HHS Action Plan to Prevent Healthcare-Associated Infections: RESEARCH

I. Introduction

A broad, comprehensive research agenda to support a national effort to prevent healthcare-associated infections (HAIs) needs to address the issue from a number of aspects. Increased understanding of the basic science underlying HAIs and their associated pathogens will be critical for informing prevention efforts. A coordinated research agenda needs to be developed in order to strengthen the scientific understanding of these infections. Research into the epidemiology of HAIs needs to be broadened. Gaps in the existing epidemiologic knowledge base should be identified with corresponding research projects targeted to fill those gaps.

To build upon an expanded understanding of the basic science and epidemiology of HAIs, the effectiveness of current infection control practices in hospitals should also be evaluated. New techniques to prevent HAIs need to be identified. Better implementation of existing practices is needed where the scientific basis for these practices already exists. Interventions that utilize technology to promote HAI prevention and provide clinical decision support, as well as the human and organizational factors affecting adoption of effective interventions in hospitals, need to be studied.

Specific projects for enhancing the implementation and impact of existing, evidence-based practices can then be identified, prioritized, and executed. Lastly, and perhaps most importantly, completely new and innovative approaches will be needed to combat current and emerging challenges related to these infections.

Thus, the two broad goals of the research portion of the initiative were to: 1) identify gaps in the existing knowledge base of current infection control practices in hospitals and, 2) develop a coordinated research agenda to strengthen the science for infection control prevention in hospitals.

II. Current State of the Art and Identified Gaps in Knowledge and Practice

A. Cross Cutting Issues

In preparation for identifying specific research areas, the working group identified gaps in the existing knowledge base of current infection control practices in hospitals. Several cross-cutting issues emerged:

1) Adherence to Current Prevention Recommendations Has Been Suboptimal

   Adherence to current prevention recommendations in healthcare settings has been generally suboptimal, even when knowledge of recommended practices

is sufficient. Several lines of evidence suggest that merely increasing adherence to *currently recommended practices* can result in a dramatic reduction in infection rates, at least for some infection types.

A better understanding of the barriers to adherence, and strategies to overcome those barriers, are needed to promote improvements such as the following:

a. The use of technology to improve adherence
b. Better understanding of human and organizational factors that affect adoption and implementation of effective strategies
c. Standardized methods (i.e., performance methods) that are feasible, valid, and reliable for measuring and reporting compliance with broad-based HAI prevention practices that must be practiced consistently by a large number of healthcare personnel (e.g., compliance hand hygiene, isolation precautions, environmental cleaning practices) in order to prevent infections

2) Demonstrating Preventability through Multicenter Demonstration Projects Has Proven to Be an Effective Strategy for Influencing the Widespread Adoption of Recommended Practices

Preventability is defined for this purpose as the proportion of all cases of a certain HAI that can be demonstrated as possible to prevent through the careful and concerted implementation of current or existing recommendations and/or guidance.

Recent multicenter demonstration projects involving large numbers of healthcare facilities working collaboratively to decrease HAIs by simultaneously implementing a multifaceted prevention program have been able to demonstrate, through standardized data collection, deep reductions in central-line associated bloodstream infections (CLABSIs) in ICUs.

These projects have answered important questions regarding the preventability of this particular infection type, and have likely directly influenced practice across the United States by setting new expectations for prevention. Additional prevention demonstration projects involving other targeted infections, such as surgical site infection, *Clostridium difficile* infection, and methicillin-resistant *Staphylococcus aureus*, would be helpful.

3) Limitations in Current Surveillance Strategies Exist and There is a Need to Use Electronic Data in Measuring Processes and Outcomes

A critical component of an effective prevention program is use of standardized process and outcome data as a means to inform those responsible for implementing the program and evaluate its impact. Unfortunately, many of

the current healthcare-associated infection surveillance strategies are labor intensive and subject to limitations as a result of poor inter-rater reliability in applying standard definitions and variable implementation of case-finding strategies.

In addition, current case-finding strategies are largely focused on identifying infections that are manifested during an inpatient stay or as a result of specific surgical procedures. Such strategies may not capture an important and potentially large proportion of healthcare-associated infections that, although the direct result of care delivered during an inpatient stay or in the ambulatory care setting, have their onset in the community.

Strategies that make use of existing electronic data sources for creating process and outcome measures may have a number of important potential advantages, including decreasing the burden of data collection, reducing error introduced by poor inter-rater reliability, and providing the ability to track adverse events longitudinally over the spectrum of a particular patient's healthcare delivery. More research on the use of electronic data for surveillance of healthcare-associated infections is needed.

4) Multicenter Collaborative Trials to Establish the Efficacy of Preventive Interventions are Needed

In addition to multicenter demonstration projects designed to document preventability using current or existing prevention recommendations, there is a need for additional multicenter collaborative trials that are carefully designed and conducted to establish the efficacy of new preventive interventions and further enhance our understanding of the efficacy of existing interventions.

5) Additional Research is Necessary to Strengthen the Scientific Basis for the Acquisition of Healthcare-Associated Pathogens

The scientific basis for the acquisition (including basic pathogenesis, transmission, and colonization) of numerous healthcare-associated pathogens is poorly understood. Many current practices are based on empiric observation. More biologically plausible preventive measures may be derived from additional basic, epidemiological, and translational research.

B. Issues Regarding the Specific Tier 1 Procedures and Organisms

The current state of the art and specific gaps in knowledge and practice across three areas:

1) Basic and/or Laboratory Science;
2) Epidemiology; and

3) Prevention Practices are presented for the following healthcare-associated infections:

   a. Central Line-Associated Bloodstream Infections
   b. Surgical Site Infections
   c. *Clostridium difficile* Infections
   d. Catheter-Associated Urinary Tract Infections
   e. Ventilator-Associated Pneumonia
   f. Methicillin-resistant *Staphylococcus aureus*

1) Central Line-Associated Bloodstream Infections (CLABSIs)

Current State of the Art Practice
Detailed recommendations on the prevention of CLABSIs have been developed by the Centers for Disease Control and Prevention (CDC) and Healthcare Infection Control Practices Advisory Committee (HICPAC).[1] Recent investigations have demonstrated that adherence to recommended catheter insertion practices are usually followed by a dramatic reduction in infection rates, suggesting that the preventable fraction of CLABSIs is large.

Efforts to implement "bundles" of catheter insertion practices have been quite popular in the intensive care setting, and although the rates of adherence are largely unknown, data from the National Healthcare Safety Network (NHSN) suggests that the rate of CLABSIs has been decreasing annually across all ICU types reporting data to that system. Although data suggest that the vast majority of CLABSIs occur outside of the ICU, precise data about catheter use and CLABSI rates in this setting, including among non-hospitalized patient populations, is sparse.

Current Gaps in Knowledge and Practice
- Basic and/or Laboratory Science
  - Biofilms and their relationship to the pathogenesis of device-associated infections
  - The prevention of biofilm formation or disruption/removal of biofilms in situ
  - Effective strategies and/or techniques for the early detection of CLABSI and for the differentiation of CLABSI from other bacteremias
- Epidemiology
  - A better understanding of CLABSIs occurring outside the intensive care unit is needed
  - Improved methods for surveillance that allow capture of adverse events associated with catheters regardless of patient location are needed
- Prevention Practices
  - What strategies could be developed to inhibit or destroy biofilms as a means of preventing device-associated infections?

[1] http://www.cdc.gov/ncidod/dhqp/gl_intravascular.html

- Use of antibiotic lock solutions: Are they effective? Are there unintended consequences (e.g., antimicrobial resistance)? Are there certain patient populations that should be targeted for this practice?
- What is the impact of daily chlorhexidine bathing on CLABSI rates, and does this practice lead to a shift in pathogens causing CLABSI by selecting for certain gram negative organisms that have intrinsic tolerance or antimicrobial resistance?
- What is the impact of chlorhexidine-impregnated sponge dressings?
- How should antimicrobial-impregnated catheters be optimally utilized?
- How do we optimize post-insertion catheter care?
- How do we assure that catheters are promptly removed when no longer clinically necessary?
- How do we optimize catheter care in non-hospitalized patients?

2) Surgical Site Infections (SSIs)

Current State of the Art Practice
Detailed recommendations on the prevention of SSIs have been developed by CDC and HICPAC.[2] Overall SSI rates have been relatively stable over recent years, although for some procedures, there has been a shift in pathogens for many cardiac and orthopedic procedures SSI [*Staphylococcus aureus* being the major pathogen, with an increasing proportion caused by Methicillin-resistant *Staphylococcus aureus* (MRSA)]. Adherence to current recommendations on the use of peri-operative antimicrobial prophylaxis is generally suboptimal.[3]

Current Gaps in Knowledge and Practice
- Basic and/or Laboratory Science
  - Biofilms and their relationship to the pathogenesis of infections following procedures involving implantation of devices
  - The prevention of biofilm formation or disruption/removal of biofilms in situ
  - The role of Nitric Oxide, innate adaptive immune response, cytokines, and endotoxemia in the pathogenesis of SSI
- Epidemiology
  - Surgical care has been shifting to the outpatient setting in recent decades and post-operative inpatient stays are becoming shorter. These trends raise challenges in detecting SSIs, as no standardized methods for post-discharge and outpatient SSI surveillance exist, and common approaches to case finding may be inadequate. There is data suggesting that SSI rates reported to the NHSN may be underestimated. More standardized methods for SSI case finding are needed, including those that are exportable beyond acute care to ambulatory care centers.

[2] http://www.cdc.gov/ncidod/dhqp/gl_surgicalsite.html
[3] Bratzler D, Houck P, Richards C, Steele L, Dellinger EP, Fry DE, Wright C, Ma A, Carr K, and Red L. Utilization of Antimicrobial Prophylaxis for Major Surgery: Baseline Results from the National Surgical Infection Prevention Project. *Archives of Surgery* 2005; 140:174-182.

  - There are limitations in current risk-adjustment strategies for comparing inter-facility surgical site infection rates. Better risk adjustment strategies are needed.
  - Most of the current prevention recommendations focus on pre- and intra-operative practices. Some recent data suggest that post-operative care may be important in determining whether or not a surgical incision becomes infected. A better understanding of post-operative risk factors for SSI might lead to an important new approach for SSI prevention.
- Prevention Practices
  - There is uncertainty as to how the trend towards increasing resistance among staphylococcal infections in cardiac and orthopedic procedures should influence optimal antimicrobial prophylaxis practices (e.g., when should vancomycin be included? Should other agents be used?)
  - The effectiveness of certain pre-operative prevention practices requires further study:
    - Pre-operative bathing with antiseptics;
    - Pre-operative screening for staphylococcal colonization and/or routine attempts to decolonize patients with antimicrobial agents prior to surgery;
    - Role of maintaining intra-and peri-operative normothermia;
    - Role of supplemental oxygenation during surgery;
    - Antimicrobial dosing in obese patients; and,
    - Determining whether antimicrobial strategies are different for surgery as compared with device implantation.

3) *Clostridium difficile* Infection (CDI)

Current State of the Art

As identified by CDC, CDI infection rates have been increasing in recent years, mostly due to transmission of a single, fluoroquinolone-resistant epidemic strain with enhanced virulence characteristics. Prevention strategies primarily focus on optimizing antimicrobial use, and in preventing transmission using basic infection control precautions. Since *Clostridium difficile* spores can persist on environmental surfaces, the role of environmental cleaning is likely to be important.

Current Gaps in Knowledge and Practice

- Basic and/or Laboratory Science
  - Role of immunity in preventing CDI and the most effective vaccine strategies
  - Evaluate for the presence of metronidazole resistance in *C. difficile* isolates
  - Role of the gut flora, precisely what component of the gut flora, is protective
  - Changes in the ecology of gut flora in the setting of cancer chemotherapy and antimicrobial therapy

  - Role of proctitis and/or nontoxigenic *C. difficile* in reestablishing gut flora ecology
  - Basic biology of the sporulation and germination of *C. difficile*
  - Development of valid animal models of *C. difficile*-associated diarrhea (CDAD)
  - Roles of Toxin B and binary toxin in pathogenesis
- Epidemiology
  - Better assessments of incidence/burden of CDI in the United States, including setting of onset and in relation to healthcare exposures
  - Methodology for measuring transmission and burden of CDI in non-acute care settings (e.g., long term care facilities)
  - Better understanding of the epidemiology of antimicrobial use in inpatient settings
  - Role of asymptomatic carriers in healthcare transmission is unknown
  - Role of *C. difficile* in neonatal/infant diarrhea
  - Better understanding of the incubation period before CDI develops after *C. difficile* acquisition
  - Relative importance of different sources of *C. difficile* transmission in the healthcare setting (e.g., environment versus healthcare workers) and in relation to CDI burden
  - Better understanding of CDI in the community
- Prevention Practices
  - Develop and assess the impact of a *C. difficile* environmental cleaning bundle, role of sporicidal agents (e.g., bleach)
  - Determine the role of extending duration of contact precautions beyond duration of symptoms in reducing transmission of *C. difficile* in healthcare facilities
  - Define optimal measures to reduce unnecessary antimicrobial use
  - Role of gastric acid suppression

4) Catheter-Associated Urinary Tract Infection (CAUTI)

Current State of the Art
Detailed recommendations on the prevention of UTIs have been developed by CDC and HICPAC.[4] Between 15% to 25% of hospitalized patients may receive short-term indwelling urinary catheters. In many cases, catheters are placed for inappropriate indications, and healthcare providers are often unaware that their patients have catheters, leading to prolonged, unnecessary use.

An estimate of annual incidence of HAIs and mortality in 2002, based on a broad survey of U.S. hospitals, found that urinary tract infections made up the highest number of infections (> 560,000) compared to other HAIs. Although morbidity and mortality from CAUTI is considered to be relatively low compared to other HAIs, the high prevalence of urinary catheter use leads to a large cumulative burden of infections with resulting infectious complications and deaths. In addition, bacteriuria

[4] http://www.cdc.gov/ncidod/dhqp/gl_catheter_assoc.html

frequently leads to unnecessary antimicrobial use, and urinary drainage systems are often reservoirs for multidrug-resistant bacteria and a source of transmission to other patients.

Current Gaps in Knowledge and Practice

- Basic and/or Laboratory Science
  - Biofilms and their relationship to the pathogenesis of urinary catheter-associated infections
  - The prevention of biofilm formation or disruption/removal of biofilms in situ
  - Effective strategies and/or techniques for the early detection of CAUTI
- Epidemiology
  - Quantification of the contribution of urinary tract infection and bacteruria to antimicrobial use
  - Role of urinary catheter systems as a reservoir for antimicrobial resistant bacteria and how different types of catheters affect the reservoir composition
  - Quantification of unnecessary urinary catheter use
- Prevention Practices
  - Role of newer catheter materials and technology in prevention of CAUTI
  - Appropriate catheter use in incontinent patients
    - Risks and benefits of periodic use of condom catheters in incontinent male patients
    - Risk of local complications (e.g., skin maceration, phimosis) with the use of condom catheters
    - Appropriate use of urinary catheters to manage skin breakdown in incontinent patients or nursing home residents
  - Role of antiseptics in preventing CAUTI (periurethral cleaning, methanamine)
  - Alternatives to indwelling urethral catheters and bag drainage (suprapubic catheters, urethral stent in bladder outlet obstruction, catheter valves)
  - Optimal methods for preventing encrustation in long-term catheterized patients who have frequent obstruction (catheter materials, irrigation, oral urease inhibitors, methanamine)
  - Use of portable ultrasound in patients with low-urine output to reduce unnecessary catheter insertions or irrigations (in catheterized patients)
  - Use of new prevention strategies in patients requiring chronic catheterization such as bacterial interference

5) Ventilator-Associated Pneumonia (VAP)

Current State of the Art

Detailed recommendations on the prevention of VAP have been developed by CDC and HICPAC.[5] The National Nosocomial Infections Study (NNIS) database from 1992 to 1997 demonstrated that VAP accounted for 27% of ICU infections in the 112

[5] http://www.cdc.gov/ncidod/dhqp/gl_hcpneumonia.html

participating ICUs. By 2008, VAP had become the most common nosocomial infection seen in the intensive care unit in several studies and is one of the major causes of severe healthcare-associated morbidity and mortality among ICU patients.

Unlike most other ICU infection syndromes that have relatively low mortality rates, the mortality rate for ventilator-associated pneumonia ranges in most studies between 20% to 50%. For patients hospitalized in the critical care unit, VAP contributes disproportionately both to poor outcomes as well as to substantially higher costs of care. Current approaches to preventing VAP rely on evidence-based strategies that minimize intubation, minimize the duration of mechanical ventilation, as well as minimizing the risk of aspiration of oropharyngeal pathogens.

Multiple resistant microorganisms are playing an increasingly important role in the pathogenesis of VAP, particularly among infections occurring after the first week in the ICU. These pathogens contribute significantly to the increased costs, morbidity, and mortality seen with this syndrome.

Current Gaps in Knowledge and Practice

- Basic and/or Laboratory Science
    - Gaps in knowledge about the pathogenesis of VAP lead to inconsistency of both definition as well as diagnosis of the syndrome
    - Biofilms and their relationship to the pathogenesis of ventilator-associated pneumonia
    - The prevention of biofilm formation or disruption/removal of biofilms in situ
    - Better understanding of the contribution of endotracheal tube composition to infection pathogenesis
    - Poor understanding of the role of various host factors in the defense against VAP
    - Evaluation of the effects of mucosal and pulmonary immunity on the prevention of VAP
    - The effect of inflammatory lung injury on the susceptibility to VAP
- Epidemiology
    - Lack of a clear understanding of the relative contributions of the large number of complex and confounding variables/risk factors that influence the development of VAP
    - Need a better understanding of the role of broad-spectrum antimicrobials in the development of VAP caused by multiple-resistant pathogens
    - Relationship of endotracheal tube-induced bacterial sinusitis to VAP
    - Understanding the natural tension between the need for adequate nutrition and the increased risk for aspiration and VAP associated with enteral nutrition
    - Identify and evaluate proxy measures for VAP (i.e., acute lung injury) for inter-facility comparisons that do not require stringent diagnostic approaches
- Diagnosis

    - No "gold-standard" diagnostic technique
    - Role of diagnostic bronchoscopy with culture
    - Role of various microbiological culturing techniques, including quantitative cultures
- Prevention Practices
    - Role of oral decontamination
    - Role of gastric decontamination
    - Secretion management/role of subglottic suction
    - Role of H-2 blockers and sucralfate
    - Role of positioning the patient
    - Degree to which less-invasive ventilatory support (e.g., CPAP, high oxygen therapy, even iron lung) could reduce the need for positive pressure ventilation via endotrachael tube or tracheostomy and whether this could improve overall outcomes
    - Role of antimicrobial impregnated endotrachael tubes
    - Impact of internal ventilator filters and ventilator breathing circuit filters on the risk of VAP
- Implementation
    - Impact of bundles for improving adherence

6) Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Current State of the Art
Methicillin-resistant *Staphylococcus aureus* (MRSA) remains an important cause of healthcare-associated infections, and is endemic in most US hospitals. In addition to adding to the total burden of *S. aureus* infection, healthcare-associated MRSA infections are associated with increased morbidity and mortality when compared to infections caused by methicillin-susceptible strains. MRSA has also emerged as an important cause of infection in the community. 59% of all purulent skin infections evaluated in U.S. emergency departments are caused by MRSA. MRSA infections, both healthcare- and community-associated, are generally caused by a very limited number of strains, suggesting that most cases result from direct or indirect person-to-person transmission of MRSA.

It is widely held that the major reservoir for transmission in the healthcare setting is infected or colonized patients, and that patient-to-patient transmission occurs indirectly via transient carriage by healthcare personnel or through contaminated shared equipment. In 2005, there were an estimated 94,000 invasive MRSA infections in the United States. These were associated with nearly 18,000 deaths. Of these invasive infections, 86% were associated with healthcare delivery, and two-thirds of the healthcare-associated infections had their onset outside the hospital setting.

Although the optimal strategy for prevention and control of healthcare-associated MRSA has not been fully determined, it seems likely that successful control requires a multifaceted approach that may vary according to individual characteristics of a

healthcare facility, as outlined in the CDC guidance document "Management of Multidrug-resistant Organisms in Healthcare Facilities, 2006."[6]

Current Gaps in Knowledge and Practice

- Basic and/or Laboratory Science
  - Effective vaccine target antigens
  - Determinants of colonization/carriage (host, organism, environment)
  - Host determinants in the development of invasive versus soft tissue disease
  - Virulence facts associated with MRSA HAI
- Epidemiology
  - Better understanding of colonization and transmission dynamics within the healthcare setting
    - Are there patient characteristics that influence their risk of serving as a reservoir of transmission?
    - Are there patient characteristics that influence the risk of acquiring MRSA carriage?
  - Better understanding of the inter-relationship of healthcare facilities within a region or system in sustaining transmission
  - Better understanding of the impact of community MRSA emergence on healthcare-associated MRSA infection
  - Preventability of endemic MRSA colonization/infection
  - Better understanding of the epidemiology of healthcare-associated MRSA infections that have their onset outside of hospitals
  - Role of fomites in the healthcare-associated transmission of MRSA HAI
- Prevention Practices
  - What is the impact (both intended and unintended) of suppressing or eradicating colonization for the purpose of either preventing infection in colonized individuals or preventing transmission to others?
  - What is the optimal role for active surveillance for detecting asymptomatic carriage?
  - How can transmission be measured? (i.e., how does a healthcare facility know when it is effectively preventing transmission?)
- Implementation
  - Optimal approach to antibiotic-use controls

III. Criteria for Setting Research Priorities

In order to identify a set of initial research projects that would result in the highest overall impact on the HAI of interest and therefore should be given high priority in the near-term, criteria was addressed that took into account both existing knowledge and gaps that, if addressed, would allow more effective interventions to reduce the impact of an individual HAI.

[6] http://www.cdc.gov/ncidod/dhqp/pdf/ar/mdroGuideline2006.pdf

Four major criteria were addressed when evaluating proposed projects:

1) Contribution to Understanding
    - Will the project fill a knowledge gap?
        Prevalence or Epidemiology: Known/Unknown
        Severity: Known/Unknown
        Mechanism of Disease or Infection: Known/Unknown
        Effectiveness of Present Intervention: Known/Unknown
    - What level of evidence will the project yield? Will the evidence likely change behavior?

– Evidence → Weak
  → Strong → Compliance
  → Non-compliance → Barriers to compliance

    - Will the project impact be long- or short-term?

– Demonstrated impact → Short-term
  → Long-term

    - Will the evidence be generalizable?
    - Will the project lead to sustainable changes in behaviors, infections, or costs?

2) Feasibility
    - Are resources (human, technologic, technical, etc.) available to perform the project?
    - Is there an ability to leverage resources?
    - Will the proposed research intervention be scalable to other environments?
    - Will the proposed study lead to interventions that could potentially reduce burden?

3) Cost
    - Are the costs of the project justifiable for the potential health impact?

4) Public Impact
    - Are the project results easily understood and of value to policy-makers?
    - Are the impacts of projects on the general public easily understandable?
    - Is the impact measured in cost, quality of life, redirected resources, etc.?

IV. Proposed Initial Priority Research Projects

In order to develop a list of the research projects that should be given the highest priority for possible initial investment, the gaps in knowledge and practice outlined in Section II were each considered in the context of the criteria for setting research priorities discussed in Section III.

The following list of high priority research projects emerged from that process and represents a research portfolio that addresses gaps in basic science, epidemiology, practice, as well as each of the priority infection types identified by the HHS Steering Committee for the Prevention of Healthcare-Associated Infections. These initial priority projects should not be construed as sufficient to adequately address all HAI prevention research needs, but rather an *initial step* in what should be an ongoing, long-term approach to research that enables continuous learning of HAI prevention.

The scientific understanding of HAI prevention is rapidly evolving, and therefore the *next steps* in HHS-supported research should be determined after consideration of information and knowledge gained from these initial projects and other ongoing research efforts. These determinations should be made on a rolling basis by an interagency group (see Section V).

Recommendations on Projects:

- Projects that Address Specific Knowledge Gaps (Basic Science, Epidemiology, and Practices)

    a. Basic Science
        i. Design and implement broad-based studies that define and clearly delineate the pathogenesis of device-associated infection
        ii. Develop strategies for preventing and/or eliminating biofilms associated with medical devices

    b. Epidemiology
        i. Perform studies of the epidemiology of bloodstream infections that occur outside of the hospital, including those related to hospitalization. These studies would include an assessment of patient characteristics and risk factors for bloodstream infection that could lead to new prevention strategies.

        ii. Establish preventability
            1. Establish preventability of CDI through a regional hospital collaborative intervention to reduce endemic rates through employment of tiered evidence-based recommendations (e.g., transmission reduction and risk reduction through antimicrobial stewardship), peer-to-peer learning, and

standardized electronic collection and feedback of CDI rate data using the NHSN to assess impact

2. Establish preventability of unnecessary antimicrobial use through a multi-center collaborative intervention. These efforts could include coordinated development and implementation of clinical diagnosis and antimicrobial use paradigms in the treatment of CAUTI and VAP, as well as in the prevention of SSI (i.e., surgical antimicrobial prophylaxis) with the aim of reducing overall antimicrobial use.
3. Establish preventability of SSI through a multi-center collaborative intervention to reduce rates. These efforts could include coordinated development and implementation of strategies to implement existing evidence-based recommendations, peer-to-peer learning, and standardized electronic collection and feedback of SSI rate data using the NHSN to assess impact.

c. Practices
   i. Perform a large, simple, cluster-randomized study to assess whether ICU-wide application of a MRSA decolonization strategy is effective at reducing healthcare-associated infection and mortality compared to targeted decolonization strategy guided by active surveillance for MRSA colonization

- Projects Designed to Enhance the Implementation and Impact of Existing, Evidence-Based Infection Control Practices

d. Multidisciplinary investigation of the human cultural and organizational barriers at the unit and institutional level that inhibit the successful implementation of prevention measures

e. Improving measurement to support and evaluate prevention practices
   i. Perform studies to develop and evaluate novel and potentially automatable strategies for measuring healthcare-associated infections, transmission of epidemiologically important pathogens, and related processes of care using electronic data sources routinely captured during the course of patient care
   ii. Evaluation and validation of standardized post-discharge surveillance methodology that can be used in both inpatient and ambulatory care settings
   iii. Identify and evaluate proxy measures for VAP (i.e., acute lung injury) for inter-facility comparisons that do not require stringent diagnostic approaches
   iv. Develop standardized methods (i.e., performance methods) that are feasible, valid, and reliable for measuring and reporting

compliance with broad-based HAI prevention practices that need to be practiced consistently by a large number of healthcare personnel (e.g., hand hygiene, isolation precautions, environmental cleaning practices)

V. Long Term Prioritization, Coordination, and Evaluation of Research Efforts

Highlights of the broad areas of current HAI-related responsibilities for the HHS components involved in the Plan's development are illustrated in Appendix C.

Addressing the longer term research needs for healthcare-associated infections for the nation will require a coordinated effort across the Department and with external stakeholders. Many agencies within the Department such as the Agency for Healthcare Research and Quality (AHRQ), CDC, Centers for Medicare and Medicaid Services (CMS), and National Institutes of Health (NIH) have funded research to address healthcare-associated infections and their underlying causes. However, no mechanism currently exists to coordinate these efforts.

Research on the basic science, epidemiology including risk factors, testing of prevention methods and implementation of evidence-based practices, and effects of payment and coverage policy should be linked, so findings from each area can inform and build upon findings in the other areas. For example, if CDC finds a potential population or setting a risk factor for a healthcare-associated infection, this information could help establish potential priorities for AHRQ-funded research on prevention or implementation of evidence-based practices. Synergies will also emerge, i.e., AHRQ could fund research assessing the effect of a CMS change in payment policy or NIH findings could point toward a potential CDC-funded prevention strategy. This coordination will reduce potential duplication and enhance the impact of each agency's work.

Specifically the following mechanism for coordination is proposed:

The Healthcare-Associated Infections Research Working Group is chartered and meets quarterly. This group would have at least two representatives from AHRQ, CDC, CMS, and NIH and representatives from other HHS Operating and Staff Divisions or federal agencies, as needed. The committee would have three main objectives:

1) Coordinate and prioritize research efforts to reduce healthcare-associated infections nationwide

2) Design a plan and metrics for evaluating progress within the research domain to address healthcare-associated infections

3) Serve as a contact point to communicate to external stakeholders on this issue so HHS's efforts are coordinated and linked to a broader national coalition

The proposed Healthcare-Associated Infections Research Working Group should set up criteria and a plan for evaluation of the HHS research program to address healthcare-associated infections. The evaluation should assess the research program and the projects it has specifically funded. Metrics of accomplishment could include documented improvements in care, published articles, dissemination of findings through conferences or other means, or other research products.

It is important to note that successful research may demonstrate negative results or bring up more questions as well as demonstrate effective interventions. The Research Working Group will set up a priori criteria to evaluate the Department's research program on HAIs and a plan for the timing of evaluation, such as annually. The evaluation of the program should lead to adjustments to the program in subsequent years.

VI. Conclusion and Vision for the Future: Creating a Learning Healthcare System in the United States

The large knowledge gaps that exist in HAI prevention are, in part, the result of barriers to new generation of knowledge that currently exit in U.S. healthcare. In a background paper developed and presented at an Institute of Medicine workshop sponsored Roundtable on Evidence Based Medicine and entitled, "Leadership Commitments to Improve Value in Health Care," Platt and colleagues argue that evidence generation, i.e., *learning what works and what does not*, should be established as a normal part of health care in the U.S.

The authors outline major challenges confronting the development of knowledge to support the learning healthcare system. These include: 1) Limited investment for research and development towards understanding how well various strategies work in practice, or how to assure that the right preventive or therapeutic regimen is offered to individuals who need it; 2) Difficulty in using much of the existing data, even when it exists in electronic form, because of fragmentation among organizations that control the data, variation in the way different organizations interpret the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, Institutional Review Boards' varying interpretations of regulations governing the use of these data for research, and proprietary concerns of data holders; 3) Important limitations in the quality and generalizability of the existing data; and 4) Lack of a full understanding of the strengths and weaknesses of the different research methods, ways in which to strengthen them, and the situations in which they are best applied.

While knowledge gaps do exist, there is much that has been accomplished. The research plans proposed in this section have begun to identify the gaps in the existing knowledge base of current infection control practices in hospitals, a necessary first step in the process to develop a coordinated research agenda that will strengthen the science for infection control prevention practices in hospitals. It is critical that we understand why adherence to current HAI prevention recommendations has been suboptimal, that we

fully understand the specific limitations that exist in current surveillance strategies, and that we have explored how electronic data can be used to measure process and outcomes.

The proposed research projects address the gaps identified in the basic sciences, epidemiology, practices, and the priority infection types identified in the first phase of the initiative. They lay the foundation for further steps that will be informed by the results of the initial projects and other ongoing research. An ongoing challenge will be the identification of projects that will enhance the implementation and impact of existing evidence-based infection control practices. The Department is committed to collaborating within HHS and with external stakeholders to assess current research methods, funding levels, information technology use, and researcher training and to present solutions to facilitate and accelerate knowledge generation. The overall goal is to support the research required to aggressively combat healthcare-associated infections and protect the safety of all Americans.