and elk. Human prion diseases include classic forms of Creutzfeldt-Jakob Disease (CJD), the types most commonly occurring throughout the world, including the United States, and variant Creutzfeldt-Jakob Disease (vCJD), a type of human prion disease that emerged in the United Kingdom in the mid-1990s associated with eating meat products contaminated with the agent of BSE.

Multiple mechanisms are used to conduct national human prion surveillance. These mechanisms are interrelated, but separate, and each provides specific information that contributes to the overall picture of what is happening in the United States regarding human prion disease. These surveillance mechanisms consist of the following: 1) receipt and follow-up of spontaneous case reports to CDC, usually from clinicians, either directly or through state and local health departments, 2) routine analysis of national CJD mortality data, 3) funding state-of-the-art diagnostic neuropathological testing of clinically suspected cases of human prion disease at the National Prion Disease Pathology Surveillance Center (NPDPS), and 4) collaborative surveillance studies focused on subpopulations of special public health concern, including persons less than 55 years of age, human growth hormone recipients, CJD donor blood recipients, and hunters in the longest known CWD endemic states.

Up to 12 state or local health departments have been supported by the CDC prion disease program funding in previous years. Recipients have been selected based on population size; occurrence of a cluster of human cases increasing public and health authority concerns; proximity to Alberta Canada, the epicenter in North America for BSE; the occurrence of a case of BSE in the state; the presence of CWD in the state; and a state's interest and ability to conduct enhanced human prion surveillance. In addition to direct support for surveillance in selected states, indirect support in all states is provided through the NPDPS.

The national human prion disease surveillance system in the United States has shown increasing annual numbers of CJD cases that have reflected both the increased sensitivity of surveillance and the aging of the U.S. population. As a result of this surveillance and improved surveillance internationally, the annual age specific rate of CJD is estimated to be about 1 to 1.5 cases per million persons, although rates of up to two cases per million are not unusual. For the approximately 315 million persons in the United States, mortality data indicate the occurrence of between 300 and 500 U.S. prion disease deaths per year. Of these, about 85% represent sporadic disease unrelated to any known environmental exposure. Five to 15% of these deaths occur as a result of inheriting a mutation in the gene that codes for the prion protein, and declining proportions of these deaths (less than 0.75%) are attributable to prion exposures resulting from a known medical procedure (e.g., surgery, receipt of a contaminated pituitary hormone or dura mater graft).

### Purpose

Implement and maintain an active prion surveillance system in the U.S.:

- Detect, or provide reassurance about the continued absence of, new forms of human prion disease emerging in the U.S., particularly variant CJD and possibly human chronic wasting disease.
- Provide comprehensive data on the normal incidence and trends of human prion diseases to inform prion disease-related public health policies (e.g., blood safety policies, hospital infection control policies).
- Provide education, support, and consultations to physicians and families dealing with patients clinically suspected or confirmed as having a human prion disease.

These objectives are met through collaborations with state and local health departments working to:

- Increase the number of autopsies performed on suspected and clinically diagnosed cases of prion disease.
- Maximize reporting of cases of suspected prion disease through education and provision of technical support to pathologists, neurologists, funeral and mortuary directors, and other appropriate professions.
- Enhance surveillance for persons less than 55 years of age suspected of having prion disease. This includes a) review of medical records, MRI results and EEG findings by CDC prion staff, b) follow-up on prion diagnostic test results from the NPDPS, and c) additional follow-ups of reported cases for possible routes of prion transmission.
- Develop relationships with the CJD Foundation or comparable patient groups and with hospitals and funeral homes to educate family members, medical care personnel and funeral home staff about prion diseases. Such education would include guidance on controlling risk with appropriate infection control measures and help to reduce undue fears and stigmatizations.
- Conduct surveillance to help assess risk for possible CWD in hunters of Colorado and Wyoming where CWD is endemic among deer and elk.

## **Outcomes**

### ***Provide new knowledge***

- CDC's surveillance program is increasing knowledge about prion diseases both directly through a) determination of the normal disease incidence and prion disease types in the country, including the recent recognition of a new type of prion disease, and through b) the provision of difficult to obtain tissues to investigators at other institutions, including NIH, to facilitate ongoing research in this field.

### ***Develop staff expertise***

- Effective coordination and exchange of information and data between state health departments, the National Prion Disease Pathology Surveillance Center, the CJD Foundation or comparable patient groups and with hospitals and funeral homes to educate family members, medical care personnel and funeral home staff about prion diseases.
- Effective collaborations between pathologists, neurologists, funeral and mortuary directors, and other appropriate professionals within the state dealing with persons diagnosed with human prion disease and provision of education about CJD surveillance and the role of state health departments, CDC and the National Prion Disease Pathology Surveillance Center.
- Where appropriate, effective coordination and exchange of information and data between the state Department of Health and state Department of Natural Resources.

### ***Control outbreaks of infectious diseases***

- Confirm unusual occurrences of human prion diseases by timely conducting follow-up investigations of reported clusters of suspected CJD cases reported to state departments of health or of unusual individual cases, especially cases in persons less than 55 years of age, suspected

iatrogenic CJD cases, suspected cases of variant CJD or of an emerging prion disease (e.g., possible human chronic wasting disease).

#### ***Develop/modify treatment guidelines***

- Presently there are no effective treatments for human prion diseases.

#### ***Develop/modify intervention recommendations***

- A key benefit of this surveillance system includes the collection of data that will either support or lead to modifications of current recommendations to prevent spread of prion diseases. Current guidelines attempt to prevent spread of prion diseases by blood, grafts, and surgical equipment. They also address prion safety for hunters of cervids in CWD endemic areas and prion safety during the institutional and home care of patients and for pathologists and workers in funeral homes. The CDC prion disease surveillance program enables better science-based focusing of concerns related to the risk of variant CJD from consumption of BSE contaminated beef. It also enables improved policies related to public health and cattle trade. Multiple false reports of variant CJD have been ruled out by the CDC surveillance system, preventing undue concerns among the U.S. public and among international beef trading partners. The CDC prion disease surveillance program provides an important ongoing measure of the success of the ongoing, costly control measures put in place by the USDA and FDA to reduce the potential for exposures of cattle and humans to the BSE agent. It provides reassurance to those who continue to question the effectiveness of such control measures.

#### **Strategies and Activities**

1. Conduct enhanced surveillance for CJD and the possible emergence of new variant forms of CJD.
2. Maintain regular contact with the National Prion Disease Pathology Surveillance Center at Case Western Reserve University.
3. Work collaboratively with pathologists, neurologists, funeral and mortuary directors, and other appropriate professionals within the state to maximize communications and reporting of suspected and diagnosed cases of CJD.
4. Provide educational sessions to pathologists, neurologists, funeral and mortuary directors, and other appropriate professionals within the state to maximize knowledge and reporting of suspected and diagnosed cases of CJD.
5. Develop relationships with the CJD Foundation or comparable patient groups and with hospitals and funeral homes to educate family members, medical care personnel and funeral home staff about prion diseases.
6. Work collaboratively with CDC and other sites funded for enhanced surveillance of CJD and other prion diseases.
7. Collect, analyze, and disseminate data (e.g., reports, manuscripts, and presentations).
8. Complete bi-annual line list reports of all persons with a suspected or confirmed diagnosis of CJD, indicating which reports the EIP site's project area accepts as a case (i.e., definitive, probable, possible, neurologist diagnosed) and for those cases, whether the following information is included: a) Year of death, b) State of residence, c) Sex, d) Age, e) Date of birth, f) CJD Status, g) Was the case diagnosed by a neurologist?, h) Is the case still under investigation and if yes, please explain, i) Was CJD noted on the death certificate?, j) Was an Autopsy performed?, k) Was a Biopsy performed?, l) Were specimens sent to NPDPSC?, m) Were specimens sent to another laboratory?, n) Were clinical data for cases < 55 years of age sent to CDC?, o) Was the CJD Surveillance Report Form completed for cases < 55 years of age? In addition, for states with long-standing endemic chronic wasting diseases in free ranging cervids, include the following information: p) Was the patient identified in the hunter registry?,

- q) How was the patient/decedent identified (NDI, surveillance)?, r) Was the decedent's family interviewed?, and s) Did the patient hunt in a CWD endemic area?
9. Track and report data to CDC.
  10. Obtain scientific data to support development of evidence based and cost-effective policies.
  11. Increase the number of autopsies performed on suspected and clinically diagnosed cases of prion disease.
  12. Report immediately to CDC any newly suspected or confirmed case of CJD in a person less than 55 years of age as well as any case of suspected or confirmed CJD that may be the result of iatrogenic transmission. For these cases, submit the pertinent portions of the medical record to CDC. Pertinent sections of the medical record includes the admission summary, discharge summary, EEG reports, MRI reports, neurology consultation notes, psychiatry consultation notes, pathology reports from a biopsy, and pathology reports from autopsy.
  13. To facilitate cross checking of different data sources and to identify all diagnosed CJD cases in the project area, CDC strongly encourages that at least annually, the Prion Surveillance Coordinator have access to the Department of Vital Statistics' death certificate-derived data from any death certificate on which one of the following codes or terms appears anywhere on the death certificate:
    - ICD-9 046.1 for deaths before 1999
    - ICD-10 A81.0 for deaths from 1999 to the present.
    - 'jakob', 'jacob ', 'creutz', 'crutz', 'critzfield', 'cjd', 'spongiform', 'spongioform', 'spongeform', 'sponaiform', 'tse', 'prion'
    - 'gss', 'gerstman', 'gertsman', 'straussler', 'strausler', 'scheinker', 'ffi', 'familial insomnia', 'familial fatal insomnia'
  14. For states with long-standing endemic chronic wasting diseases in free ranging cervids, only: Meet with the Department of Natural Resources to conduct CWD related education and other activities aimed at persons who hunt within the state and those who consume venison provided by these hunters.
  15. For states with long-standing endemic chronic wasting diseases in free ranging cervids, only: Maintain a list of new game management units or hunt areas where CWD-positive cervids have been found.
  16. For states with long-standing endemic chronic wasting diseases in free ranging cervids, only: Produce an annual summary describing hunter registry data (hunters, submissions, matched mortality records, and the result of the CJD analyses), including updated results of expected vs. observed CJD analysis.

### **Evaluation and Performance Measurement**

1. Number of investigations conducted based on information received via active surveillance systems.
2. Number of suspected and clinically diagnosed cases of prion diseases for which biopsy or autopsy was conducted.
3. Number of suspected or confirmed cases of CJD in persons less than 55 years of age as well as any cases of suspected or confirmed CJD that may be the result of iatrogenic transmission reported to CDC within two weeks of the report to the state department of health.
4. Number of cases less than 55 years of age or who is suspected of having or is diagnosed with CJD
5. Number of educational sessions provided to pathologists, neurologists, funeral and mortuary directors, and other appropriate professionals within the state.

6. Number of contacts with the CJD Foundation or comparable patient groups, hospitals and funeral homes to educate family members, medical care personnel and funeral home staff about prion diseases.
7. Number of bi-annual line list reports of all persons with a suspected or confirmed diagnosis of CJD
8. Review at least annually state death certificate data and report number of new cases found, number of cases found that had already been reported to prion surveillance, and number of cases reported to prion surveillance that are not found by death certificate review.
9. For states with long-standing endemic chronic wasting diseases in free ranging cervids, only: Number of meetings with the Department of Natural Resources and description of what was accomplished at these meetings.
10. For states with long-standing endemic chronic wasting diseases in free ranging cervids, only: Production of an annual list of new game management units or hunt areas where CWD-positive cervids have been found.
11. For states with long-standing endemic chronic wasting diseases in free ranging cervids, only: Submit an annual summary describing hunter registry data.



**Arbovirus: Defining the burden of arboviral diseases in the United States**

**Background**

Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies, or midges. More than 100 arboviruses are known to cause human disease. While most infections are subclinical, symptomatic illness manifests as one of three primary clinical syndromes: systemic febrile illness, neuroinvasive disease (e.g., meningitis, encephalitis, or acute flaccid paralysis), or hemorrhagic fever.

Human disease cases due to the following arboviruses are nationally notifiable: California serogroup (e.g., La Crosse and Jamestown Canyon), chikungunya, dengue, eastern equine encephalitis, Powassan, St. Louis encephalitis, western equine encephalitis, West Nile, and yellow fever viruses. Colorado tick fever virus is of regional importance and disease is a reportable condition in five states. Although West Nile virus is the leading cause of arboviral encephalitis in the United States, the other reportable arboviruses cause sporadic disease and local or regional outbreaks. In 2014, more than 2,500 travel-associated chikungunya virus disease cases were reported to ArboNET from U.S. states. In addition, several other arboviruses are new or emerging causes of disease (e.g., Heartland, Bourbon, and Zika viruses).

Arboviral surveillance data are reported by state health departments to CDC through ArboNET. ArboNET is a passive surveillance system. It is dependent on clinicians to consider the diagnosis of an arboviral disease, obtain the appropriate diagnostic test, and report positive results to public health authorities. Diagnosis and reporting are incomplete, and the true incidence and burden of arboviral diseases is unknown.

**Purpose**

Better define the public health and economic burden of arboviral diseases in the United States, and to identify and improve public health prevention and control measures. Preference will be given to collaborative projects across multiple EIP sites for one or more of the proposed activities.

**Outcomes**

***Provide new knowledge***

- New diagnostic assays or specimen types for more timely clinically-relevant diagnosis and simpler interpretation of arboviral test results without confounding of issues of cross-reactivity, secondary infection, or prior vaccination.
- Better understanding of the clinical spectrum, geographic distribution, and public health importance of Heartland and Bourbon viruses.

***Control outbreaks of infectious diseases***

- An effective primary prevention or control measure to reduce the burden of West Nile virus disease in the United States.

***Develop/modify treatment guidelines***

- Evidence-based clinical management guidelines or therapy to reduce hospitalization and death due to West Nile virus neuroinvasive disease.

## **Strategies and Activities**

Applicants may address one or more of the following:

1. Perform a controlled study to evaluate the effectiveness of a community-based intervention (e.g., comprehensive vector control) to reduce the incidence of West Nile virus disease.
  - a. Coordinate with other EIP sites to define geographic areas with higher numbers of West Nile virus disease cases.
  - b. Develop a strategy to reduce the incidence of West Nile virus disease.
  - c. Implement the strategy in selected areas.
  - d. Evaluate the effectiveness of the prevention or control strategy.
2. Perform a controlled study to evaluate clinical management guidelines or therapy to reduce the morbidity and mortality of West Nile virus neuroinvasive disease.
  - a. Identify collaborating clinical institutions and providers and/or professional organizations (e.g., Infectious Diseases Society of America) with access to adequate numbers of West Nile virus neuroinvasive disease cases.
  - b. Develop clinical management guidelines or identify a therapy.
  - c. Implement the guidelines or administer the therapeutic in randomly selected patients.
  - d. Evaluate the effectiveness of the guidelines or therapy in reducing the severity of disease or death.
3. Evaluate the utility of molecular testing on urine specimens for the diagnosis of acute arboviral diseases.
  - a. Identify collaborating healthcare facilities with adequate numbers of West Nile virus or other arboviral disease cases.
  - b. Collect acute urine and serum at the time of initial clinical presentation for suspected arboviral disease.
  - c. Collect a convalescent serum specimen at 7–21 days after onset of fever.
  - d. Evaluate the acute urine for arboviral RNA by RT-PCR or NAAT and the acute and convalescent sera for arboviral IgM and neutralizing antibodies.
  - e. Evaluate the sensitivity and specificity of molecular testing on acute urine for the diagnosis of acute arboviral infection.
4. Evaluate the incidence, epidemiology, clinical features and risk factors for Heartland or Bourbon virus.
  - a. Identify collaborating healthcare facilities or an existing project or specimen set (e.g., specimens collected from patients with acute febrile illness or suspected tick-borne disease).
  - b. Collect clinical and epidemiologic data.
  - c. Collect and evaluate specimens for evidence of acute Heartland virus disease.
  - d. Describe the epidemiology, geographic distribution, clinical spectrum, and outcomes of patients with Heartland virus disease compared to enrolled patients without Heartland virus infection.

## **Evaluation and Performance Measurement**

Evaluation and performance measures will be developed in consultation with CDC and, as applicable, other participating sites, for the above activities. Examples of appropriate measures include:

1. Regular participation in conference calls with CDC and other sites for approved activities
2. Number and proportion of facilities, providers, etc., enrolled
3. For Strategy/Activities #1 & #2: Number of enrollees in which strategies/guidelines are implemented.
4. For Strategy/Activities #3 & #4: Number of enrolled facilities, providers, etc., for which all specimens and/or data are collected
5. For Strategy/Activities #3 & #4: Completion of data quality assessments

## **Congenital Cytomegalovirus (CMV) Infection**

### **Background**

Congenital CMV infection is the most common infectious cause of disability worldwide. Congenital CMV is diagnosed by testing newborn saliva or urine for CMV, but this is not performed routinely anywhere in the U.S. due to lack of infrastructure to test saliva or urine, and thus most congenital CMV remains undiagnosed. Newborns in the U.S. are routinely screened for a variety of birth defects using dried blood spots (DBS) which could possibly be useful to screen for CMV, however there is currently no validated test to use DBS to screen newborns for CMV.

### **Purpose**

Establish the clinical sensitivity of DBS for detection of congenital CMV in newborns.

### **Outcomes**

#### ***Provide new knowledge***

1. This study will establish the best clinical specimen for screening newborns for CMV regardless of the outcome. If DBS exhibit good clinical sensitivity, that will be the best specimen because DBS are already collected on all US newborns and would not require new infrastructure. If DBS do not show adequate sensitivity, saliva will be the specimen of choice because it is the current specimen of choice for select testing and research studies but lacks any infrastructure for large-scale screening.
2. Clinical follow-up in this study (4 years) will add to the knowledge of late-onset sequelae from congenital CMV infection. Very few studies to date have included clinical follow-up beyond one year.

#### ***Develop/modify guidelines***

1. Results of this study will make a key contribution to guidelines for newborn screening for CMV. Currently CMV screening is not recommended in part due to the lack of a high-throughput test. If DBS show adequate sensitivity that would establish the existence of a high throughput test.
2. Clinical follow-up of CMV+ children may help form standardized guidelines for management of CMV-infected children which are currently lacking.

### **Strategies and Activities**

1. Obtain parental consent and obtain a saliva specimen and a DBS specimen from infants within 2 weeks of birth prior to discharge at 1-3 hospitals.
2. Testing of saliva will be performed in-state and testing of DBS specimens will be performed at CDC with the option for paired testing in-state.
3. Obtain information on signs of congenital CMV infection in the newborn period including newborn hearing screening results of the participating infants from the infant's hospital record. Contact information for participation in follow-up component of the study will be collected from patients at the time of enrollment).
4. Assess clinical sensitivity of DBS specimens by comparing CMV PCR results from the paired DBS and saliva specimens and correlating them with sequelae of congenital CMV infection such as

hearing, cognitive and vision delays collected during annual follow-up (for up to 4 years) as recorded in the participant's medical record and through hearing screening.

5. Develop and conduct (optional) additional activities to assess parental understanding and acceptance of newborn screening for CMV.

### **Evaluation and Performance Measurement**

1. Number and proportion of children delivered in the participating hospitals that are enrolled.
2. Number and proportion of enrolled children with DBS and saliva samples.
3. Number and proportion of enrolled children with valid DBS and saliva samples that have provided consent for collection of follow-up data from medical provider and valid provider contact information.
4. Number and proportion of enrolled children with valid CMV lab results who are assessed for sequelae at birth and receive annual clinical evaluations for CMV-associated delays.