# The Respiratory Protection Effectiveness Clinical Trial

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# Incidence of Respiratory Illness in Outpatient Healthcare Workers Who Wear Respirators or Medical Masks while Caring for Patients

***The Respiratory Protection Effectiveness Clinical Trial: The ResPECT Study***

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# A Introduction

## *A1 Study Abstract*

Prevention strategies are key in limiting the transmission of respiratory pathogens such as influenza. Among non-pharmacologic interventions, there is intense interest in the use of facial protective equipment (FPE) – medical masks (MMs) or N95 respirators (N95s) - as a key component of personal protective equipment (PPE) when faced with seasonal influenza, epidemic or pandemic respiratory illness. Patient isolation, cohorting, and healthcare personnel (HCP) use of PPE, including FPE, have been found important. However, their relative protective effect is unknown, especially in the outpatient setting. In 2003, the Severe Acute Respiratory Syndrome (SARS) outbreak and the role of healthcare-associated transmission stimulated a series of evaluations examining which interventions were critical in decreasing spread of this respiratory virus among HCPs. While data emerged supporting the use of respirators for procedures with a risk of extensive exposure to respiratory secretions, the need for such respiratory protection outside of these settings was not adequately studied. Studies from epidemic respiratory illness season in the healthcare setting are missing and recommendations for respiratory protection among HCPs are controversial and not evidence-based. Public health groups and healthcare delivery organizations are uncertain about appropriate respiratory protection for HCPs in the event of an influenza pandemic or other infectious diseases epidemic. To plan for such an eventuality and to best manage limited supplies of FPE, evidence is needed to guide planning activities and policy makers. This project aims to answer a key question about FPE use: How do respirators (N95s) protect HCPs in the outpatient setting against influenza, influenza-like illness, acute respiratory illness, and other respiratory infections and illnesses, as compared to medical masks (MM)? This study will have the following outcomes:

- An analysis to determine the more effective facial protective equipment, N95s or MM, to prevent disease transmission in the outpatient setting during a seasonal influenza outbreak, epidemic or pandemic event.
- An analysis of the incidence of organism-specific rates of respiratory pathogen infections and illnesses in the outpatient setting during influenza season.
- Occasional secondary analysis that use de-identified or limited data sets from the ResPECT database to support the central objectives of the study and to extend the scope of the project.

## *A2 Primary Hypothesis*

***Null Hypotheses:*** The incidence of (1) laboratory confirmed influenza (LCI) or (2) influenza-like illness (ILI), acute respiratory illness (ARI), laboratory confirmed respiratory illness (LCRI) and laboratory detected respiratory infection (LDRI) *will not be* different between HCPs who practice 2007 guidelines (medical masks) or 2009 guidelines (N95 respirators).

***Alternative Hypothesis:*** The incidence of (1) laboratory confirmed influenza (LCI) or (2) influenza-like illness (ILI), acute respiratory illness (ARI), laboratory confirmed respiratory illness (LCRI), and laboratory detected respiratory infection (LDRI) *will be* different between HCPs who practice 2007 guidelines (medical masks) or 2009 guidelines (N95 respirators).

# B Background

## *B1 Prior Literature and Studies*

**Introduction:** Despite widespread use of respiratory protective equipment in the U.S. healthcare workplace, there is limited and inconclusive clinical evidence that respirators prevent HCP from airborne infectious diseases. Scientific investigation of this issue has been quite complicated, primarily because the use of respirators has become "the standard of care" for protection against airborne diseases in some instances, even without sufficient evidence to support their use. The key question remains: How well do respirators prevent airborne infectious diseases? The answer to this important question has medical, public health, political and economic implications.

Key challenges posed by this gap in knowledge include an uncertainty among public health groups and healthcare delivery organizations about appropriate respiratory protection for HCPs who care for patients with confirmed or suspected respiratory infections. This lack of knowledge posed pragmatic challenges and became source of controversy during the 2009 H1N1 influenza pandemic and stands to hold equal or greater significance in the event of a future pandemic.

This study aims to determine the relative effectiveness of two interventions, medical masks and N95 respirators, to protect HCPs against influenza and other respiratory infections. This will be among the first studies to compare respirators to medical masks in high-risk outpatient settings. HCPs in outpatient settings are more likely to come into contact with more patients with influenza, are more likely to experience higher numbers of sick HCPs, and are more likely to show an epidemic curve of influenza infections that is representative of the community at large. The primary study goal is to determine whether there are differences in the incidence of laboratory-confirmed influenza when healthcare workers wear respirators or medical masks while caring for patients in the outpatient setting. As secondary outcomes, we will also determine whether there are differences in the incidence of ILI, ARI, LCRI, and LDRI Indirectly, this project may also help gain understanding about modes of viral transmission, because respirators presumably prevent airborne transmission while medical masks do not.

Bacterial superinfection is a common, morbid, and potentially mortal complication of influenza (Chertow, 2013). Autopsy studies demonstrated bacterial infection in nearly all deaths resulting from the 1918 influenza pandemic. During the 2009 H1N1 influenza pandemic, bacterial superinfection complicated 55% of fatal cases. Palacios *et al* found that presence of *S. pneumoniae* in a nasopharyngeal swab specimen correlated with severe disease in previously healthy, low risk patients with 2009 pandemic strain influenza (Palacios 2009). There is clinical concern for bacterial superinfection after other respiratory virus infections, but the supporting evidence is limited (Randolph 2004). As noted, the data on bacterial superinfection is gleaned largely from autopsy series and cases of severe disease. Less is known about the events occurring early in bacterial colonization and infection of humans with influenza.

Colonization of the nares or pharynx with *Streptococcus pneumoniae, Staphylococcus aureus, Hemophilus influenzae, Streptococcus pyogenes*, and other bacterial pathogens is presumed to be the antecedent to infection (Wertheim 2005; Simell 2012). Changes in the resident microbiota following viral infection may present an opportunity for more pathogenic bacteria to invade. To date, studies of bacterial superinfection have focused on the epidemiology of multiple pathogens, or on the pathophysiology of single pathogens. We propose to characterize the bacterial communities of the nares and oropharynx in healthy subjects prior to, during, and after natural infection with influenza and other respiratory viruses. We will use culture independent methods to comprehensively profile bacterial diversity in all specimens.

The Veterans Health Administration (VHA) and the Centers for Disease Control and Prevention (CDC) have a vested interest in the results of this clinical trial, with both providing funding and sharing resources for its implementation. The CDC is charged with providing guidelines to protect HCPs from infectious diseases while the VHA employs a large population of HCPs. The results stand to have broad health policy implications that will reach well beyond the funding organizations on a global scale. The Johns Hopkins University (JHU) (Baltimore, MD) served as the initial Data Coordinating Center (DCC) for this clinical trial. We will transfer the DCC to the University of Texas Southwestern Medical Center (Dallas, TX) where the co-Principal Investigator (TMP) is now on staff.

**Historical Context:** Influenza, respiratory syncytial (RSV), coronavirus and other respiratory pathogens lead to serious complications resulting in substantial morbidity and mortality, especially among the frail and chronically ill. Human-to-human spread of respiratory diseases can be explosive for several reasons, including the transmission characteristics of these viruses, the population density of ill patients in healthcare settings, the types of exposures within healthcare settings, and the administrative and physical structure of healthcare facilities. These influences on transmission were evident during the 1918 influenza pandemic and became increasingly evident during the 2009 H1N1 influenza epidemics and the 2003 SARS outbreak (caused by a coronavirus). Additionally, patients in healthcare facilities who acquire influenza, RSV and other respiratory viruses, suffer increased morbidity and mortality. During the pandemic of 1957, influenza A impacted a Chicago hospital, causing one-third of the patients and staff-members on affected units to become ill with influenza. Leclair *et al.* found that the incidence of nosocomial RSV increased with the intensity of hospital exposure. Sartor and colleagues describe a small outbreak on a 23-bed internal medicine unit where 41% of the patients and 23% of the HCPs developed influenza. The authors noted that 14 person-days of

sick leave occurred, 8 scheduled admissions were canceled and all emergency admissions were canceled for 11 days. Keech and colleagues found that people with influenza and ILI were confined to bed an average of 2.4 days, missed 2.8 days of work, and took a mean of 3.5 days after the onset of symptoms to resume normal activity. Costs of outbreaks are difficult to truly estimate, but the outbreak reported by Sartor *et al*. cost $34,179, approximately $3,798 per patient. Estimates also suggest that students miss about 22 to 189 million school days annually due to upper respiratory illnesses, commonly called "colds". Accordingly, parents miss about 126 million workdays annually to stay home and care for their ill children. Together, the total economic impact of cold-related work loss exceeds $20 billion per year.

While most clinical studies suggest influenza is transmitted from person-to-person via large respiratory droplets, several recent exhaustive reviews of the world's literature suggest routes of transmission are variable, depending on virus characteristics, host-virus interactions, and environmental conditions. Many studies indicate that that the predominant mode of transmission is via large droplets that are generally greater than 10 microns in diameter, remain suspended in the air for short periods of time, and are not typically inhaled into the trachea or lower into the pulmonary tree. Still, other modes of transmission may also occur, including contact and small droplets (sometimes called aerosols) that are generally less than 10 microns in diameter, typically remain airborne for longer periods of time as "droplet nuclei," and may be inhaled deep into pulmonary tree. In addition, this later form of transmission may be more likely in the setting of procedures which potentially aerosolize secretions.

It is generally agreed that the predominant mode of transmission for most other contagious respiratory pathogens, such as RSV and corona virus, is via large droplets, with small droplets (aerosols) playing a much smaller but clinically significant role. Indirect contamination from the environment (e.g., fomites) or direct contact contamination (e.g., hand-to-hand or hand to conjunctiva) may also be important with many respiratory pathogens.

**Prevention Strategies:** Healthcare facilities face challenges in preventing transmission to HCPs who are exposed to infectious patients, colleagues and family members. Unfortunately, some pathogens, including influenza, can be transmitted when the infectious person is asymptomatic, although symptomatic transmission is believed to be the more common route. The timing of when transmission is most likely to occur has not been defined for many respiratory pathogens.

For many of these pathogens, vaccines or chemoprophylaxis may not be available, requiring institutions to use other infection prevention techniques. Recommended prevention and control methods for the pathogens in this study include both primary strategies (e.g., vaccination, chemoprophylaxis, use of barriers), when available, and secondary strategies (e.g., hand hygiene, isolation, environmental disinfection, screening and cohorting). Nonpharmacologic interventions are promoted by many public health organizations and guidelines include the use of hand hygiene, patient isolation, and respiratory etiquette. The

challenge for infection prevention and control and public health emergency experts is in making data-driven and cost-effective recommendations to prevent transmission in a variety of healthcare settings. Hence, key areas of interest for healthcare epidemiologists and policy makers include (1) determining the most appropriate types of PPE for HCPs, (2) delivering data to HCPs that will help convince them to comply with infection control recommendations, and (3) actually implementing FPE usage, taking economic, logistical, and occupational factors into consideration. The first issue is central to determining policy recommendations at institutional, national and international levels. At a local level, these decisions determine planning and supply chain needs for healthcare facilities for both seasonal and pandemic respiratory viral outbreaks.

Among non-pharmacologic interventions, there is continued interest in the use of "facemasks" as a key component of personal protective equipment (PPE). While masks were used in the Middle Ages (between the approximate years of 400 and 1500 A.D.) to prevent transmission of plague, it was not until the mid-1980's that Hall *et al.* demonstrated that the use of masks and goggles decreased healthcare-associated transmission of RSV. Control measures for influenza in long term care settings have focused primarily on two methods: immunoprophylaxis for generally healthy HCPs and chemoprophylaxis for patients. Still, the importance of patient isolation, cohorting, and use of FPE by HCP including eye goggles or faceshields and masks is widely recognized and practiced.

**Gaps in Knowledge:** The relative importance of facemasks (medical masks), respirators and contact precautions (without masks or respirators) has not been definitively proven, prompting disagreement and controversy in the scientific and health policy communities. In 2003, SARS and the role of healthcare-associated transmission stimulated a series of evaluations to identify which interventions had been critical in decreasing spread of the SARS coronavirus among HCPs. Jefferson *et al.* summarized studies that evaluated the utility of non-pharmacologic interventions used during the SARS epidemic. Transmission was reduced 55% by frequent hand hygiene, 78% by wearing masks, 57% by wearing gloves and 77% by wearing gowns. Still, with only one exception, these studies did not determine the protective effect of N95 respirators relative to other types of prevention; the word "masks" were either undefined or represented by multiple types of medical masks and respirators. One study that is often cited as showing a statistically significant decrease in infections with N95 respirators had such small subject numbers and so few measured events that drawing definitive conclusions is not warranted.

In 2007, the World Health Organization (WHO) proposed draft guidance recommending a complement of strategies that included the use of medical masks for many respiratory pathogens, including novel influenza strains and the SARS coronavirus. These recommendations were based on the experiences of several countries to prevent and control SARS infections and the lack of data showing superiority of respirators compared to medical masks. Data emerged from the SARS events supporting the use of respirators for certain procedures, such as intubations, which are known to produce aerosols of respiratory secretions. While these data were valuable, they focused narrowly on infection control measures for SARS. Similar studies are needed in the setting of other pathogens, such as influenza.

MacIntyre and colleagues recently published a prospective cluster-randomized trial that compared medical masks and non–fit-tested respirators to standard practice (no masks) in

preventing ILI in households (MacIntyre *et al*. 2009). Among 286 adults, from 143 households, who were exposed to children with clinical respiratory illness, self-reported adherence to mask or respirator use significantly reduced the risk for ILI-associated infection, but only in the subset of the population reporting adherence to mask or respirator use. However, adherence with mask or respirator use was poor; <50% of participants wore masks or respirators most of the time as instructed. Across the entire study population, including those who were not adherent, the authors reported that household use of face-masks or respirators was low and ineffective for controlling seasonal respiratory disease. What is not known, however, is whether the observed ineffectiveness was due to non-compliance or insufficient respiratory protection from medical masks. Unfortunately, new knowledge gained from completion of this Australian study was limited. This study lacked the power to compare any effects of masks with those of respirators. Thus, it was not informative on this issue.

MacIntyre *et al*. also conducted a study among 1936 front-line hospital HCPs in Beijing, initially reporting that use of N95 respirators was significantly more effective than use of masks in preventing clinical respiratory illness (MacIntyre *et al*. 2011). However, due to low outcome incidence, the study lacked the power to address influenza, either from the standpoint of laboratory-confirmed respiratory viral infection, clinical respiratory illness, and influenza-like illness. It was also initially reported that fit-testing did not improve N95 effectiveness, perhaps because a large proportion of the population was documented to have a good fit with the initially-chosen respirator. However, the authors later retracted their findings, citing methodological, analytic, and sample size limitations.

The most recent research continues to fuel the debate over appropriate prevention against influenza and respiratory pathogens. Loeb *et al*. (2009) conducted a trial comparing influenza rates among 446 Canadian nurses individually randomized to wear either an N95 respirator or a surgical/medical mask, finding that masks were no less effective at preventing laboratoryconfirmed influenza than N95 respirators. However, nurses randomized to the use of masks did experience a strong trend ($p = 0.06$) towards higher level of influenza-like-illness and a statistically significantly higher level of fever ($p = 0.007$) compared to those wearing N95s.

Although the Loeb study found no significant differences in the prevention of laboratoryconfirmed influenza, many of the cases were identified by serology and the majority of serologically detected cases were asymptomatic. A main goal of proper FPE usage is the prevention of symptomatic influenza, resulting in the current study's emphasis on obtaining data quickly on symptomatic individuals. Loeb et al. acknowledged frequent non-occupational (*e.g.,* home and community) exposures to influenza-like illness in both arms, but no analysis was done to assess the levels of risk associated with these home exposures. Additionally, Loeb *et al.* conducted their study in a cohort of HCPs with relatively low influenza vaccination rates, did not directly assess exposure risks by quantifying nursing contacts with patients with febrile respiratory illness, and was unfortunately terminated prematurely (April 23, 2009) when, in

response to growing concern about the H1N1 outbreak, the Ontario Ministry of Health and Long Term Care recommended N95 respirators for all HCPs caring for patients with febrile respiratory illness.

Perl & Srinivasan's (2009) simultaneously published editorial in JAMA stressed that the lack of clinical trials on the transmission of influenza hampers the appropriate authorities from making definitive recommendations for PPE. Two cluster randomized trials of medical masks versus N95 respirators in healthcare settings have been performed in Beijing, China. The first trial (McIntyre 2011) was conducted from December 2008 to January 2009 and enrolled 1441 healthcare workers. The second trial (McIntyre 2013), conducted from December 28, 2009 to February 7, 2010 enrolled 1669 healthcare workers. These trials found no significant difference between groups assigned to medical masks or N95 respirators for ILI or laboratory confirmed influenza. The incidence of influenza during the study periods was low, limiting the power of the trials to identify significant differences. A meta-analysis (Smith 2013) of the three available RCTs also identified no significant difference in influenza like illness or laboratory confirmed influenza.

Importantly, based upon numerous laboratory studies, most scientists believe that N95 respirators provide superior prevention because of their tight facial fit design and generally higher filtration efficiencies. After all, respirators are designed to reduce exposure to small, inhalable particulates while medical masks are not. However, considering all published studies to date, the clinical data produced thus far by the public health and medical communities from across the world have been inconclusive. One possibility that may help explain this gap between expectations and contemporary clinical evidence is pragmatic in nature: HCPs, in general, may not tolerate respirators as well as medical masks, prompting them to remove respirators for longer periods and/or more frequently, possibly increasing the likelihood of exposure and infections. Of note, removing respiratory protective equipment in this fashion is often in violation of public health and institutional guidelines (non-compliance). Importantly, in the context of this limitation with respirators, it is conceivable that medical masks could provide the same or higher levels of protection than N95 respirators.

Unfortunately, clinical trials conducted in real patient-care environments during a respiratory virus epidemic ("flu season") are lacking. Accordingly, the public health recommendations for respiratory protection among HCPs are, in part, based on expert opinion, sometimes leading to controversy. A key challenge posed by this gap in knowledge includes uncertainty about appropriate respiratory protection for HCPs in the event of seasonal or pandemic influenza. To plan for such an eventuality and to be able to best manage limited supplies of respirators, evidence is needed to guide policy developers and decision-makers. One of the most important lessons learned from the SARS crisis was the importance of protecting HCPs with appropriate personal protective equipment. It is important to recognize that in Toronto, a SARS commission convened by the Canadian government found that 72% of SARS cases occurred in a hospital setting, 43% of cases involved HCPs, and of the 100 healthcare providers who became infected with SARS, three died. Since this time, Suwantarat *et al.* found that another coronavirus causing Middle Eastern Respiratory Syndrome (MERS) has been associated with significant transmission to HCPs, further supporting the importance of solving this issue. Transmission in several settings in Middle East settings has resulted from conflicting recommendations issued by Public Health

authorities including the CDC and WHO. What remains to be answered for the vast majority of pathogens is what type of protection is most appropriate.

## ***B2 Rationale for this Study:*** *THE 2009-10 H1N1 INFLUENZA PANDEMIC*

During the 2009-10 H1N1 influenza pandemic, the use of respiratory protection became one of the most frequently discussed and debated topics. Many healthcare organizations found themselves without sufficient N95 respirators to meet national and/or local guidelines for use. Perhaps worse was a highly variable difference in the number of N95 respirators stockpiled by organizations; some hospitals had many and others had few. The uncertainty and lack of evidence-based respiratory protection policies, in part, caused organizations to prepare differently, resulting in disparate levels of access to N95 respirators and, in some cases, interference with healthcare operations.

In in midst of the 2009-10 H1N1 influenza pandemic, the WHO recommended in most instances the use of medical masks for HCPs exposed to H1N1-infected patients (except during aerosolgenerating procedures), while the CDC took a somewhat contradictory stance, recommending instead that HCPs wear N95 respirators in most instances. The notoriety of this contradiction increased when many state and local health departments in the U.S. sided with the WHO. In an open letter published on November 5, 2009, the Society for Healthcare Epidemiology of America (SHEA), IDSA, and the Association for Professionals in Infection Control and Epidemiology (APIC) jointly expressed their dissatisfaction with the CDC position. Increasing the controversy, the National Academy of Sciences Institute of Medicine (IOM) issued findings from a consensus meeting that called for (a) HCPs to favor N95 respirators over medical masks for novel H1N1 influenza and (b) intensive research without delay to determine which is more effective. Although the CDC initially recommended and later reiterated its position that medical facilities should favor the use of N95 respirators, on a practical level, large sectors of the US healthcare workforce continued to essentially ignore these guidelines, wearing medical masks, and in some instances no protection.

In October 2009, The CDC issued Interim Guidelines that addressed the insufficient supplies of N95 respirators in many settings. This updated guidance recommended that supply shortages should prompt prioritization of FPE usage at the institutional level, calling for HCPs to wear devices at least as protective as N95 respirators in high-risk settings such as when performing aerosol-generating procedures. In lower risk settings when there were clear shortages or impending shortages of respirators, facilities were permitted to use medical masks as a primary means of HCP protection against influenza. Facilities were advised to make a “good faith” effort to procure an adequate supply of respirators, and continue to implement a hierarchy of controls, including source control, engineering, and administrative measures, encourage vaccination, and continue other work practices recommended by the CDC.

In July 2010, CDC guidance was modified to call for U.S. HCPs to wear an N95 respirator when coming into close contact with patients who were, or may have been, infected with 2009 H1N1 influenza. This modification occurred after CDC posted in the Federal Register a notice that proposed a change such that (a) medical masks would be the primary means of respiratory protection worn by HCPs against influenza while (b) devices at least as protective as N95 respirators would be worn by HCPs who perform (or help perform) procedures that produce bioaerosols (e.g., intubation, suction). The 2009 H1N1 pandemic was officially declared over on August 10, 2010 by the CDC, rescinding the previous recommendations that were applicable only during the 2009 pandemic. As a result, N95 respirators are no longer required as the primary means of protection against influenza, per CDC recommendations. All HCPs are no longer required to wear N95 respirators when interacting with patients with confirmed/suspected influenza, allowing the current study to proceed. Subsequently, the CDC guidelines have remained largely unchanged. Patients with respiratory pathogen symptoms should be provided with medical masks as soon as they enter a healthcare setting, HCPs should don a medical mask when entering the room of a patient with suspected or confirmed influenza, and HCPs performing aerosol-generating procedures should wear an N95 or equivalent. If facilities or organizations wish to provide a different type of FPE (e.g. to meet evolving CDC guidance and local policies) than the standard medical mask, it should at least provide the same protection of the nose and mouth as a facemask (e.g., N95, PAPR, etc.).

Despite the controversies, most who opined in 2009-10 about HCP respiratory protection against influenza acknowledged that the best course forward would be one that bases respiratory protection guidelines on scientific data. The National Academy of Medicine (formerly the Institute of Medicine or IOM) articulated its position in multiple documents, including its 2009 Letter Report, *Respiratory Protection for Healthcare Workers in the Workplace against Novel H1N1 Influenza A,* where it clearly states the importance of research, noting that continued research asking the most important and pressing questions should be a top priority. Our protocol is designed to determine the most appropriate respiratory protection for US healthcare workers. This approach is strongly endorsed by Dr. John Howard, Director of the National Institute of Occupational Safety and Health (NIOSH), and Dr. Ken Shine, Chair of the IOM Committee on Respiratory Protection for Health Care Workers in the Workplace against H1N1 Influenza, who both wrote letters in support of this clinical trial. Although the H1N1 20092010 influenza pandemic has ended the need for this research remains essential. This study will focus on the relative protective effects of the CDC's 2007 seasonal influenza guidelines versus the CDC's 2009 H1N1 pandemic influenza guidelines.

Since this time, further controversy has developed around the appropriate prevention practices for Middle Eastern Respiratory Syndrome (MERS) caused by a novel coronavirus with differences between the CDC and the WHO guidelines (CDC 2015; Chung 2014; Hsu 2014; WHO 2015). The emergence of another pathogenic respiratory virus that impacts HCP health has further pushed the scientific community to strive to answer the question of respiratory protection for HCP for influenza and other respiratory viral infections.

**Non-Compliance with Respiratory Protective Measures:** The CDC and other influential public health organizations recommend in most scenarios that HCPs utilize droplet precautions when caring for patients who are ill with respiratory diseases. Only a few diseases require airborne

precautions. Droplet precautions consist of a gown, gloves, eye protection (glasses or goggles) and a medical mask. Exceptions include tuberculosis, measles and a small set of diseases known to be capable of airborne spread, in which case a respirator (N95 respirator or equivalent) is recommended. On a practical level, this means HCPs should wear a medical mask whenever they enter a room of a patient with respiratory symptoms, unless the worker is certain the patient is not infected (no mask needed) or the patient is suspected or known to have tuberculosis or one of the less common airborne diseases (respirator needed). However, it is widely acknowledged that HCPs often do not fully adhere to these recommendations; compliance rates with personal protective equipment recommendations are near 30%. Interestingly, lower rates of FPE compliance are often observed among senior staff and longtime employees, possibly due to a feeling of increased invulnerability. This trend is also reflected in lower hand hygiene and vaccination rates among more senior HCPs. Limited tolerability may also play a role.

**Attitudes/Opinions/Beliefs**: There is minimal data on the impact of attitudes and opinions among HCP about respiratory protective measures in an outpatient setting. An IOM report concluded that "Experience with… efforts to improve infection control… have demonstrated that the efficacy of an intervention alone does not guarantee its success. The best respirator or medical mask will do little to protect the individual who refuses, or who misunderstands how… to use it correctly."

Despite the crucial role that FPE plays in limiting nosocomial spread of respiratory pathogens, few studies have examined seasonal respiratory pathogen protection compliance rates, individual HCP attitudes and beliefs about FPE use, or the specific impact of safety climate in this setting. In a recent comprehensive review of the infection control literature regarding protecting workers from respiratory pathogens, The British Columbia Interdisciplinary Respiratory Protection Study Group found that "organizational and individual factors can explain much of the variations in self-protective behavior in health care settings, especially with respect to applying universal [standard] precautions. It seems likely that these factors were also important safety determinants during the SARS outbreaks but they have not been extensively studied". This group also noted that "safety climate is being increasingly recognized as one of the most important determinants of safe work practice in terms of preventing exposures to [blood and body fluids] but has been little studied in other types of nosocomial transmitted diseases. Respiratory tract diseases, in particular, have not been well studied in this regard." Thus, it would be interesting to collect data on HCPs attitudes and opinions concerning FPE use and the relationship of these beliefs on the incidence of respiratory infection. This data could possibly lead to policies that improve knowledge about FPE use among HCPs, especially in an outpatient setting.

Number of Study Arms: The consequences of widespread non-compliance among HCPs and the impact on the efficacy of measures remain controversial. On the surface, therefore, it would

follow that infection control researchers would want to assess the impact of non-compliance. To make an unbiased assessment of FPE effectiveness, a randomized clinical trial would ideally include three arms: a respirator arm, a medical mask arm and a negative control (no respiratory protection) arm. However, there is often a dearth of evidence, in part, because the ideally designed clinical studies (*e.g.*, randomized, double-blind trials) are challenging to conduct in a clinical (operational) context. Ethical considerations often preclude designs that randomize individuals to "no protection" when the standard of care (or operational policy) calls for some level of protection. This challenge has been discussed elsewhere in detail. With this ethical limitation in mind, the protocol that follows is designed with two arms, not three.

**HCP Exposure Risk Assessment:** This study will also investigate the relationship between HCP infection rates and their reported exposure to patients with suspected or confirmed respiratory illness, aerosol-generating procedures, or household members with respiratory pathogen symptoms. Loeb et al. *(*2009) bears several important parallels to the current study but did not directly assess exposure risk by quantifying contact with individuals or procedures that may introduce a higher risk for infection. Studying this relationship may reveal important information concerning transmission, prevention, and absolute and relative risks of respiratory viral infection. The proposed study aims to assess and account for the frequency and level of risk associated with non-occupational exposures.

# C Study Objectives

This study aims to determine the relative effectiveness of two interventions to protect HCPs against infections and illnesses caused by influenza and other respiratory pathogens.

## C1 *Protective Effects*

### 1.a Primary

To determine and analyze the magnitude of the change, if any, in incidences of laboratory confirmed influenza in HCPs wearing N95 respirators (2009 guidelines) compared to medical masks (2007 guidelines).

### 1.b Secondary:

- To determine and analyze the magnitude of the change, if any, in incidence of ARI, ILI, LCRI and LDRI in HCPs wearing N95 respirators compared to medical masks.
- To examine the relationship between incidence and possible risk factors, including compliance, attitudes and opinions of HCPs and workplace exposures.

## C2 *Incidence Determination*

### 2.a Primary

- To improve understanding about the burden of infections and illnesses caused by influenza and other respiratory pathogen among HCPs working in outpatient settings.

### 2.b Secondary:

- To measure the incidence of ARI, ILI, LCRI, and LDRI in selected outpatient settings.
- To measure the changes in the participant's nasal/oropharyngeal microbiome over the course of the study.

# D Study Design and Methods

## *D1 Overview*

This study will assess and compare the effectiveness of respiratory protective equipment among HCPs in the outpatient setting in a variety of geographic/climatic conditions.

We propose a study with a prospective timeline (Appendix L), non-blinded, cluster randomized interventions (with the unit/clinic as the unit of randomization), a two-arm, "head-to-head" comparison, multiple sites and multiple geographic locations, with longitudinal cohorts recruited for multiple years.

This study will be conducted in outpatient clinics, emergency departments and/or urgent care settings in multiple geographic locations. The outpatient setting has been chosen because it is the front line in the event of an influenza epidemic. Patients typically report to either their primary care physician, urgent care facility or the emergency department for respiratory infections. It has been shown that the highest rate of infection in healthcare workers is in this outpatient setting. The Study Team aims to balance the sites to include medical, pediatric and VA study sites. We will employ stratified randomization for FPE assignment, to assure generalizability of results across clinic types. The types of clinics/clusters included will be dependent on the clinics that meet the requirements and agree to participate in the study, but we will attempt to recruit a variety of outpatient clinics to ensure a generalizable study group. Each study site will utilize a Master Study Protocol with synonymous text to produce a local IRB application.

Subjects will be recruited and randomized to one of two study arms, medical masks (2007 and 2010 CDC seasonal influenza guidelines) or N95 Respirators (2009 N95 pandemic influenza guidelines). Sites will be randomized each flu season such that sites may use different types of FPE each flu season. The duration of the intervention (mask wearing) period of the study is dependent on surveillance and incidence of viral respiratory illness at each site. The intervention period may potentially be shortened due to site-specific/regional incidence and surveillance, but it is not anticipated to extend longer than 16 weeks. The duration of viral respiratory season varies widely from year-to-year, so flexibility in the duration of the study intervention period is vital in allowing us to capture the height of viral respiratory season. The duration of the intervention period may therefore be lengthened or shortened based on incidence and surveillance data available at each site. Each subject will agree to participate in

the study for up to 16 weeks per flu season, in which the "pre-study period" is a screening and educational period. During the pre-study period, participant demographic information will be collected (baseline survey), a survey on knowledge, attitudes, and beliefs regarding FPE will be administered (pre-study survey), a blood sample will be collected for baseline serology testing, and subjects will be educated about the study, including the fit testing process. Weeks 1-16 are the "intervention period." A cluster-randomized design will be utilized such that a group ("cluster") of approximately 16 people will be assigned (randomized) to wear the same device (Medical Mask or N95) for up to 16 weeks (potentially shorter) while working in the study site location (Appendix A). Participants will also be asked to provide upper respiratory specimen during the intervention period. During this time, the research team will also observe participants' adherence to mask use and hand hygiene. Two weeks after the final week of wearing FPE (hereafter referred to as "post-study period"), subjects will be asked to provide a final serological sample and to complete a post-study survey. Participants may participate in successive flu seasons until the study is completed.

Being able to wear OSHA-compliant and NIOSH-approved respiratory protective equipment when in contact with patients is considered a pre-employment condition for all study sites under consideration. Therefore, the potential participants should have experience wearing medical masks and respirators and should be capable of safely wearing the respiratory equipment for the study period. It is expected that a small percentage of subjects will be excluded because they have facial hair that precludes OSHA-accepted fit testing (likely < 5% of eligible subjects), or they will have been advised by an occupational or other qualified healthcare provider to avoid wearing certain types of respirators for medical or other reasons (likely < 1% of eligible subjects).

## *D2 Study Site Selection and Randomization Scheme*

### 2.a Cluster Randomization Scheme: Clinical Unit of Analysis and Eligibility

Previous studies utilized a traditional individually randomized design (in a healthcare setting) or cluster, randomized design (in a home setting), a methodological tool that may be utilized in suitable circumstances. For this study, a "cluster design" will be used.

A group of people (a "cluster") will serve as one unit of randomization as described in the **General Methods** section of this protocol (Appendix A). Ideally, most or all staff working in selected clinic locations will agree to participate via informed consent. All HCPs (subjects) within that cluster will wear the same type of device (Medical Mask or N95) for the intervention period.

This study focuses on illness and infection in the healthcare workplace, a setting known for propagating influenza outbreaks. The principal and co-investigators believe a clusterrandomized design is essential to optimize the validity, reliability and generalizability of the results. Others have proposed individual randomization schemes in which each person (not each clinical unit) is randomized to one of the intervention arms. Justification has often centered on an individually randomized study often requiring fewer subjects to achieve statistical significance. In this setting, staff working alongside each other in the same clinic would routinely wear different

respiratory protective devices for long periods. While possible to design as a research study, this approach is unlikely to resemble the events in a real clinic during an infectious disease outbreak. Some have also expressed concern that different devices being worn in the same location could negatively influence compliance with assigned study arms.
Individual randomization may increase the likelihood of bias toward the null hypothesis. Because transmission may occur from patient-to-worker and from worker-to-worker, identifying the contribution of each exposure type to the risk of acquiring infection would be exceedingly difficult. Compared to cluster randomization, an individual randomization scheme may be more likely to cause patients and other HCP to raise questions or objections. Patient requests or other staff requests for modification of respiratory protection among the staff would be expected to cause cross-over and bias toward the null hypothesis.

Overall, to maximize compliance and ensure generalizability, the investigators have selected a cluster randomization, in collaboration with CDC partners, members of the Study Advisory Board and the Study Science Board, in which all subjects on the same clinical unit are outfitted with the same type of protective devices. Although the model of N95 may vary at each study site and within each cluster, the type of respirator (NIOSH-certified, negative pressure, N95 filtering face pieces) will not change.

Selection of clinic sites will be based on the size of the clinic. Each cluster/clinic will have a median of approximately 20 HCPs. Selection of clinic sites will also be based, in part, on the interest-level and enthusiasm of the HCP-subjects and the numbers of patients who present for healthcare with a diagnosable respiratory illness. For purposes of this study, “primary care” will be defined as “a healthcare delivery site at which family practice, internal medicine, emergency medicine, or general practice clinicians (or nurse practitioners and physician assistants with similar training) evaluate and treat patients who typically arrive on their own accord (not via referral) and from which referrals to subspecialty services are typically requested” (See Appendix K). While most clusters will naturally consist of consented HCP-subjects who work in a particular clinic location, some large clinics may be designed in functional partitions that are amenable to this study’s analysis scheme. When deemed appropriate by the study team, large clinics may be further sub-divided into more than one cluster for study purposes.

The participating center would register their clinical sites/clusters with DCC who meets the eligibility criteria for the cluster as described above. The clusters would be assigned to one of the two arms using a system established by the DCC).

## *D3 Study Subject Selection:*

Seven institutions have been identified as participating centers: the Johns Hopkins Health System (JHHS) in Baltimore, MD; Denver Health Medical Center, and Children’s Hospital

Colorado in Denver, CO; and the Department of Veterans Affairs (VA) sites in Denver, CO; Washington, DC; NY, NY; and Houston, TX. Additional sites need to be added. Additional sites will be assessed by certification criteria (Appendix K) and must have an adequate number of outpatient visits/clinics (at least 25 that employ 20 or more HCPs), history of collaboration with other sites on large clinical trials, and research infrastructure experience with clinical studies. We aim to recruit at least 500 participants per study site per influenza season, based on a 2530% dropout rate. Depending on the capability of selected study sites to accrue subjects, up to 10 (ten) sites may be included altogether.

## 3.a **Inclusion Criteria**

(1) Clinical site leadership has agreed to have one or more staff participate in the trial
(2) Subject meets the definition of "healthcare personnel"
(a) Provides healthcare to patients and/or
(b) Typically positions themselves within 6 feet of patients ("close contact") and (c) Is a full-time employee (average of ≥ 24 hrs/week) working 75% of the time at a study site (and *not* employed at another location where the study is being conducted).
(3) Subject able to read and sign informed consent
(4) Subject agrees to all requirements of the protocol, including fit testing and diary keeping
(5) Subject's age 18 or greater
(6) Subject passes fit testing for one of the study supplied respirator models and agrees to use that model for the entire intervention period of the study (if in the respirator arm).

## 3.b **Exclusion Criteria**

(1) Subject self-identified as having severe heart, lung, neurological or other systemic disease that one or more Investigator believes could preclude safe participation.
(2) Known to *not* tolerate wearing respiratory protective equipment for *any* period.
(3) Facial hair, or other issue such as facial adornments, precluding respirator OSHA-compliant fit testing or proper mask fit during the study period
(4) Advised by Occupational Health (or other qualified clinician) to *not* wear the same or similar respirator or medical mask models used in this study.
(5) In the opinion of the Investigator, may not be able to reasonably participate in the trial for any reason (e.g. anatomic changes to nose).
(6) Self-identified as in, or will be in the third trimester of pregnancy, during the study period.
(7) Subject rotating in 2 different ResPECT study clinic sites /clusters during the study period.
(8) Subject works less than 24 hours/week in the cluster/clinic in which they are recruited.
(9) Subject work less than 75% of the intervention period in that clinic.
(10) Subject is a previous participant of the ResPECT Study, but does not consent for data from previous flu season(s) to be linked.

## *Subject Recruitment Plan and Consent Process*

HCP-subjects in each clinic will be made aware of the study through emails (Appendix V), telephone calls (emails and telephone calls will be used to contact HCP who express interest in

the study and those HCP who have previously participated in study), posters ("flyers") distributed at each potential study location, the primary referral hospitals associated with the clinics, and other locations HCPs frequent (Appendix B). Participants will receive emails and telephone calls throughout the study to alert them of study updates, planned times for specimen collection, and to address issues that the participants have. Another social medium we may use to optimize recruitment and retention is a ResPECT Study Facebook page occasionally posting information such as survey reminders, blood draws, or swab timing for clinics (example post: "We are nearing the half-way point! Please make sure you complete your Weekly Diary and Days Worked Surveys by <date>!! If you have questions, contact the ResPECT Study staff at respect@jhmi.edu or (410) 614-6206.)" The point is to leverage our social media contacts and widen the scope of information systems with which to communicate updates and important events to participants (see Appendix AA). The Facebook page will protect privacy by being a unidirectional information source – staff will post notifications, but participants will be unable to post messages on the page. The caveat being participants "liking" the page will show up in their news feed depending on their own privacy settings. We will have the following disclaimer on the page informing participants of the privacy policy: The Johns Hopkins Health System and Johns Hopkins University School of Medicine do not edit or control the content of posted comments by third parties on this web site. However, Johns Hopkins reserves the right to remove any such postings that contain objectionable or inappropriate content. The Facebook page and email addresses will be deactivated at the end of the study.

The protocol, forms, and all written materials about the study will be approved by the local Institutional Review Board(s). The definition of eligible "healthcare personnel" for the purposes of the study will be any person who is a full-time employee (average of ≥ 24 hours/week), at least 18 years old, and who is employed by or works at the study site and interacts with patients. Interaction in this context will mean the provision of clinical care, typically positioning oneself within 6 feet of patients, or entering into a small-enclosed airspace shared with patients, such as a typical patient treatment room (e.g., "close contact"). We will cover all operating hours of participating clinics. Covering clinics such as emergency departments may require staffing outside of standard operating hours.

Subjects will be recruited by the Study Coordinator or his/her designee or self-referred to the Study Coordinator in a response to emails, telephone calls, or flyers. Initial recruitment will mainly occur through educational meetings. Consent forms will be distributed to clinic directors prior to these meetings for dissemination among interested individuals. Research staff will present the project during staff meetings, change-of-shift meetings, and other meetings/visits at the participating clinics. The research staff will go over the consent forms to ensure participants fully understand the meaning of the forms, answer any questions, and ensure that each potential participant has adequate time to review the forms. If any potential participants would like additional time to review the forms or consider enrolling, research staff will arrange to follow up with them later. During these educational meetings, the research staff will explain to

each potential subject the risks of wearing a respirator for prolonged periods. Visual demonstrations of study requirements (e.g. how to properly put on, wear, and take off a respirator/mask; nasal and throat swab procedures) will also be presented to ensure that potential participants understand all study requirements before they agree to consent. Study staff may also provide paper copies of the surveys and emails during the enrollment process and/or bring computers to show participants what the e-mails they'll receive from the study will look like, as well as how to access and complete the weekly and daily surveys.

## *D4 Respiratory/Facial Protective Devices*

### 4.a Data on respirators and mask

The following models will be used in this study. They were selected because these models:

(a) Are commonly used by the VA medical centers and
(b) Are commonly used by JHHS, Denver Health and the Children's Hospital Colorado medical facilities and
(c) Are commonly used in many settings from across the U.S.

N95 Respirators:

1. 3M Corporation 1860, 1860S, and 1870 models
2. Kimberly Clark Technol Fluidshield PFR95-270, PFR95-274 Medical

Masks:

1. Precept 15320
2. Kimberly Clark Technol Fluidshield 47107 (preferred)

(a) Data provided by the National Personal Protective Technology Laboratory at NIOSH indicate:3M 1860: 0.72% avg. penetration
(b) 3M 1870: 0.32% avg. penetration
(d) (c) Kimberly Clark PFR95-170: 1.38% avg. penetration Precept model 15320: 12.9% avg. penetration
(e) Kimberly Clark Technol Fluidshield 47107: 10.3% penetration.

NIOSH N95 approval criterion is ≤ 5% penetration (*i.e.*, ≥ 95% efficiency), suggesting the practical difference between 0.32% and 1.38% penetration is negligible.

The filter airflow resistance for the medical mask was 4.1 (Precept) and 4.5 mmH2O (Kimberly Clark), while the filter airflow resistances for the N95 filtering face piece respirators ranged from 8.9 to 11.7 mmH2O. The practical significance of these numbers is limited because human test subjects typically have difficulty detecting differences between these low levels of airflow resistance. Each study site will purchase the appropriate FPE each flu season to ensure availability of the FPE models in the study at the participating clinics/clusters.

**FIGURE 1 Basic* Elements of Recommended Personal Protective Equipment**

| ***2007 CDC Influenza Guidance*** | ***2009 CDC H1N1 Influenza Guidance*** |
|---|---|
| *Types of Precautions* | *Types of Precautions* |
| Standard Precautions | Standard Precautions |
| Droplet Precautions | Airborne Precautions |
| Medical Mask | N95 Respirator |
| Gloves | Gloves |
| Gown | Gown |

**This figure is for quick comparisons; for further details, see the original sources: references 47 and 48.*

## 4.b **Fit testing**

NIOSH defines a respirator fit test as the use of a protocol to qualitatively or quantitatively evaluate the fit of a respirator on an individual. In compliance with JHH/OSHA regulations, subjects will be required to fill out an amended version of the 1910.134 OSHA Respirator Medical Evaluation Questionnaire (Appendix M). Subjects randomized to the N-95 arm will be fit-tested prior to the intervention period using the study supplied respirator and an OSHAaccepted fit-test kit (i.e., 3M™ FT-10 Saccharin Fit Test Kit, 3M, St Paul, MN, USA) that meets the manufacturers' instructions for fit-testing. The fit-tests used at each facility may vary but all will be OSHA-accepted. As participants will change masks frequently during the course of a work shift, subjects will be educated about how to properly perform seal checks on their masks to ensure a proper fit. Participants will be asked to refrain from eating or drinking for 15 minutes before the test; males will be asked to be freshly shaven, and to remain without facial hair for the duration of the study (Appendix Q). Instructions will be given as to how to properly don, doff, and adjust FPE, and manufacturer-recommended fit checks will be explained. Participants will be given specific instructions regarding when to reuse and replace their FPE. Participants will be instructed to don new respirators or masks before each close-contact with a patient with suspected or confirmed respiratory pathogen infection. Subjects will be allowed to choose which N95 respirator they will use – either 3M 1860 (regular or small), 3M 1870, or PFR95270/PFR95-274 Kimberly Clark N95 (regular or small). In instances in which subjects who are fittested using either qualitative or quantitative methods cannot detect the Saccharin solution, Bitrex will be used instead. Subjects who fail all N95 respirator fit-tests or cannot detect either Bitrex or Saccharin will be considered screening failures and will be excluded from the study. Alternative respirators will not be provided as part of this protocol.

## *D5 Attitudes and Opinions*

Participants will be asked to complete surveys about their attitudes and opinions concerning FPE both before and after the study. A standardized form will be used (Appendices E & H).

## *D6 Adherence to Respirator or mask use and hand hygiene*

Trained research assistants will observe clinics to determine adherence to correct FPE use and number of respirator/mask changes required. Participants will be instructed to don a new respirator/mask each time they come into close contact (within 6 feet) of a patient with suspected or confirmed respiratory pathogen infection. Hand hygiene frequency will also be observed. Unannounced observations will occur in each clinic throughout the intervention period of the study; these visits will take place during all operating hours of each participating clinic. A standardized system will be used to measure FPE and hand hygiene compliance (Appendices I and Z) using HandyAudit compliance measurement iPad application. These observations may be made using paper or electronic methods but must ultimately be submitted via HandyAudit.

As discussed, a patient-based observation system (see Appendix Y) may also serve as an additional method for assessing HCP compliance with FPE and HH, especially when these observations are difficult or impossible to attain by study staff (i.e. behind closed doors or in areas with limited visibility).

To encourage and remind participants of mask wearing, study sites may hang posters with a "Mask Up" slogan (see Appendix BB) in clinics and high traffic areas of the hospital. These posters reiterate CDC mask wearing guidelines for HCPs in close contact with patients presenting with signs and symptoms of respiratory infection. The intent of this campaign is to maximize mask-wearing compliance among study participants.

## *D7 Risks and Benefits*

Respirator or medical mask wear is completely voluntary; therefore, any subject may remove his/her respiratory protective equipment at any time for any reason for any duration. While CDC guidance specifies (and OSHA regulation enforces) the settings and conditions in which these protective devices are to be worn, employees are afforded the right to remove the equipment. Still, it is the subjects' best interest to remove these devices at appropriate times, such as during break periods or when not interacting with patients.

**POSSIBLE RISKS:** The problems posed by N95 respirators and medical masks in this study are primarily related to discomfort and annoyance. The risks of wearing a respirator are minimal. Subjects wearing respirators or medical masks who engage in low-level exertion, the type typical for HCPs, should not experience limits of endurance or exertion capacity. Subjects who exert themselves at a moderate or high-level workload for a prolonged period (highly unusual for HCPs) may need to remove their protective equipment for all or some of the remaining study session. While the risks of ischemic events, such as a myocardial infarction or cerebrovascular accident, cannot be completely excluded, the risks of these events have been conventionally understood to be extremely low. Studies quantifying the risks of such rare events while wearing respirator protection in the healthcare sector have not been conducted. However, HCPs who can perform the occupational duties required to care for patients are believed to be capable of wearing a respirator without adverse incident.

While there are no known data that support exclusion of pregnant women from this study, the investigators raised concerns about the possibility of a change in respirator fit caused by the typical facial changes during pregnancy. The primary concern is that the fit may become inadequate during the latter stages of pregnancy. Because of a theoretical risk posed by illfitting respirators during pregnancy, HCPs who will be in the 3rd trimester of pregnancy during the study period are excluded from the study.

Mild discomfort is the primary risk associated with upper respiratory specimen swabs (throat and nasal swabs). Gagging or aspiration may theoretically occur, although the investigators are not aware of well-documented cases in the public domain. Other rare occurrences may include bleeding or emesis.

There is a risk associated with the collection and handling of PHI. All PHI data will be coded at the earliest opportunity, transmitted and stored according to institutional guidelines, and the code key will be destroyed at the end of the study.

Risks associated with having blood drawn are slight but may include excessive bleeding, fainting or feeling light-headed, hematoma, and rarely, infection. Trained personnel will collect blood for serological testing.

**POSSIBLE BENEFITS:** The study is designed to help answer an important question regarding the safety of all HCPs. All participants will meet fit-testing criteria (as determined by the "Inclusion/Exclusion" protocol). They will also be fit-tested for the N95 respirator specifically for the study. The fit-testing documentation provided by ResPECT Study staff may also be submitted to each participating site to fulfill a clinic's mandatory fit-testing renewal requirement. Because OSHA-designed fit-testing provides a means for education about respiratory protection and fit-testing can help equip HCPs with a safe work environment, the study could offer the benefit of enhanced workplace safety. Otherwise, there is no known direct, immediate benefit to subjects.

## *D8 Early Withdrawal of Subjects/Data/Follow-up for Withdrawn Subjects*

If a participant is unable to complete the study, due to illness (other than a respiratory pathogen illness) or non-compliance with the data collection and sampling required for this study, they will be removed from the study. If participants fail to submit more than three entire weeks of surveys (i.e. no weekly survey and no daily surveys) and/or fail to comply with three warnings from study personnel during observations (i.e. improper use of FPE, failure to correct HH) they will be subject to an administrative withdrawal at the discretion of the site PI.
In the event a participant becomes ineligible but is still willing to participate (i.e. – changes location but still willing to be involved with the study) AND has completed at least eight weeks of the study intervention period, the final blood collection and post-study survey will be

completed before removal from the study. All post-study collections will be reviewed and completed at the discretion of the site PI.

## *D9 Study Data Collection tools*

The data will be collected on electronic data capture forms (HandyAudit and REDCap). Findings may be validated with a telephone call, email, or a face-to-face contact by study personnel.

| | Forms | Study time point | Appendix | Filled by |
|---|---|---|---|---|
| a) | Pre-study Inclusion/Exclusion Screening | Pre-study | C | Research team/participant |
| b) | Baseline Survey | Pre-study | D | Participant |
| c) | Preliminary Survey | Pre-study | E | Participant |
| d) | Amended Fit-testing Medical Questionnaire | Pre-study | M | Participant |
| e) | HSE Fit Test Evaluation Form | Intervention | Q | Research Team |
| f) | Enrollment Checklist | Pre-study | P | Research Team |
| g) | Weekly Diary | Intervention | G | Research Team |
| h) | Daily Exposure Form | Intervention | F | Participant |
| i) | Symptomatic Event Report Form | Intervention | N | Participant/Research Team |
| j) | Subject Compliance Monitoring Forms:<br>FPE Observation Form | Intervention | I, Y, Z | Research Team |
| k) | Subject Compliance Monitoring Forms:<br>Hand Hygiene Observation Form | Intervention | I, Y, Z | Research Team |
| l) | Post Study Survey | Post-study | H | Participant |
| m) | Supplemental Vaccination Questions | Post-study | CC | Participant |

### 9.a **Pre-study Inclusion/Exclusion screening**

All potential participants will be required to complete a pre-study screening form to determine their eligibility to participate in the study (Appendix C). If HCPs are determined to not be eligible to participate in the study due to a potentially complicating health condition, they will be provided information about proper respiratory protection (Appendix J).

### 9.b **Baseline Survey**

The baseline survey (Appendix D) will collect contact information, demographic information, recent exposure (risk factor) history, vaccination status, smoking status, history of systemic

disease (respiratory/heart/neurological) and information about medication use. Participants will be required to complete this survey prior to the study intervention period.

### 9.c Preliminary Survey

The pre-study attitudes, beliefs, and opinions survey (Appendix E) will collect participants' knowledge, attitudes, beliefs, and opinions about FPE. Participants will be required to complete this survey prior to the study intervention period.

### 9.d Amended Fit-Testing Medical Questionnaire

In compliance with OSHA regulations, subjects will be required to complete an amended version of the 1910.134 OSHA Respirator Medical Evaluation Questionnaire (Appendix M) prior to being fit tested.

### 9.e HSE Fit-Test Evaluation Form

This form will be completed by the research team to evaluate the participants for fit testing. (Appendix Q)

### 9.f Enrollment Checklist

This will be a checklist (Appendix P) to ensure that the participants enrolled in the study intervention period meet the study entry criteria. The data collected during the pre-study assessments including; Inclusion/Exclusion criteria, Fit-testing, and Baseline survey will determine if a participant can be enrolled into the study or is a screen failure.

### 9.g Weekly Diary

During the intervention period (Table 2), the information will be collected once weekly (Appendix G) updating their influenza vaccination status, symptoms, treatment and exposure.

### 9.h Daily Exposure Form

A daily exposure form (title "Monday Exposure Form, Tuesday Exposure Form, etc; Appendix F) will be used to help participants recall and record exposure risks, signs and symptoms of respiratory illness and periods of daily FPE wear. The daily exposure form will ask about respiratory illness among household members, work colleagues and other contacts. Participants will complete the daily exposure form every day to track the existence or absence of respiratory or influenza-like symptoms on each date worked at the study site.

While data from this study will be kept confidential and will not be reported to managers and will not be used to enforce furloughs for ill participants, we will encourage participants who

become ill to consult with their local occupational/employee health departments concerning their illness.

## 9.i Symptomatic Event Report Form

Subjects who self-identify as having any sign(s) or symptom(s) of influenza (as defined in Table 3) will be asked to complete a Symptomatic Event Report Form (Appendix N). Trained study staff will then determine if the subject should undergo an upper respiratory specimen collection using nasal/throat swabs for data collection purposes.

Participants reporting signs or symptoms of respiratory disease (including influenza) in their weekly symptom diary/daily exposure diary will be contacted by study personnel to schedule an upper respiratory specimen swab (throat and nasal swabs). Those participants who are not working or are unable to come to work will be instructed to use their take-home kit (Appendices R, S, T, and U).

## 9.j Subject Compliance Monitoring Forms

Data will also be gathered on FPE compliance and hand hygiene (HH) compliance. Data will be collected by trained study staff using the electronic HandyAudit compliance monitoring system (https://www.handyaudit.com/) or using standardized forms if the HandyAudit system is unavailable (Appendix I, Appendix Z). FPE and HH compliance data collection will occur during unannounced observation visits within clinic operating hours. This information will be used to analyze the relationship between levels of compliance with FPE and HH and incidence of respiratory disease. Participants will be asked to wear FPE whenever they have close contact (within 6 feet or sharing a small enclosed airspace) with an individual with suspected or confirmed ILI. They will also be asked to don new FPE before each new close-contact patient interaction. The study team will aim to achieve five FPE and five HH observations per site, per week. These data were collected using HandyAudit (Handimetrics, Toronto, CAhttps://www.handyaudit.com/handyaudittechnology.html).

## 9.k Post-Study survey

After the intervention period, there will be a post-study period when the participants will complete a post-study survey regarding attitudes, beliefs, and opinions about FPE and the study. (Appendix H).

## 9.l Adverse Event Submission Form

An adverse event (AE) is any adverse change from the patient's baseline (pre-study) condition, which occur during the course of the study and, after the consent form has been signed, whether the event is considered to be related to the study intervention or not. The research team will complete an AE submission form (Appendix O) upon reporting of such events.

## *D10 Study specimen collection, test methods, storage and shipping*

The high cost of this study requires prioritization of achievable endpoints and target data. In an effort to optimize the use of available funds, a subset of lab tests for identification of respiratory pathogens through serologic testing will be performed while the remainder will be stored for future completion when additional funding becomes available (more information is available in the section on funding source). The lead study team (principal and lead site investigators) determined that all sites will send remaining samples to UT Southwestern (UTSW) and the VA North Texas for storage. Future sample testing will be determined by the lead study team. Samples from VA sites will be stored in space leased by the VA North Texas at UTSW. All storage facilities are in compliance with VA North Texas requirements.

Excess samples remaining after study tests have been completed may be released to ResPECT investigators for analyses of other respiratory organisms, after approval by the lead study team and local IRBs. As new respiratory pathogens are identified, specimens may be used for additional testing as dictated by changing epidemiology. According to record retention policies, the VA requires that records are retained until six years after the end of the calendar year in which the study closed. The lead study team will comply with the record retention policies at the VA, as well as the policies at each individual site.

### 10.a **Blood Specimen Collection**

Blood samples will be collected by trained personnel at two time points; one at the beginning of the intervention period and second at the end of the intervention period. The samples collected were originally stored for serology testing and sent to Dr. Geoffrey Gorse at Saint Louis University at agreed upon intervals for analysis. Dr. Gorse's lab operates in a VA-leased space at Saint Louis University and complies with all VA St. Louis Healthcare System regulations. To maintain data integrity and ensure study longevity, the lead study team determined that all sites will send remaining blood samples to UTSW and the North Dallas VA for storage. VA samples will be stored in space leased by the North Texas VA at UTSW. As new respiratory pathogens are identified, specimens may be used for additional testing as dictated by changing epidemiology.

### 10.b **Respiratory Specimen collection**

The specimen will be taken from the upper respiratory passages that will be collected and stored using the standard methods. The respiratory specimens will be collected from throat and nasal passages. No nasopharyngeal aspirates will be performed for the purposes of this study. If it is determined that subjects are unable to come to work and participate in specimen collection when they experience respiratory pathogen symptoms, participants will use "take-home" specimen collection kits, which will be provided to them upon enrollment, (Appendix R) and procure a respiratory specimen themselves. The kits will include instructions on dangerous goods shipping (Appendix S), self-specimen collection (Appendix T), and shipment packaging (Appendix U) so that the specimens can be sent to the research lab.

**Laboratory Specimens and Test Methods**

***Respiratory Pathogen Identification***

Swab specimens (secretions/swabs in viral transport medium) will be processed and stored within 48 hours at each study site. Frozen samples will stored at Johns Hopkins University and the Denver VA/the University of Colorado at agreed upon intervals. Storage and laboratory testing will occur at both Johns Hopkins and the Denver VA/the University of Colorado. Samples will then be sent to UTSW for storage, where they will be stored for future use.

***Nucleic Acid Extraction, PCR***

Samples will be processed for nucleic acid extraction using multiplex PCR assay(s) at JHU to identify human respiratory pathogens (Table 4). St. Louis testing is done using assays to determine serum hemagglutination inhibition (HAI) antibodies to multiple strains of Influenza A and B viruses. Excess samples were stored for further analysis by ResPECT investigators at their respective institutions. These will be transferred to UTSW where they will be used for additional studies based on the determination of ResPECT investigators. Samples may be destroyed at the discretion of the lead study team.

## 10.c **Study Specimen Storage and Shipping**

Because Dr. Perl, study co-PI and original lead site investigator at the lead clinical site, has left JHU for UTSW, the study lead team has determined that all respiratory and blood samples will be transferred from the other ResPECT sites to UTSW for storage. UTSW will house and catalogue the samples according to good laboratory practices in a freezer farm in the institution's ID Division and space leased by the North Texas VA. Samples will be stored in one of several -80°C upright freezers. Protocols for specimen cataloguing and storage will be developed with the Johns Hopkins University under the direction of Charlotte Gaydos, who also now serves as the lead site investigator at JHU. A laboratory based, inventory database and tracking system will be put in place and will be used to track samples. Freezer temperatures will be monitored daily for temperature deviations. A materials transfer agreement (MTA) has been signed by JHU, UTSW and the New York VA. The study team will check with individual site IRBs to ensure this MTA suffices for all sites.

# E Study Procedures

## *E1 Certification and Registration of the clinical Sites/Clusters:*

The participating sites will certify (Appendix K) and then register these clusters with DCC. DCC will then randomize the clusters to one of the two arms and send the randomization scheme to the participating site.

## *E2 Screening for Eligibility*

The anticipated duration of this study is four respiratory virus seasons. Enrollment of subjects will commence as soon as possible after IRB approval, with the intention that the study will cover four respiratory virus seasons. The start of the actual intervention period will be determined by year and site based upon influenza surveillance at the participating site, as well as state and regional health departments. The clusters would be assigned by one of the two arms using a system established by the DCC.

HCPs who agree to participate will be asked to provide written informed consent and agree to participate for up to 16 weeks with the option to voluntarily withdraw at any time, for any reason.

Once consented, participants will be screened for exclusion (Appendix C), and to ensure that they are healthy enough to participate in the study. Non-English speakers and those with a language or hearing impairment will be excluded from the study. Once participants are consented, they will be asked to fill out the baseline survey and preliminary attitudes/opinions/beliefs survey, will provide their initial blood draw, and will be fit-tested if they are being recruited at a site that has been designated as an N95-wearing clinic. Ideally, all these (pre-study assessments) initial procedures will occur during their initial enrollment but may have to be performed later date in the study. During the pre-study period, fit testing will be done to confirm eligibility of participants at the site randomized to wear N95 respirators. There will not be a pre-participation physical examination. However, during the informed consent process, the Study Coordinator will explain to each potential subject the risks of wearing a respirator for prolonged periods and the procedure of collecting upper respiratory specimen.

Contacting participants may include (but is not limited to) following up with participants about form compliance, fielding questions, ensuring payment and scheduling, and contacting participants who alert us that they have become symptomatic. The list of participating HCPs and the intervention schedule will be kept confidential to protect HCPs from repercussions for either declining or accepting participation in the study.

## *E3 Schedule of Study Assessments*

### 1) Pre-study Period assessments

Prior to the initiation of the intervention period, participants will be expected to provide an initial serological sample for comparison with their final serological sample for influenza titers. Study preparation/screening and education will also take place during this time. Participants will also be required to complete a baseline survey and preliminary attitudes, beliefs, and opinions survey.

i. Consent form: After explaining the study to the potential participant as discussed in the previous section, consent from the agreeing participant would be obtained. The study participant will sign two copies of the consent form, one for the study use and other would be given to the study participant for their record.
ii. Pre-study Inclusion/Exclusion screening
iii. Enrollment checklist iv. Baseline survey
v. Preliminary survey
vi. Fit-testing: Fit testing will include education on how to properly don and doff FPE, perform user seal checks, and when masks should be reused or replaced. Education on donning and doffing respirators and medical masks will be through handouts at fittesting and one-on-one discussion during the fit-testing process. In compliance with JHH/OSHA regulations, subjects will be required to fill out an amended version of the 1910.134 OSHA Respirator Medical Evaluation Questionnaire (Appendix M). We will only include clinics whose managers/leaders have agreed to the inclusion of their clinical site(s) in the study. The researcher will complete a fit test evaluation form (Appendix Q) to assess if the participant passes the fit testing requirement.
vii. Initial blood draw: approximately 15-20cc of blood will be drawn from the subject for baseline (at enrollment) influenza titers. Blood for serum titers will be drawn, processed and stored per laboratory protocol.
viii. Educational component: All subjects will be counseled on influenza vaccination per their local policy if they have not received it for the current season. Subjects wishing to be vaccinated will be encouraged to do so at the earliest possible time, so that seroconversion occurs by the study start. All subjects will be counseled on influenza vaccination in accordance with local policies and procedures (*e.g.,* no change in recommendations despite study participation). All subjects will be educated about standard precautions.

## 2) Intervention Period Assessments:

The intervention period will consist of 12-16 weeks of participants wearing their assigned FPE. Depending on the observed incidence of viral respiratory disease, the intervention period may be extended (or otherwise modified) if the incidence of influenza remains significantly elevated.

As discussed in the methods section, the duration of the intervention (mask wearing) period may be shortened or lengthened based on incidence and surveillance data available from each site. Flexibility in adjusting the duration of the intervention period is vital to allow for the maximum capture of data during viral respiratory season, which may be different at each site, each year. Consenting HCPs in each of the included clinics will be enrolled for the duration of the intervention period and will be asked to follow the cluster randomization scheme.

i. **Daily Exposure Form:** All participants will be asked to complete the daily exposure diary for each day during the intervention period regardless of whether the participant worked that day. This diary will collect participant symptom information, participant exposure to symptomatic patients/co-workers, hand hygiene frequency, and frequency of wearing N95s/medical masks.

ii. **Weekly Diary:** All participants will be asked to complete the weekly diary. This diary will capture participant symptom information, participant exposure to symptomatic household members, and flu vaccination status

iii. **Symptomatic Event Report Form:** If a participant develops respiratory/flu-like symptoms, a symptomatic event report form will be completed by either the participant/research staff.

iv. **Respiratory Specimen:** All subjects will be asked to consent to respiratory specimen collection, regardless of respiratory symptoms. Specimens from the upper respiratory passages, that may include a nasal and throat swab, will be collected from participants during this time. No nasopharyngeal aspirates will be performed. Randomized upper respiratory specimens will be collected 2-6 times during the study period: 2-3 times on a random basis, while 1-4 triggered respiratory specimens will be collected when symptoms are reported by participants. Participants may have two upper respiratory specimens collected in a single week, should they report symptoms, but will also be scheduled for a randomized swab. All swabs will be processed and stored for analysis at a later date. Should funding be made available, we plan to perform PCR testing on all respiratory specimen secretions, including the randomly collected specimens from asymptomatic subjects. First, we will be performing PCR testing on the samples from subjects having signs or symptoms of a respiratory infection including influenza. Respiratory specimens obtained from asymptomatic randomized participants will be stored for later PCR testing and analysis. While serology may detect up to 75% of asymptomatic cases, serology cannot identify infection with organisms other than influenza. PCR testing of samples from participants with signs or symptoms of influenza will allow us to accurately determine the organism that is causing the symptoms.

v. **FPE/Hand Hygiene Compliance Monitoring:** During unannounced visits to study clinics, research assistants will complete the subject compliance forms and may verbally correct participants who are observed donning/doffing/wearing FPE incorrectly or who are not following proper hand hygiene procedures to maximize compliance and protection of healthcare workers and patients. We may also be employing an additional patient-based hand hygiene and FPE monitoring system to assess practices on a clinic-wide basis (see Appendix Y). Forms may be distributed to participating sites asking their patients to record the HH and FPE practices of HCP during interactions. This information will be collected anonymously with respect to HCP and the patients.

Subjects with signs or symptoms of respiratory infection will be advised to consult with the local occupational/employee health department as per institutional guidelines. In many cases the Occupational Health Clinic would be expected to recommend employee sick leave for a short period (1 or more days). When absent from duty, subjects will be asked to continue completing their exposure and symptom forms. However, we plan to have an online survey/form system that will be integrated into the data collection scheme within the first flu season. When the subject-employees return to work (e.g., the Occupational/Employee health Department permits

the employee to return to duty), s/he will resume donning of the assigned protective devices and will resume their testing.

### 3) Post-Study Period Assessments

Two weeks after the conclusion of the intervention period, a post-season serological sample will be collected and a post-study survey will be completed. Although participants will only be required to wear FPE, provide upper respiratory specimen, and be observed for the initial intervention period, the entire course of the study will continue for two weeks after the intervention period to allow for the final visit for final serology and the post-study survey. It is anticipated that study participants will enroll for subsequent respiratory virus seasons. However, if participants withdraw prior to the completion of 4 respiratory virus seasons, replacements can be recruited on a season-by-season basis.

i. Post-Study Survey: All participants will be asked to complete a post-study survey. This form will collect participants' post-study attitudes, behaviors, and opinions on FPE usage and vaccination status at the end of the study period.
ii. Final Blood draw: Approximately 15-20cc of blood will be drawn from the subject at the end of the study (before termination). Blood for serum titers will be drawn, processed and stored per laboratory protocol.
iii. Supplemental Vaccine Questions: All participants will be asked to complete an additional survey about selected vaccinations for preventable diseases that can be acquired in the healthcare environment, in addition to the questions asked in the pre- and post-study surveys.
iv. Sub-study consent: Participants who participated in the main portion of the study will be asked to take part in a study extension, in which any additional respiratory specimens collected elsewhere may be accessed and tested for respiratory pathogens.

## *E4 Subject Stipends or Payments*

Subjects will be compensated for the time necessary to complete the entire study, resulting in a maximum possible compensation of $599 (Appendix W). HCPs' compensation will be prorated by duration of participation, contingent on the completion of the nasal and throat swabs, preliminary and post-study surveys, daily exposure diaries, weekly symptom diaries, and serological testing at the beginning and end of the study. Subjects who voluntarily withdraw from the study or are removed from the study mid-week, because of illness or other investigator-identified issue will receive compensation prorated according to completed study requirements. Subjects who do not meet eligibility requirements at screening will not receive compensation and will be withdrawn from the study. Receipt of the final $135 compensation at the end of the study will be prorated according to overall participant performance. Subjects who have withdrawn from the study before the endpoint, voluntarily or at the direction of the investigator, will not receive the additional $135. The compensation will be issued to study participants via checks mailed to their home addresses and will be issued twice during the study period, once after the $6^{th}$ week of intervention and again after all study activities are complete.

The research team may also implement incentives such as providing food or gift cards to participants to thank them for their participation and assistance, rewarding the clinic with the highest compliance, etc.

## *E5 Study Timetable*

See Table 2

## *E6 Safety and Adverse Events*

### 6.a Definitions and Classification of Adverse Events

Definition of Adverse Event: An adverse event (AE) is any adverse change from the patient's baseline (pre-study) condition, which occurs during the trial, after the consent form has been signed, whether the event is considered related to study procedure or not.

#### i Relationship

At each site, the principal investigator will assess the relationship of each adverse event to the research procedure, based on available information, using the following as guidelines:

a) Unrelated: No temporal association, or the cause of the event has been identified; or the study procedure cannot be implicated
b) Probably not related: the cause of the event has been identified;
c) Possibly related: Temporal association is present, but other etiologies are likely to be the cause; however, involvement of the study procedures cannot be excluded
d) Probably related: Temporal association is present; other etiologies are possible, but unlikely
e) Related: Temporal association is present
f) Other: unknown

#### ii Severity and Expectedness

The following AE definitions will be used:

Unanticipated/Unexpected Event: (Any untoward event that is not identified with the current investigator brochure or study protocol) Awareness of sign, symptom, or event, but discomforts enough to cause interference with usual activity and may warrant intervention.

Serious Adverse Event: Any untoward medical occurrence that results in death, is life-threatening, requires patient hospitalization, prolongs existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital abnormality.

## 6.b Data Collection and Reporting Procedures for Adverse Events

**Data collection procedures for adverse events**

Any event experienced by a participant in a given week will be documented in the weekly diary. Participants will complete the weekly symptom diary, and any event experienced during that week will be noted. The Research team will assess if the reported event meets the definition of adverse event. If the Study Coordinator or Principal Investigator learns of any hospitalizations or other adverse events or serious adverse event between study visits, an Adverse Event Submission Form will be completed (Appendix O). Information regarding the type of report will be collected initial and a follow-up, the date and description of the AE. All adverse events and Serious Adverse Events between the time of study entry (consent) and the end of post-study period will be collected and reported. Patients will be monitored for all ongoing unresolved adverse events until they are either resolved, or in the opinion of the Principal Investigator, the patient is medically stable.

**Reporting procedures**: All serious adverse events and unexpected/unanticipated events(s), will be submitted to local IRB according to their reporting policy. In addition, a summary of the adverse and serious adverse events will be sent to the sponsors/agency/DCC annually.

## 6.c Data and Safety Monitoring Board (DSMB)

Three independent researchers will constitute a Data Safety Monitoring Board (DSMB). The members of the board are expected to include the following members. The board composition could change at any time. Members with similar qualifications will be included to replace exiting members.

- Dr. Tia Powell, MD is a psychiatrist and bioethicist. She is the Director of the Montefiore-Einstein Center for Bioethics. Previously she has been the Executive Director of the New York State Task Force on Life and the Law, and the Director of Clinical Ethics at Columbia-Presbyterian Hospital in New York City. She graduated from Harvard University and Yale Medical School. She was a member of the Institute of Medicine Committee that reviewed a CDC and OSHA request to clarify the recommended guidelines for protection of HCPs exposed to novel H1N1 influenza.
- Dr. Elizabeth Colantouni Johnson, PhD is an Assistant Professor with joint appointments at the Johns Hopkins School of Medicine in the Department of Anesthesiology and Critical Care Medicine (ACCM) and at the Johns Hopkins School of Public Health in the Department of Biostatistics. She is a member of the Quality and Safety Research Group within ACCM. She earned her PhD at the Johns Hopkins Bloomberg School of Public Health of the Johns Hopkins University, her MS in Statistics at North Carolina State University and her BS at Virginia Tech.
- Daniel Morgan MD, MS is a physician and epidemiologist in Baltimore, Maryland. He is Associate Professor of Epidemiology and Medicine at the University of Maryland School of Medicine, Chief Hospital Epidemiologist at the Baltimore VAMC and a fellow at the Center for Disease Dynamics, Economics and Policy (CDDEP). His work is funded through the Department of Veterans Affairs, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Agency for Healthcare Quality and Research (AHRQ).

DSMBs typically make recommendations about study cessation/modification to avoid exposing subjects to an inferior intervention. This often occurs when the study results pass a statistical threshold demonstrating one arm to be inferior. In this context, the DSMB will be charged with identifying an appropriate time for protocol termination/modification based on available interim data about the incidence of influenza and respiratory infections. If one respiratory protective device is found to change the incidence of disease in a clinically significant fashion (e.g., $p$=0.05), the DSMB will weigh the risks and benefits of continuing or prematurely terminating the study. The DSMB will meet approximately yearly for respiratory virus seasons 1 and 2, and on an as needed basis after that time (e.g., December, May). One member of the team will be selected to be the primary liaison with the DSMB.

# F Statistical Plan

## *F1 Study Outcome Definitions*

The following definitions align with the definitions in the study's analysis plan, posted on clinicaltrials.gov here: https://clinicaltrials.gov/ct2/show/study/NCT01249625?show_desc=Y#desc. The most recent analysis plan was uploaded and registered to ClinicalTrials.Gov in June of 2017.

**Laboratory-confirmed influenza illness (LCI):** A laboratory-confirmed influenza illness is defined as laboratory confirmation of influenza infection by either: (A) detection of influenza virus by RTPCR in an upper respiratory specimen swab collected ideally within 48 hours of symptom onset but at least within seven days of symptom onset or (B) influenza seroconversion defined as a 4fold rise in hemagglutination inhibition antibody titers from the pre- to post-season serological samples.

**Acute Respiratory Illness (ARI):** The first secondary outcome is the incidence of ARI as a clinical syndrome. ARI is defined as the occurrence of signs or symptoms of respiratory infection, as defined by Table 2 in the published protocol, with or without laboratory confirmation.

**Influenza-Like Illness (ILI):** The second secondary outcome is the incidence of ILI as a clinical syndrome. ILI is defined as temperature of 100°F [37.8°C] or greater plus cough and/or a sore throat, with or without laboratory confirmation.

**Laboratory Confirmed Respiratory Illness (LCRI):** The third secondary outcome is LCRI attributable to any of the pathogens listed in Table 4. LCRI is defined as ARI combined with

laboratory confirmation by RT-PCR of any of the pathogen listed in Table 4 in an upper respiratory specimen swab after symptoms were reported and within seven days of the original symptomatic report. Events with multiple viruses detected will count as a single event of LCRI. If a swab that tested positive but was not associated with a symptomatic event (i.e. was not collected between symptom onset and seven days after symptom onset) then the incident does not count as a LCRI event. If an individual seroconverts to influenza, had symptoms at some time during the study, and does not have a PCR-confirmed pathogen event already, then we will assign them a single LCRI event.

**Laboratory Detected Respiratory Infection (LDRI):** The fourth secondary outcome is LDRI attributable to any of the pathogens listed in Table 4. For a participant with or without symptoms, an LDRI is defined as: 1) detection of a respiratory pathogen by PCR or other laboratory methods, or 2) serological evidence of infection (e.g. seroconversion) with a respiratory pathogen during the study surveillance period(s). In a case where two or more pathogens are identified in the same specimen, each pathogen will be considered to represent a separate infection (e.g., 2 pathogens as 2 events, 3 pathogens as 3 events) for that study participant for that time-point. Sequential detection of the same pathogens by PCR or other laboratory method in swabs collected at least 21 days apart will be considered separate infections.

## *F2 Study Outcome Measurements:*

### 2.a Measurement of the Protective Effects:

- Investigators will compare the incidence rates of LCI, ARI, ILI, LCRI, and LDRI among HCPs who were randomized to wear respirators versus medical masks as discussed in the following statistical section.

- Investigators will examine the relationship between incidence and possible risk factors, including compliance, attitudes and opinions of HCPs and workplace exposures. The analysis plan will account for the frequency and level of risk associated with nonoccupational exposures.

### 2.b Incidence Determination

- Investigators will determine incidence rates of LCI among HCPs in outpatient setting.

- Investigators will determine incidence rates of ARI, ILI, LCRI, and LDRI among HCPs in outpatient setting.

## *F3 Effect Size*

This study is powered to detect a statistically significant difference between two randomized intervention arms, where the primary outcome is laboratory-confirmed influenza. We aim to detect a 25% reduction (i.e., a relative risk of 0.75) in the incidence of laboratory confirmed influenza among subjects wearing an N95 respirator compared to subjects wearing a medical mask. These figures were chosen by balancing the goals of the study that are sometimes in

competition with each other, including (a) the anticipated mean incidence of laboratory confirmed ILI virus infection in all study locations, (b) level(s) at which one intervention is considered superior to another from a scientific perspective, and (c) the level(s) at which one intervention is considered superior to another from an ethical perspective, such that study discontinuation becomes necessary. Clinicians and clinical scientists in the Infectious Diseases and Occupational Medicine communities were informally surveyed for their opinions about the magnitude reduction necessary to sway policy, such that one device would be considered better than another. Most clinicians reported 15-25% would be necessary to change practice.

## *F4 Sample Size Determination and Power*

We chose the size of our sample based upon the expected attack rate of our primary outcome (lab-confirmed influenza) in our population. We estimate that over a year, 20% of unvaccinated individuals in the medical mask group will experience laboratory confirmed influenza. We assume that 65% of our population will be vaccinated. Among vaccinated individuals in the medical mask group we assume that vaccine is 65% effective in preventing influenza infection. Vaccine efficacies at the higher end of what has been seen (86% in health care workers) will lead to a reduction in the yearly attack rate to 8.8%, and efficacy on the lower end of what has been seen (51% in the general population) will lead to an increased yearly attack rate of 13.4%. This variation is smaller than what we might expect due to variations in the severity of influenza epidemics and vaccine uptake, and falls within the range of potential outcomes we consider in our sensitivity analysis (Table 5).

Hence, we expect a yearly attack rate of 11.55% {11.55% = 0.35*0.2+0.65*(1-0.65)*0.2}. Based on this yearly attack rate, we expect a 4-year attack rate of 38.80% {38.80%=1-(1-(0.35*0.2+0.65*0.35*0.2))$^4$}. We aim to detect a 25% reduction (i.e., a relative risk of 0.75 within each season) in the incidence of laboratory confirmed influenza among subjects wearing an N95 respirator compared to subjects wearing a medical mask.

We estimate the sample size needed to detect a significant difference in the incidence of laboratory confirmed influenza using the approach described by Ukoumunne. The sample size is given by

$$pn = 2*(z_{\alpha/2} + z_{\beta})^2 \frac{\pi_0(1-\pi_0)+\pi_1(1-\pi_1)}{(\pi_0-\pi_1)^2}(DEFF)$$

where p=the number of clusters (to be calculated) n=number of people in each cluster (estimated from the units targeted for inclusion to be

16) $z_{\alpha/2}$=1.96 for an alpha=0.05 $z_{\beta}$=0.84 for beta=0.8

$p_0$=cumulative proportion with lab confirmed influenza over four seasons in group 1 (medical mask group) (assumed to be 0.388 for LCI)

$p_1$=cumulative proportion with lab confirmed influenza in group 2 ( N95 respirator group) (assumed to be 0.304 for LCI)

DEFF=design effect (calculated to be 2.5)

The Design effect is calculated as:

$$1+\rho(n-1)$$

where $\rho$ is the intra-class correlation coefficient (assumed to be 0.1) and n is the average number of people in each cluster. The design effect provides an adjustment for the correlation of outcomes within clusters.

Using the above assumptions, we estimate that we need 157 independent clusters (clinics) with a median size of 16 individuals each to detect a relative risk of 0.75 between N95 and medical masks at preventing laboratory-confirmed influenza infection. Using this model, the total number of individuals participating each season would need to be 2506, with total personseasons accumulated over the course of the study of 10,024. For our secondary outcome of laboratory confirmed respiratory illness (LCRI), the total number of individuals participating each season would need to be 1,276, with total person-seasons accumulated over the course of the study of 5,104. (See Table 6). We expect some loss to follow-up (20-25%) and thus would target clusters of 20 individuals each cluster. These main power calculations have been confirmed using the Cluster Power software package for R.

We have performed an analysis of the sensitivity of our study design to variations in the fouryear attack rate of laboratory confirmed influenza, as well as our power to assess secondary outcomes under both high and low attack rate scenarios. These results are shown in Table 5.

## *F5 Statistical Methods and Analysis Plan*

***Descriptive statistics***

Standard descriptive statistics will be used to describe baseline characteristics and follow-up measures, both overall, and within each group. Summary statistics such as means, medians, and ranges will be produced for all measured continuous variables. Frequencies will be computed for all categorical and ordinal variables. Graphical methods including stem-and-leaf diagrams and box plots will be used to examine distributions, identify potential influential points, and guide the choice of transformations if warranted.

***Raw incidence calculations***

Using the outcome data discussed above, we will obtain estimates of the following quantities for all study participants and for each of the two study groups:

- the incidence of laboratory-confirmed influenza (rate across the whole season),
- the incidence of acute respiratory illness (rate by person-weeks),
- the incidence of influenza-like illness (rate by person-weeks),
- the incidence of laboratory-confirmed respiratory illness (rate by person-weeks),
- the incidence of laboratory-detected respiratory infection (rate by person-weeks).

***Incidence comparison between study groups***

To compare the above incidence rates among HCPs who were randomized to wear respirators versus medical masks, we will fit two different types of models.

*Logistic regression model*

A dichotomous variable will indicate whether or not a subject became infected with laboratoryconfirmed influenza during the entire influenza season. We will use logistic regression to model the difference in seasonal influenza infection between the N95 and medical mask groups, using generalized estimating equations (GEE) to account for cluster-specific correlation. If $Y_{ij}$ is an indicator of whether subject *i* in group *j* developed laboratory-confirmed influenza, and
$MASK_{ij}$ is an indicator of which mask the individual wore, then we would fit a version of this model

$$\text{logit}\left[\Pr(Y_{ij}=1 \mid MASK_{ij})\right] = \beta_0 + \beta_1 MASK_{ij}$$

with an exchangeable correlation structure within each unit to account for clustering. Additional covariates may be added to the model to adjust for possible confounding variables.

Count variables will measure the number of ARIs, ILIs and LCRIs that a subject developed across the study period and corresponding variables will track person-time. We will use Poisson loglinear regression to model the difference in seasonal respiratory infection rates between the N95 and medical mask groups, using GEE to account for cluster-specific correlation. Assuming that $D_{ij}$ is the number of illnesses experienced by subject i in group j, and $N_{ij}$ is the total person-time contributed, we model the expected number of illnesses as follows:

$$\log\left[E\left(D_{ij} \mid MASK_{ij}\right)\right] = \log N_{ij} + \beta_0 + \beta_1 MASK_{ij}$$

e

This model will be fit with an exchangeable correlation structure within each unit to account for clustering. Additional covariates may be added to the model to adjust for possible confounding variables.

## *F6 Missing Outcome Data*

Efforts will be made to keep missing data to a minimum, and participants who withdraw from treatment will be encouraged to continue on study in order to provide complete follow-up information. An intent-to-treat analysis, in which all available data on all randomized participants are included, will be used for the primary comparison of treatments.

Information necessary to complete the intention-to-treat analysis will be collected. Methods with potential outcome framework will be used as a secondary analysis. This data will be used to evaluate the effect of wearing respirators by accounting for the limited wear time or change in behavior during the course of the study that falls outside the study protocol.

Since periodic changes in infection control guidance and practice may occur over the study years, participants will be expected to adhere to the most up-to-date guidance issued by the Centers for Disease Control and Prevention (CDC) and local policies at each study institution, at a minimum. This may result in cross-overs (e.g., wearing an N95 instead of a MM) which will be accounted for in an intention-to-treat analysis after study termination.

The characteristics at the time of randomization for those participants without complete followup will be examined. To assess the potential biases introduced by differential withdrawal among different respirators, a comparison of withdrawal rates and time to withdrawal will be included as an ancillary analysis to the primary outcome comparison. The processes are further explained in the analysis plan.

## *F7 Planned sensitivity analyses*

### 7.a Potential outcome analysis for laboratory-confirmed influenza

To account for the unavoidable additional uncertainty regarding the missing data from our primary outcome, we will conduct a sensitivity analysis that randomly assigns binary outcomes to participants who did not complete the study. Specifically, we will create a two-dimensional grid on which we vary the influenza attack rates in participants who dropped out of the study for both the MM and N95 arm, separately. We will fix the MM dropout attack rate between half and twice the observed MM attack rate, based on complete data. We will fix the N95 dropout attack rate between half and twice the observed N95 attack rate, based on complete data. By varying these two parameters across the grid, and for each combination, calculating the adjusted odds ratio (averaged across n=50 imputed datasets for each point on the grid), we will observe the sensitivity of our results to values of the missing data.

### 7.b Analysis of differential withdrawal

The characteristics at the time of randomization for those participants without complete followup will be examined. To assess the potential biases introduced by differential withdrawal among different respirators, a comparison of withdrawal rates and time to withdrawal will be included as an ancillary analysis to the primary outcome comparison.

# G Data Handling and Record Keeping

## *G1 Confidentiality and Security*

*Data Management and Privacy:*

Data will be entered into a password protected database with unique identifiers assigned to each study participant. Paper data collection instruments will be stored in a locked filing cabinet. The data will be entered into a secure database. The specific database/data collection system used may vary at each site due to site-specific privacy/database/IRB guidelines. However, all data collected (i.e. surveys, specimen collection data) will be standardized. JHU has been identified as the data collection center and will serve as a clearinghouse for data while the study active (i.e., recruiting participants). Once participant recruitment interaction is complete, REDCap and cluster data will be securely moved to and stored at the UTSW, which will become one of the data management centers along with UF. After all data are collected and all analyses completed, linkage between participants and their unique identifier will be destroyed. During the course of the study, protected health information that is collected will be disclosed only to study personnel, unless otherwise required by law. All personnel have taken (and will continue to maintain) required training for HIPAA protection and research ethics.

A tracking system using coded identifiers will be implemented to facilitate tracking of sample compliance and sample movement between study sites, laboratories, and/or other pertinent locations. Coded identifiers will be matched year-to-year to link participants' data. This information will be stored and accessed in compliance with federal and study site requirements.

## *G2 Case Report Forms and Source Documents*

All subject-specific data recorded in diaries, forms or other record (including infection status) will be de-identified and kept confidential.

## *G3 Data Management*

Study data will be collected and managed using an electronic database which is a secure, webbased application designed exclusively to support data capture for research studies. This application provides: 1) an intuitive interface for data entry (with data validation); 2) audit trails for tracking data cleaning and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages (SPSS, SAS, Stata, R); 4) procedures for importing data from external sources; and 5) advanced features, such as branching logic and calculated fields.

Hosting and Security

During the active recruitment period, the application was hosted on servers administered by Johns Hopkins University. The servers were protected by both a hardware firewall and a web application firewall. In addition, they had multi-level intrusion detection, network security audits, and secondary hardware on standby for immediate replacement. All data transmitted between the client browser and web servers were encrypted using an SSL connection. They also ensured that server updates were applied in a timely manner and that the data were regularly backed-up and stored securely off-site.

UTSW and UF will become the data management centers, as was decided by the lead study team. The electronic database will be moved to a secure server hosted at UT Southwestern, and the study files will be transferred from JHU using an encrypted external hard drive. The study files will be securely stored on a password-protected, limited access network drive at UT Southwestern.

Data storage facilities managed by the Information Resources (IR) Department at UTSW will house the ResPECT database. The facilities agreement with UTSW's IR provides for an enterprise class data center equipped with uninterruptible power supplies (UPS) with automatic generator backup power in the event of a utility failure. In addition to state-of-the-art network security, the facility provides excellent physical security with 42 digitally recorded cameras monitoring every square inch of floor space, keycard access, and NACI federal background checked operations staff on-duty 24 hours a day, 365 days a year.

UTSW has state-of-the-art environmental controls and safety monitoring systems including fire detection with various levels of suppression, and the perimeter of the building is protected by a two-hour firewall. Authorized personnel have 24x7 access to their systems housed in the data center. In addition, IR maintains backup data sets in a data vault, in the event of a catastrophic failure. The locations of the backup sets are logged, tracked, and audited using a media management system.

A backup copy of the data will also be securely stored on an encrypted external hard drive at UF.

Authentication and User Rights

To access the ResPECT study website, all users of the web-capture system must have a valid username and password. Each user account has rights that can be granted or denied including: data import, data export, data comparison, data logging, file repository access, user rights assignment, data access groups assignment, lock/unlock records, and super user. In addition, they can be granted read, edit or no data entry rights for each data entry form.

The standard REDCap audit trail cannot be disabled. REDCap records all data activity, including the access username, timestamp, and a detailed description of the action. In compliance with FDA 21 CFR Part 11, an additional level of audit information is available using e-signatures and required descriptions of reasons for change. Once a data collection instrument has been locked for a given record in the project, a user with e-signature privileges may then apply an esignature to that form. If a record has been e-signed, then it denotes that its data has been both locked (to

prevent further changes) and authorized (i.e. by a user with e-signature privileges). In addition to e-signatures, a required "reason for change" can be enabled which requires the user to enter a description of the reasons for the changes being made. The e-signature history and the required reasons for change descriptions are both stored in REDCap's data audit trail.

# H Limitations

There are several possible limitations for this study:

(1) Available scientific literature supports a wide spectrum of respiratory illnesses involving HCPs. Our screening tool may miss persons who are infected with influenza or other respiratory pathogens if they are asymptomatic or minimally symptomatic. However, the presence of asymptomatic HCPs with respiratory infections should not affect the comparison of the effectiveness of the interventions as they should be equally distributed among the arms. We also hope to capture a significant portion of asymptomatic disease through serological testing for influenza titers, and by performing and storing respiratory swab specimens on all participants, with analysis of these stored samples carried out should funding be made available. However, currently only samples from participants who meet the criteria of being symptomatic with ILI will undergo analysis by PCR testing.

Still, as some organisms may be less likely to cause signs and symptoms, infections from these specific organisms may be more difficult to document.

(2) Self reporting of symptoms in the daily diary may under or overestimate illness especially among HCPs where there is a culture of "presenteeism."

(3) Compliance with not only respiratory personal protective measures, but with other behaviors such as hand hygiene and isolation, could all be important effect modifiers and could bias or confound results towards or away from the null. However, we would expect that the use of these normal protective measures would not be impacted by this study.

(4) We are including HCP populations that have a high rate of influenza vaccination that will require an increased sample size (accounted for in the calculations) using the conservative influenza incidence rates in this protocol.

(5) We are limited by our diagnostic strategy. We will attempt to obtain swabs from upper respiratory passages on all participants but will be limited by their willingness to have sampling done.

(6) Because we are having subjects wear personal protective equipment while at work, but not at home or in the community, it is possible that non-occupational exposures could nullify ("wash-out") any otherwise detectable differences in study arms. The probability of a Type I

(false positive) epidemiologic error is greater than would be expected if HCPs were to wear their respiratory protective measures 24 hours per day for the study duration. However, we will be assessing the level of risk exposure at home (Appendix D) that will allow us to account for to potential risk of infection outside of the workplace.

(7) Some subjects will probably choose to be compliant with guidelines, while some of their colleagues are non-compliant. All workers will be required to comply with the minimum requirements of the CDC guidelines and OSHA regulations. Since those wearing medical masks may not be complying with existing federal and institutional guidelines, it stands to influence other workers to do the same. Further, the presence of our study stands to raise awareness about the importance of wearing respiratory protective equipment, possibly introducing bias toward the null (Hawthorne effect). Such a "minority of compliance" could introduce error into our analyses, including sample size under-estimation.

(8) Only two medical mask models are used. The models used in this study exhibit better capture efficiency than most medical masks. Thus, other models of medical masks may not perform as well as this model and thus the data may not be generalizable to all hospital settings where poorer quality masks are used.

# I Anticipated Products and Impact

## *I1 New Knowledge*

- An assessment of the incidence rate of organism specific respiratory viral infections during respiratory season in all study locations.
- An analysis to determine the most effective respiratory protective equipment for use among HCPs to prevent transmission of respiratory viral illnesses during seasonal influenza season.
- In the event of a large-scale respiratory epidemic or pandemic, an analysis to determine the more effective respiratory protective equipment for use among HCPs to prevent transmission of respiratory viral illnesses during periods of prolonged wear and national equipment shortages.

## *I2 Publications and Reports*

- A publication in peer-reviewed medical journal – submission fall ~ 2017 – describing the absolute and relative effectiveness of respiratory personal protective measures.
- A publication in peer-reviewed medical journal – submission winter ~2017 describing the epidemiology of pathogens and the clinical impact of pathogens on HCPs in outpatient settings.
- A publication in peer-reviewed medical journal – submission winter ~2017 describing the knowledge, attitudes and beliefs of HCPs in outpatient settings about respiratory pathogens and FPE use to prevent their transmission.
- A report gauging national respiratory protective program changes, including resource and financial costs, that grow out of the study results

- A report that projects the development of evidence based guidelines that grow out of the study results for prevention of respiratory infection.  Additional publications may follow.

## *I3 Significance*

This study will be among the first attempts to determine the best facial protective equipment to use in a seasonal influenza outbreak, epidemic or pandemic event. This evidence-based information is needed to inform policy makers and administrators on how to prepare for these events.

# J Study Administration

At this time, nine institutions have been identified as participating centers: the Johns Hopkins Health System (JHHS) in Baltimore, MD; Denver Health Medical Center, in Denver, CO, and Children's Hospital Colorado, in Aurora, CO; the Department of Veterans Affairs sites in Denver, CO, Washington, DC, New York, NY, and Houston, TX; the University of Massachusetts, Amherst, MA; and University of Texas Southwestern, Dallas, TX. UTSW will serve as the study administrative site and house the samples and data for further analyses, and UF will also house a copy of the study data on an encrypted external hard drive. The transitions were made due to investigators moving to sites and are providing coordinating and supporting functions. Additional sites will be assessed by certification criteria (Appendix K) and must have an adequate number of outpatient visits/clinics (at least 25 that employ 20 or more HCPs), history of collaboration with other sites on large clinical trials, and research infrastructure experience with clinical studies. We aim to recruit at least 500 participants per study site, per influenza season. Depending on the capability of selected study sites to accrue subjects, up to 10 (ten) sites may be included altogether.

## *J1 Organization and Participating Centers*

### 1.a Study Site: Johns Hopkins Health System, Baltimore-Washington Region

JHHS includes 4 acute care hospitals: (1) JHH, (2) Bayview Medical Center (BMC), (3) Howard County General Hospital, and (4) Suburban Hospital; and a network of urgent care facilities and a group of outpatient primary care clinics organized under the umbrella of the Johns Hopkins Community Physicians. For this proposed study the primary sites will be the JHHS and BMC that

are located in the Baltimore area, the largest metropolitan area in Maryland (population of 1,024,645). Forty-seven percent of the population is African-American, and 52% is Caucasian. Only 9% of the population is over 65 years of age. One fifth of the population qualifies for Medicaid. We will also be approaching the network of 18 primary care facilities that constitute the Johns Hopkins Community Physicians. These facilities are located in 11 counties, providing a variety of primary care services to communities in and around Baltimore, Washington DC, and across the state of Maryland.

JHHS provides medical care to patients regardless of payer status and serves patients of both sexes and all races. Johns Hopkins Hospital is a 1026 bed hospital that includes a pediatric hospital (Johns Hopkins Children's Center), a 63-bed oncology unit (The Johns Hopkins Weinberg Oncology Center) and 8 ICUs. Johns Hopkins Bayview Medical Center (JHBMC), a 678-bed, fullservice medical center, includes a 331-bed community teaching hospital and 347 non-acute care beds, and the Baltimore Regional Burn Center. Services for seniors are concentrated in a 255bed Johns Hopkins Geriatrics Center. Clinics will be selected from this rich network of healthcare institutions and will be selected based on volume of cases of respiratory illness seen and willingness to participate. The participating JHH sites include the Harriet Lane Clinic, and the Pediatric and Adult Emergency Departments. Other proposed and participating sites include the Bayview and Howard County Emergency Departments, the Bayview Pediatric Department, JHHS clinics located in Green Spring, MD and White Marsh, MD, interested departments in JHH's Outpatient Center, and the Patient First Clinics associated with the Johns Hopkins Health System.

### *Resources at the Johns Hopkins Health System study site:*

JHHS's Hospital Epidemiology and Infection Control (HEIC) is responsible for surveillance of healthcare-associated infections and epidemiologically- important organisms (MRSA, VRE, influenza, RSV, etc.), prevention and control of communicable disease exposures, investigation and control of outbreaks, development of hospital policies to prevent and control the spread of healthcare-associated infections and epidemiologically-important organisms. All are infectious diseases-trained hospital epidemiologists with expertise in surveillance, healthcare economics and healthcare-associated infections.

Charlotte A. Gaydos, MS, MPH, DrPH will now serve as the site PI for the ResPECT Study, following Dr. Trish Perl's departure to UTSW. Dr. Gaydos is a Professor and Director of the Infectious Diseases STD Lab at Johns Hopkins University School of Medicine. She advised the study team on the appropriate handling of specimens and continues to advise on aspects of virology pertinent to the project. She has been responsible for the virological testing performed at JHU and will be overseeing the transfer of samples to UTSW.

Derek A. Cummings, PhD, who will supervise and conduct statistical and epidemiologic analyses, is an Adjunct Professor in the Department of Epidemiology at Johns Hopkins Bloomberg School of Public Health. He is also a Preeminence Professor in the Department of Biology and in the Emerging Pathogens Institute, at the University of Florida. Dr. Cummings' interests are in bridging theoretical work on infectious disease dynamics, field work on infectious diseases and public health responses to infectious disease outbreaks. He conducts research on spatial

temporal dynamics of dengue in Southeast Asia, influenza in the US and China, the impact of socioeconomic and demographic changes on disease transmission, dengue diagnostics and the dynamics of immune response as well as dengue vaccination strategies. Dr. Cummings training is in systems research and has worked on theoretical simulations of dengue, measles, chikungunya and influenza transmission. His field-work includes a community based study of influenza in southern China, a study of dengue among non-human primates in Senegal and a study of dengue in Thailand. Dr. Cummings conducts studies of influenza dynamics in southern China, health care workers in the US and in school-children in the US. Dr. Cummings has also worked to characterize transmission of multiple emerging pathogens including MERS-CoV, pandemic influenza, chikungunya and Ebola.

DCC: Initially at JHHS, the DCC for the ResPECT study includes a strong research group led by our Research Program Manager, a research coordinator, and research assistants. The group has a long history of implementing interventions within the healthcare setting. They have collaborated with the CDC and VHA and completed many projects designed to reduce the risk of healthcare-associated infections including clinical trials. This research group would be responsible for distributing the study materials and training the various participating sites on the conduct of the ResPECT clinical trial.

NOTE: The DCC will be moved to UTSW following the move of one of the co-PIs.

Surveillance data including the status of respiratory viruses are collected from several local area networks. The system contains information on demographics, length of stay, DRG's, ICD-9 codes and severity, reason for admission, previous admissions, number of preoperative days, and cost. Each system has limited access and significant security. In addition, surveillance for epidemiologically significant organisms including respiratory pathogens is performed and automated using several different surveillance/tracking/chart review systems in the JHHS. This system of healthcare information tools allow for efficient research and clinical accuracy across the many sites within the Hopkins network. These systems include (but are not limited to) Theradoc® software (Theradoc Corporation, Salt Lake City, Utah), the Johns Hopkins Hospital EPR (Electronic Patient Record), Eclipsys®/Allscripts®, the JHH POE (Provider Order Entry System), the Johns Hopkins Adjusted Clinical Groups Case Mix System, and the CDC Biosense System. If necessary, data for this project will be collected based on the systems and software available at each research site.

Occupational Health Services (OHS) is integrated across JHHS. Each site is staffed by a CRNP manager and nurses. As part of the respiratory virus policy, these personnel test ill HCPs with nasopharyngeal (NP) swabs. NP swabs are performed routinely on ill HCPs who present to work during the respiratory virus season. NP swabs are available during the day at OHS and in the emergency department in the evenings and on weekends. Investigators may pursue access to both to the results of these NP swab studies, performed per JHHS usual procedures, and to the

results of the respiratory specimen collection performed as part of the experimental studies described in this protocol.

## 1.b **Study Administration: National Personal Protective Technology Laboratory, National Institute for Occupational Safety and Health, CDC**

Lewis Radonovich, MD, formerly the Director of the VA's National Center for Occupational Health and Infection Control COHIC, a Senior Physician Scientist and Medical Officer at the National Personal Protective Technology Laboratory at NIOSH, who has served as Co-PI since study inception will continue in this role.

## 1.c Study Administration: North Florida Foundation for Research and Education (NFFRE):

A not-for- profit education foundation based in Gainesville, Florida, established in 1997 to administer and facilitate research funded from non-VA sources. The Executive Director of NFFRE, will be responsible for managing and distributing the non-VA funds to their respective locations.

## 1.c **Study Administration: Veterans Health Administration Network of Medical Facilities:**

On a nationwide scale, VA's health care system now includes 153 medical centers, with at least one in each state, Puerto Rico and the District of Columbia. The rich network of VA investigators is available for consultation and collaboration. In the past, VA investigators played key roles in developing the cardiac pacemaker, the CT scan, radioimmunoassay, and improvements in artificial limbs. Through VA's Cooperative Studies Program, researchers conduct multicenter clinical trials to investigate the best therapy for various diseases affecting large numbers of veterans.

The 1400 medical facilities in the national VA healthcare system are decentralized into 21 Veterans Integrated Service Networks (VISNs), each representing a geographic portion of the nation. Regional Network offices help integrate the activities of the medical facilities included in each VISN. Local medical center leadership is primarily responsible for the activities at each hospital and its affiliated outpatient clinics.

Almost 5.5 million people received care in VA health care facilities in 2008. In 2008, VA facilities treated 773,600 inpatients and served over 60 million outpatient visits. VA manages the largest medical education and health professions training program in the United States. VA facilities are affiliated with 107 medical schools, 55 dental schools and more than 1,200 other schools across the country. Each year, about 90,000 health professionals are trained in VA medical centers. More than half of the physicians practicing in the United States had some of their professional education in the VA health care system.

## 1.d Study Site: VA New York Harbor Healthcare System, New York NY

**Setting:** VA New York Harbor Healthcare System (NYHHS) is the first Veterans Health Administration (VHA) site and overall the second site to join the Respiratory Protection Effectiveness Clinical Trial (ResPECT) Study. It joins Johns Hopkins University (JHU) which served as the pilot site for this study and has been in operation for approximately 1 year.

**Organization:** VA NYHHS is a level 1A VHA facility. It consists of two tertiary care medical centers located in Manhattan and Brooklyn and a Community Living Center located in St. Albans, Queens. VA NYHHS also operates four Community Based Outpatient Clinics (CBOCs) located in Harlem, downtown Brooklyn, New York and Staten Island which serve New York, Kings, Queens and Richmond Counties. The Veteran population in this catchment of the New York-New Jersey Veterans Integrated Service Network #3 (VISN-3) is approximately 186, 869.

VA NYHHS operates 318 acute hospital beds, 179 Community Living Center beds and 74 Residential Treatment beds. The New York Campus is a tertiary care facility with bed services in acute medicine, surgery, acute psychiatry, neurology, rehabilitation medicine. It is also the interventional cardiology, cardiac surgery, and neurosurgery referral center for VISN-3. Its facility also includes an Emergency Room and an Ambulatory Care Center with Primary Care and all Specialty Care clinics. The Brooklyn Campus provides bed services in acute medicine, surgery, psychiatry and residential substance abuse. Specialized programs exist in comprehensive cancer care and non-invasive cardiology. The Cancer Program includes special expertise in palliative care and radiation oncology. Brooklyn also has a busy Emergency Room, Primary Care, and all Specialty Care Clinics. The St. Albans Community Living Center serves the metropolitan area with specialized geriatric care. The Center provides extended care rehabilitation, psycho-geriatric care and general nursing home care. A separate domiciliary provides psychosocial and independent living skills rehabilitation. St. Albans provides Primary Care and a limited number of specialty care clinic services (Mental Health, Dermatology, Optometry, Cardiology, Urology, Podiatry, and Dental). The CBOC in Staten Island provides Primary Care, Mental Health, Optometry and Podiatry services. The CBOCs in Harlem, lower Manhattan, and downtown Brooklyn provide Primary Care and Mental Health clinics.

VA New York Harbor's two major academic affiliations are New York University (NYU) Medical Center and SUNY Downstate Medical Center. It provides funding for 270 medical residents, as well as other disciplines, including dental, optometry, podiatry, psychology, physician assistants, nursing, pharmacy, social work, Dietician, Respiratory Therapy and Pastoral Care. In addition, approximately 850 medical students rotate through the Brooklyn and NY campuses annually.

In fiscal year 2010, VA New York Harbor Healthcare System Research Program had 199 both human and animal research projects and a budget of ~$6.0 million. Important areas of research include cardiovascular, hematology/oncology, cancer, infectious diseases including AIDS/HIV, mental health, substance abuse, rehabilitation engineering/ prosthetics, pulmonary, renal, geriatrics and optometry as well as clinical trials and co-operative studies.

In Fiscal Year 2010 VA NYHHS treated 50,705 unique patients and had 7115,382 outpatient visits. It provided 72,374 hospital days of care in its acute facilities (Brooklyn and New York); 50,047 days of care in the Community Living Center and 24,031 days of care in its Residential Rehabilitation programs.

VA NYHHS employs approximately 3,450 full time employee equivalents (FTEE). While some of the Medical Staff attending and all of its resident physicians are part-time and rotate at the affiliated hospitals, the vast majority of its primary care physicians and all of its nursing and support personnel are full-time employees.

**Resources Available:**

Michael S. Simberkoff, M.D. serves as the site PI for the ResPECT Study. He retired from the position of Executive Chief of Staff, VA NYHHS on July 1, 2016. He is now a volunteer member of the Infectious Diseases Section, Medical Staff of the New York Campus, VA NYHHS and Professor of Medicine, NYU School of Medicine. Dr. Simberkoff is Board Certified in Internal Medicine and Infectious Diseases (ID). He has extensive experience in infectious diseases research, VA Cooperative Studies (served as Study Chairman for 2 CSPs and as site PI as well as member of the Executive Committee of 2 others) as well as clinical infectious diseases. He has been the facility PI for the Veterans Aging Cohort Study (VACS) since it was initiated in 1993. Prior to his appointment as Chief of Staff, he served as Chief, Infectious Diseases, Chairman of the Infection Control Committee, and ACOS, R&D at VA NYHHS.

VA NYHHS has Employees Health Services at its Brooklyn, NY, and St. Albans campuses. It also has active Infection Control programs and practitioners at each of these sites. Infection Control reports through an Infection Control Nurse Manager to the Associate Director of Patient Care Services (Chief Nurse) and to the Chairman, Infection Control Committee.

VA NYHHS has well equipped and staffed Microbiology Laboratories at its Brooklyn and NY campuses. Both laboratories are equipped to perform some molecular testing for respiratory pathogens. Both are prepared to expand molecular testing should funding become available.

VA NYHHS has Employees Health Services at its Brooklyn, NY, and St. Albans campuses. It also has active Infection Control programs and practitioners at each of these sites. Infection Control reports through an Infection Control Nurse Manager to the Associate Director of Patient Care Services (Chief Nurse) and to the Chairman, Infection Control Committee.

VA NYHHS has well equipped and staffed Microbiology Laboratories at its Brooklyn and NY campuses. Both laboratories are equipped to perform some molecular testing for respiratory pathogens. Both are prepared to expand molecular testing should funding become available.

## 1.e Study Site: VA Eastern Colorado Healthcare System, Denver CO

**Setting:** VA-ECHCS is a tertiary care medical center serving veterans residing in Colorado, Wyoming, and Montana, and the second Veterans Affairs medical center to join the ResPECT study.

**Organization: VA-ECHCS** provides comprehensive care to 75,000 veterans, including community based primary care and a full range of referral services. It includes an acute care medical center with a full range of inpatient tertiary care service, on site primary and specialty care clinics, an active Emergency Department, two nursing homes in Denver and Pueblo, and nine community based outpatient clinics (CBOCs). There are CBOCs located in the Denver metropolitan area, Colorado Springs, and Pueblo that well serve as study clinics. VA-ECHCS employs approximately 1600 persons, of whom approximately 800 are direct care providers. There are two unions that are active at the campus, UNOS and AFGE. Both have been consulted and are supportive of the project. Dr. Bessesen has worked closely with the Nurse Executive, who also supports the participation of nurses in the study.

**Resources available:** Mary Bessesen, M.D. will serve as the site principal investigator for VA-ECHCS. She is the hospital epidemiologist, Chief of the Infectious Diseases section and a VA Merit funded investigator at VA-ECHCS. She has served as site director for multicenter studies of Clostridium difficile epidemiology and natural history, C. difficile treatment and S. aureus bacteremia epidemiology and treatment. She supervises a staff of four infection control practitioners, as well as a full-time nurse study coordinator and 2 RAs to complete the necessary protocol activities.

## 1.f Study Site: VA Michael E. DeBakey Medical Center, Houston TX

**Medical Care:** The Michael E. DeBakey VA Medical Center (MEDVAMC) serves as the primary health care provider for more than 120,000 Veterans in southeast Texas. Veterans from around the country are referred to the MEDVAMC for specialized diagnostic care, radiation therapy, surgery, and medical treatment including cardiovascular surgery, gastrointestinal endoscopy, nuclear medicine, ophthalmology, and treatment of spinal cord injury and diseases. The MEDVAMC is home to a Post-Traumatic Stress Disorder Clinic; a Network Polytrauma Center; an award-winning Cardiac and General Surgery Program; a Liver Transplant Center; a VA Epilepsy Center of Excellence; a VA Rehabilitation Research of Excellence focusing on mild to moderate traumatic brain injury; and one of the VA's six Parkinson's Disease Research, Education, and Clinical Centers. Including the outpatient clinics in Beaumont, Conroe, Lufkin, and Galveston, MEDVAMC outpatient clinics logged almost one million outpatient visits in fiscal year 2009.
**Teaching Hospital:** Nearly 3,500 health care professionals provide high-quality care to our Veterans. For more than 50 years, the MEDVAMC has provided clinical training for health care professionals through our major affiliate, Baylor College of Medicine *. MEDVAMC now operates the largest VA residency program with more than 251 slots. Each academic year, more than 1,972 students are trained through 144 affiliation agreements with institutions of higher learning in 19 states. Health care students from fields such as nursing, dietetics, social work, physical therapy, and a wide variety of medical specialties receive training here each year. This responsibility serves to enhance the quality of care provided to our Veterans. As a member institution of the Texas Medical Center * (TMC) since 1985, the MEDVAMC staff serves on

various TMC oversight committees that contribute to improved patient care and hospital operations. The majority of MEDVAMC physicians are also faculty members of Baylor College of Medicine. Many MEDVAMC programs have received national awards and honors including accreditation from Joint Commission for hospital, long-term care, behavioral health care, and substance abuse.

**Modern Facility:** Located on a 118-acre campus and built in 1991, MEDVAMC is a state-of-theart facility with 386 hospital beds, a 40-bed Spinal Cord Injury Center, and a 120-bed transitional care unit for long-term care. An automated, computer-controlled transport system delivers food, laundry, and supplies throughout the building. The six-story granite building is designed with four exterior sections and four atriums that contain patio gardens, wheelchair basketball courts, and a rehabilitation pool.

**Research & Development:** Supported with more than $16 million annually, research conducted by MEDVAMC staff ensures Veterans access to cutting-edge medical and health care technology. With 729 active research projects, the MEDVAMC Research & Development (R&D) Program is an integral part of the medical center's mission and plays a very important role in the health care Veterans receive. The production of new knowledge, techniques, and products has led to improved prevention, diagnosis, treatment, and control of disease.

**Resources Available:** Maria C. Rodriguez-Barradas, M.D. will serve as the site Principal Investigator (PI) for the ResPECT Study. She is the Director for the HIV Program and Professor of Medicine, Baylor College of Medicine. As Director for the HIV Program, she is responsible for all medical staff activities at the HIV-ID outpatient clinic at MEDVAMC, as well as in charge of the Infectious Diseases Fellows Program within the VA. Dr. Rodriguez-Barradas is Board Certified in Internal Medicine and Infectious Diseases (ID). She has extensive experience in infectious diseases research, including participation in VA Cooperative Studies (site PI for OPTIMA), in NIH funded clinical trial networks (CPCRA, INSIGHT) as well as PI for Merit Review Programs. She has been the facility PI for the Veterans Aging Cohort Study (VACS) since it was initiated in 1993. MEDVAMC has an active Infection Control program and Dr. Rodriguez participates in Infection Control activities as required. MEDVAMC has well equipped and staffed Microbiology Laboratories as well as an Infectious Diseases Research Laboratory. Both laboratories are equipped to perform molecular testing for respiratory virus pathogens. Both are prepared to expand molecular testing should funding become available.

## 1.g Study Site: VA Washington DC Medical Center, Washington, DC

**Setting**: Washington DC VA Medical Center (DC VAMC) is one of the four Veterans Health Administration (VHA) sites for the Respiratory Protection Effectiveness Clinical Trial (ResPECT) Study. The DC VAMC joined the ResPECT Study as a site in the fall of 2012.

**Organization**: DC VAMC is one of the most visible and dynamic facilities in the VA system. This tertiary care teaching facility provides acute general and specialized services in medicine, surgery, neurology and psychiatry, and also has a large long-term care facility on site. The Medical Center has a satellite Substance Abuse Clinic and three Vet Centers and a number of Community Based Outpatient Clinics.

The Medical Center's staff of 1,700 provides care to Veterans residing in the District of Columbia and portions of Virginia and Maryland. The DC VAMC cares for over 50,000 Veterans with more than 500,000 outpatient visits each year. The DC VAMC is the only VA medical center with three medical school affiliations – George Washington, Georgetown and Howard Universities. It is also affiliated with many other colleges and universities in such areas as pharmacy, rehabilitation medicine, biomedical engineering, dietetics, social work, nursing and medical center management.

The DC VAMC has a multi-million dollar research program that supports more than 100 investigators and 300 active research projects. Areas of research include mental health, substance abuse including alcoholism, hypertension, cardiovascular disease, hematology/oncology, infectious diseases including HIV/AIDS, pulmonary, nephrology, neurology, and war-related injuries.

The DC VAMC is part of the VA Capitol Health Care Network (VISN 5), which was established in October 1995, and serves Veterans from economically and demographically diverse areas within Maryland, the District of Columbia, and portions of Virginia, West Virginia, and Pennsylvania.

**Resources Available:** Cynthia L. Gibert, MD, MSc will serve as the site PI for the Respect Study. Dr. Gibert is Professor of Medicine, George Washington University School of Medicine and Health Sciences. At the Washington DC Veterans Affairs Medical Center, she is the Director of Special Projects in the Medical Service, an attending physician in the Infectious Diseases Section and a member of the IRB. For more than ten years she was the Assistant Chief of Infectious Diseases and the Director of the Infectious Diseases Clinic. Dr. Gibert is also a Senior Medical Adviser to the Veterans Affairs Office of Public Health. For 25 years, she has been involved in the conduct of NIH-funded clinical research in HIV/AIDS. Currently, she is the site PI for both the NIH-sponsored Veterans Aging Cohort Study. She served as the site PI for the OPTIMA trial a VA CSP-sponsored study. She is also a site investigator for the NIAID-funded DC Center for AIDS Research (D-CFAR) being overseen by the George Washington University HIV/AIDS Institute. Dr. Gibert is a member of the VA taskforce for multidrug resistant organisms – that has defined VA policy for both methicillin-resistant *Staphylococcus aureus* as well as *Clostridium difficile*. She is a fellow of both the American College of Physicians and the Infectious Diseases Society of America. She is board certified in both Internal Medicine and Infectious Diseases.

The Washington DC VAMC has an active Infection Control program and with four infection control practitioners. The Infection Control staff reports through the Infection Control Nurse Manager to the Medical Center Director and to the Chairman, Infection Control Committee. The Medical Center has a well-equipped and staffed Microbiology Laboratory. The laboratory is equipped to perform some molecular testing for respiratory pathogens if necessary and is prepared to expand molecular testing should funding become available. There is also a robust Occupational Health Service.

## 1.h Study Site: Denver Health & Hospital Authority, Denver CO

**Setting:** Denver Health and Hospital Authority (DHHA), is a regional, academic, level-one trauma center for the Rocky Mountain Region, and overall the third site to join the Respiratory Protection Effectiveness Clinical Trial (ResPECT) Study. It joins Johns Hopkins University (JHU) which served as the pilot site for this study and has been in operation for approximately 1 year.

**Organization:** DHHA serves the city and county of Denver, CO, and the Rocky Mountain Region. DHHA integrates acute hospital and emergency care with public and community health to deliver preventive, primary, and acute care services. DH employs approximately 5,000 people, approximately 2,500 of whom are direct care providers and serve special populations such as the poor, uninsured, mentally ill, pregnant teens, persons addicted to alcohol and other substances, victims of violence, the homeless, and those with AIDS and tuberculosis.

DHHA operates 477 acute hospital beds, and is one of the state's busiest hospitals with more than 25,000 admissions annually. DHHA's major academic affiliation is the University of Colorado Anschutz Medical Campus. Denver Health's Community Health Services manages more than 355,000 outpatient visits annually, from eight family health centers located throughout Denver neighborhoods, and 13 school-based health centers in Denver Public Schools, offering on-site medical care to elementary, middle and high school students, while DHHA's Emergency Department (Adult and Pediatric) and Adult Urgent Care Center manages more than 106,000 visits annually.

**Resources Available:** Connie S. Price, MD will serve as the site PI for the ResPECT study. She is the Chief Medical Officer at DHHA, and Assistant Professor of Medicine at the University of Colorado, School of Medicine. Dr. Price is board-certified in infectious diseases and medical microbiology. Her research and clinical interest focuses in healthcare epidemiology and methods to prevent nosocomial infections. She is an independently funded investigator who has served on numerous AHRQ task orders: As a task order lead for PBRN Task Order #16: Reducing Inappropriate Prescribing of Antibiotics by Primary Care Clinicians; as a Principle Investigator (with Dr. Savitz) on AHRQ (ACTION) Task Order 8- Improving the Measurement of Surgical Site Infection (SSI) Risk Stratification and Outcome Detection; as a Principle Investigator on AHRQ (ACTION) Task Order 7 - Reducing Hospital Associated Infections (HAI): Improving Patient Safety through Implementing Multidisciplinary Interventions in the Safety Net; a Consultant on PBRN Task Order #4: Management by Primary Care Clinicians of Patients Suspected of Having Community-Acquired, Methicillin-Resistant Staphylococcus Aureus (CA-MRSA) Infections; a Coinvestigator on Task Order #10 Model for Health Professionals Cross Training for Mass Casualty
Respiratory Needs. She chairs the Infection Control and Prevention Committee at Denver Health. She has nationally-recognized expertise in prevention of healthcare associated infectious diseases and currently is lead faculty for the State of Colorado ARRA- funded collaborative to reduce surgical site infections and *Clostridium difficile*. She is active in the Infectious Diseases Society of America and recently served in an elected position to the Board of

Directors of the Society of Healthcare Epidemiology of America. She also serves on the Colorado Healthcare Associated Infections advisory committee for public reporting of healthcare associated infections for Colorado.

DHHA Division of Infectious Diseases will also employ 3.25 FTEs for the duration of this study to complete necessary protocol activities. DHHA also has an active Infection Control program and practitioners.

## 1.i Study Site: Children's Hospital Colorado, Denver, CO

**Organization:** Children's Hospital Colorado (Children's Colorado) has defined and delivered pediatric health care excellence for more than 100 years. Founded in 1908, Children's Colorado is a leading pediatric network entirely devoted to the health and well-being of children. Continually recognized as one of the nation's outstanding pediatric hospitals by *U.S. News & World Report* and ranked 9th on its Best Children's Hospitals 2016-17 Honor Roll, Children's Colorado is known both for its nationally and internationally recognized medical, research and education programs, as well as the full spectrum of everyday care for kids throughout Colorado and surrounding states. Children's Colorado is recognized for excellence in nursing from the American Nurses Credentialing Centers and has been designated a Magnet® hospital since 2005. With more than 1,000 health care professionals representing the full spectrum of pediatric specialties, the network for Children's Colorado includes 16 regional locations including its main campus on the Anschutz Medical Campus, and more than 400 outreach clinics. For more information, visit www.childrenscolorado.org and connect with Children's Colorado on Facebook and Twitter (@ChildrensColo).

**Resources Available:** Ann-Christine Nyquist, MD, MSPH will serve as the site Principal Investigator (PI) for the ResPECT study. She is the Medical Director of Infection Prevention and Control Program and the Medical Director for Occupational Health at Children's Hospital Colorado. Dr. Nyquist is board-certified in Pediatrics and Pediatric Infectious Diseases. She is a Professor in the Department of Pediatrics, Sections of Infectious Diseases and Epidemiology at the University of Colorado School of Medicine and holds a secondary appointment in the Colorado School of Public Health in the Department of Community and Behavioral Health. Her research and clinical interest focuses in healthcare epidemiology, influenza, vaccinations and methods to prevent nosocomial infections. Dr. Nyquist served as Co-Principal Investigator for the CDC Emerging Infections study assessing pneumococcal vaccine efficacy which resulted in the Center for Disease Control and Prevention Charles C. Shepard Award for the Best Manuscript in 2006 in the Category of Prevention and Control-. From 2005-2009 she served as the site Principal investigator for the NIH Region VIII Regional Center of Excellence in Biodefense for two components of the grant: the Training Program for Clinical and Translational Research and Group Education. Nationally, Dr. Nyquist serves on American Academy of Pediatrics Committee on Infectious Diseases and the Society for Healthcare Epidemiology of America (SHEA) Pediatric Leadership Council Chair. She was an Invited Expert, representing Pediatric

Infectious Diseases Society, Department of Health and Human Services (HHS) Progress Toward Eliminating Healthcare-Associated Infections meeting. In 2007 she served on the Colorado State Health Department Pandemic Influenza Triage Working Group. Dr. Nyquist and her team recently received Children's Hospital Colorado 2011 Annual Pillar Award for Quality and Patient Safety- Infection for special recognition to staff who display outstanding performances that positively affect hospital outcomes related to their outbreak investigation of Bacillus cereus contamination of alcohol prep pads.

Children's Hospital Colorado will utilize the Children's Clinical Research Organization (CCRO) for the duration of the study to complete the necessary protocol activities. Children's Hospital has an active Infection Control program with 1.5 Physician FTEs, 4.0 FTE Infection Preventionists, 1.0 FTE Industrial Hygienist and 2.0 FTE Administrative Support. The Children's Clinical Research Organization (CCRO) at the Children's Hospital Colorado provides comprehensive research services, facilities and personnel to support the conduct and facilitation of clinical trials, including study start-up, execution and close-out. The mission of the CCRO is to improve the health of children by providing patients and health care professionals access to timely and reliable research resources to plan and execute clinical trials; as well as innovative opportunities to advance the diagnosis, treatment and prevention of pediatric diseases and their sequelae.

The CCRO team is made up of a dedicated group of clinical research professionals, including clinical research coordinators, regulatory professionals, financial administrators and management team. Services include: Study coordination: start-up and initiation, patient screening and recruitment, consenting, patient management, identification and reporting of adverse events, phlebotomy and drug administration (as appropriate and according to licensure), monitoring of patient compliance, data entry and query response, coordination of preparation for sponsor monitor visits, specimen processing and shipment, collaboration and coordination of ancillary services, project management, budget development and negotiation, collaboration with Office of Research Services contracting team and IRB submission and continuing review.

## l.l Study Site: Statistical Support: University of Massachussetts, Amherst, MA

UMass Amherst, the flagship campus of the University of Massachusetts system, sits on nearly 1,450 acres in the scenic Pioneer Valley of Western Massachusetts, 90 miles from Boston and 175 miles from New York City. The library system is the largest at a state-supported institution in New England with more than 5.8 million items. The University of Massachusetts Amherst Library System provides support for research through collections in the 28-story W.E.B. Du Bois Library and two science libraries. Numerous periodical indexes and full text databases may also be accessed electronically. The Five College online catalog provides electronic access to library catalog records at the University and the surrounding four colleges (Amherst, Hampshire, Mount Holyoke and Smith colleges). Reference librarians are available in person, online, and by telephone.

The Reich Laboratory (http://reichlab.io) is the research lab of Dr. Nicholas Reich at U. Mass. In addition to Dr. Reich, it also houses Dr. Alexandria C. Brown. Dr. Reich is Dr. Brown's primary mentor, in the Department of Biostatistics and Epidemiology. Dr. Brown has her own desk space

and computer in a shared office space with 2 other postdoctoral researchers and 2 graduate students, all of whom are working on modelling infectious disease dynamics. Weekly lab meetings allow the opportunity to present ongoing work, confront issues, and brainstorm new ideas with the lab team. Dr. Brown has a 15.6 GiB Intel® Core™ i7-4790 CPU @ 3.60GHz × 8 desktop computer with 3.9 TB of disk space. This machine is connected to the Department's Local Area Network (LAN). The LAN enables secure hard disk space for research projects that is accessible by multiple users and backed-up daily.

The School of Public Health and Health Sciences (SPHHS) is comprised of approximately 50 fulltime faculty members, including six epidemiologists and six biostatisticians. SPHHS maintains micro computer research rooms for faculty, staff and students. Fourteen PC compatible microcomputers, a file server, a scanner and two laser printers are connected to the Department's Local Area Network (LAN). The LAN enables secure hard disk space for research projects that is accessible by multiple users and backed-up daily. The following software packages have been installed on the LAN: SAS System 9.1 for Windows, Stata 9, SAS callable SUDAAN, Minitab 13.1 for Windows, SPSS 14, Microsoft Office XP, Dreamweaver MX, Endnote 6.0, NCSS 2001, Nud*ist N6, and Adobe Acrobat.

**Resources Available:** Nicholas Reich, PhD, is a biostatistician whose research operates at the interface of biostatistics and epidemiology. He has broad experience as a collaborating and independent biostatistician across many different biomedical and global health research settings. His areas of research focus have been on developing statistical methodology for analyzing and modeling disease surveillance data, and developing methods for analyzing clusterrandomized clinical trial data. He received doctoral training in Biostatistics and post-doctoral training in Infectious Disease Epidemiology at Johns Hopkins Bloomberg School of Public Health. He has served as the statistician for the ResPECT Study since its inception.

## I.m **Study Site Administration and DCC: University of Texas Southwestern Medical Center, Dallas TX**

UT Southwestern is a prominent medical education and biomedical research institution in the United States. It is located in the Southwestern Medical District, a 1,000 plus-acre campus in Dallas incorporating three degree-granting institutions - UT Southwestern Medical School, UT Southwestern Graduate School of Biomedical Sciences, UT Southwestern School of Health Professions – along with four affiliated hospitals: Parkland Hospital, Children's Health℠, Zale Lipshy University Hospital, and William P. Clements Jr. University Hospital. One of the largest medical schools in the country, UT Southwestern annually trains about 3,700 medical, graduate, and health professions students, residents, and postdoctoral fellows each year. Ongoing support from federal agencies, such as the National Institutes of Health, along with foundations, individuals, and corporations, provides approximately $422.6 million per year to fund more than 5,700 research projects. UT Southwestern faculty physicians provide patient care at UT

Southwestern University Hospitals & Clinics, Parkland Health & Hospital System, Children's Medical Center, Texas Scottish Rite Hospital for Children, VA North Texas Health Care System, and other affiliated hospitals and community clinics. Faculty and residents care for more than 100,000 hospitalized patients and oversee approximately 2.2 million outpatient visits a year, providing more than $106.7 million in unreimbursed clinical services annually.

The Division of Infectious Diseases includes 24 full time faculty members, 9 of whom are faculty preceptors. There is ample administrative support for the training program within the division which includes: 1) Division Administrator, who manages and directs the administrative and business functions of the Division and also coordinates grant submissions, budget monitoring, and personnel; 2) Division Accountant, who monitors budgets and provides monthly reports to PIs in the division; 3) Grants and Contracts Specialist, who prepares grant applications and progress reports for all divisional grants; and 4) Fellowship Coordinator, who oversees administrative duties of both the fellowship and T32 grant trainees. The Division of Epidemiology, organized within the Department of Internal Medicine, was founded by Dr. Robert Haley in 1983 and since has served a leading role in organizing and managing large multidisciplinary studies spanning the range of research from basic mechanistic to clinical and population studies. The UT Southwestern Department of Clinical Sciences is a multidisciplinary department which encourages clinical research and provides an academic, educational, and cultural home for clinical investigators across all departments and disciplines of the University. The DCS has the following 5 divisions staffed by full-time faculty: Outcome's and Health Services Research, Biostatistics, Biomedical Informatics, Community Health Sciences, and Behavioral and Communication Sciences.

**Resources Available:** Trish M. Perl, MD, MSc, serves as a co-PI for the ResPECT study. She supervised the Johns Hopkins University sites while a faculty member there and the DCC. She continues to supervise the overall conduct of the study. She is the Chief of Infectious Diseases at UT Southwestern Medical Center where she is the Jay P Sanford Professor of Medicine. She has extensive experience in clinical trials and is an expert in in health careassociated infections, antimicrobial-resistant organisms, emerging pathogens, and infection prevention. She is an Adjunct Professor of Medicine in the School of Medicine and recently left Johns Hopkins. Previously, she served for 20 years on the faculty of Johns Hopkins School of Medicine, which was one of the first Centers of Excellence for health care-associated infections. She earned her medical degree at the University of North Carolina School of Medicine, did her residency at Royal Victoria Hospital at McGill University in Montreal, and did her fellowship in clinical epidemiology and infectious diseases at the University of Iowa. Dr. Perl also did a twoyear stint with the Canadian equivalent of the Epidemic Intelligence Service, and her first outbreak investigation – an encephalopathy caused by eating mussels – was published in the *New England Journal of Medicine*.

### I.n Study Site: Statistical and Epidemiologic Support: University of Florida

The University of Florida (UF) is an American public university that sits on a 2,000-acre campus in Gainesville, Florida. The University of Florida is divided into 16 colleges and more than 150 research, service and education centers, bureaus and institutes, offering more than 100 undergraduate majors and 200 graduate degrees. The University of Florida is one of the nation's

largest research universities. The University of Florida was awarded $678 million in research expenditures, more than all other Florida universities combined, in sponsored research in 2009-10.

University of Florida Health has two campuses in Gainesville and Jacksonville. It includes two teaching hospitals and two specialty hospitals, as well as the colleges of Dentistry, Medicine, Nursing, Pharmacy, Public Health and Health Professions, and Veterinary Medicine, including a large animal hospital and a small animal hospital. The system also encompasses six UF research institutes: the Clinical and Translational Science Institute, the Evelyn F. and William L. McKnight Brain Institute, the Genetics Institute, the UF Health Cancer Center, the Institute on Aging and the Emerging Pathogens Institute. UF Health is the only academic health center in the United States with six health-related colleges on a single, contiguous campus.

**Resources Available:** Derek Cummings, PhD, MHS, MS, is an infectious diseases epidemiologist under UF's Preeminence Program, through which he serves as a full professor for the department of biology and the Emerging Pathogens Institute. Prior to his arrival at the University of Florida he worked for the school of public health at Johns Hopkins University, where he was an associate professor in the school's department of epidemiology. Cummings' research focuses on identifying the factors that influence the spread of infectious diseases in order to develop strategies to control and curb their proliferation. Cummings' work with emerging pathogens spans several nations, including southern China, Thailand, Liberia, Senegal, and Saudi Arabia. Though he has examined a variety of diseases, the bulk of his research has focused on the dengue virus and influenza.

In southern China he studied influenza A and patterns of transmission between rural and urban areas. In Saudi Arabia he studied Middle East Respiratory Syndrome (MERS). In Senegal he studied transmission of the dengue virus in non-human primate species – baboons, red monkeys, and green monkeys. Cummings has conducted extensive research on pathogens in the United States as well. He was the principal investigator in a study of seasonal shifts in transmission of influenza A, influenza B, and respiratory syncytial virus (RSV) in Pittsburgh, Pennsylvania.

**ADDITIONAL STUDY SITES**

Since it is not possible to predict the location of the future outbreaks, despite being "seasonal," multiple sites from across the U.S. will be identified for participation. In order to optimize the use of funding, several criteria will be used to guide the selection process (Appendix K).
Ideally, study sites would have the following characteristics:

- Site has at least 25 clinics (EDs, outpatient clinics, etc.) that employ 16 people or more. Or, have fewer clinics that are easily divisible into 25 separate work environments, with 16 or more people working in each work environment.

(This is based on 400 participants per site, per year.)

- Site needs to have a track record of research.
- Site needs to have an active research staff that can conduct the study without undue delay.
- The site needs to show past ability to do collaborative research.
- Site should have a track record of clinical trials.
- Site should have a history of collaborative research efforts with one of the Principal Investigators
- Site should have a pediatric component in their set of possible study locations (because the incidence of infectious diseases is highest in these settings). This criterion would not apply to VA study sites.
- Active respiratory protection program including training and annual fit testing in place

## *J2 Funding Source and Conflicts of Interest*

Two US Federal Government Agencies provided most of the funding for this project. Together, the Centers for Disease Control (National Institute of Occupational Health and Safety) and the Veterans Health Administration (Office of Public Health and Environmental Hazards) have expressed commitment to approximately $10M. It is well-understood by representatives at both agencies that funds reaching beyond $10M could be required to reach the primary endpoint, especially if the incidence of measured outcomes happens to be relatively low in the study-site locations when data is collected. However, in a setting with high-than-usual counts of influenza or ILI, the primary endpoint could be achieved in less than a 4-year period as described. If accessible funding draws low, a group of key CDC decision-makers will determine whether to continue pursuing some or all of the study endpoints, and how. The Biomedical Advanced Research and Development Authority (BARDA) provided an additional $350,000 in funding in fiscal year 2017.

There are no known conflicts of interest, financial or otherwise.

## *J3 Committees/Science Board*

While many of the key questions about the design and conduct of this clinical trial have been answered, a variety of questions and issues will be raised during the course of the study. To ensure that each question or issue receives impartial and equitable attention from the Investigators, an independent Science Board (SB) will be developed. The Members of this Board, each an eminent scholar and/or opinion leader, will offer their personal opinions about challenging and complicated questions or concerns about the study while it is being conducted. Any changes made by the SB on the protocol or the conduct of the study will be reviewed and approved by the coordinating center's IRB, the IRB at NIOSH, and the local IRBs for each site before the changes are implemented in the conduct of the study.

In contrast to the narrow focus of the Data Safety Monitoring Board (DSMB), topics addressed by the SB will be open and unrestricted and may involve a wide variety of scientific, sociological, economical or political topics. Members of the SB may change over the course of the Study.

Science Board Members:

Michael Bell, MD – Centers for Disease Control
Arnold Monto, MD – University of Michigan School of Public Health
David Weissman, MD – Centers for Disease Control/ National Institute for Occupational Safety and Health
Mark Loeb, MD – McMaster University

Trish M. Perl, MD, MSc – University of Texas Southwestern
Lew Radonovich, MD – Centers for Disease Control and Prevention

# K Publication Plan

As this is a large, multicenter study, authorship rules need to be defined in advance. All publications of information or data related to this project will come under this rule. Publications by an investigator of results from his or her institution's part of the study should involve collaboration with the other participating investigators and the ResPECT Study Consortium and should include input from the principal investigator(s), and his or her colleagues. Such input should be reflected in publication authorship, and agreement regarding order of authors' names should be tentatively established before drafting the manuscript. Additionally, publications must comply with confidentiality obligations owed to the sponsor.

The members of the ResPECT Study Consortium must have the opportunity to review and comment on all proposed abstracts, manuscripts, or presentations regarding this study ideally 60 days prior to submission for publication/presentation. During this 60-day period, Consortium members may respond with any requested revisions. Any information identified by the members of the Consortium as confidential must be deleted prior to submission. If reasonably requested, members of the Consortium will take reasonable steps to expedite the review process to meet publication deadlines. Submission may be made upon notification by the Consortium that such review has been completed and after issues found in the review and/or information identified by the Consortium as confidential is deleted. The ResPECT Study Consortium also has the right to publish the results of this study.
All manuscripts submitted for publication must have "The ResPECT Study Consortium" listed in the authorship section. The members of the ResPECT Study Consortium will be identified under acknowledgements at the end of the manuscript.

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# M Attachments

## *M1 Tables*

Table1 **Protocol Activities by Week**

| | **Pre-Study Period** | **Intervention Period (weeks)** | | | | | | | | | | | | **Post-Study Period** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Week** | ≥5 weeks before study begins | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12-16 | ≥2 weeks |
| **Event** | -Recruitment<br>-Consenting<br>-Lead-in Education<br>-FPE Training | I | I | I | I | I | I | I | I | I | I | I | I | |
| **Data Forms** | -Screening<br>-Fit-testing Q<br>-Baseline Survey<br>-Pre-study survey | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | L<br>O | Post-study survey |
| **Specimen Collection** | B | R | R | R | R | R | R | R | R | R | R | R | R | B |

**Key:**
B = Blood Draw
I = Randomized Intervention FPE
R= Upper Respiratory specimen, randomized and triggered as indicated.
L = Weekly diary and Daily Exposure forms, and Symptomatic Event Report form if needed.
O =FPE and Hand Hygiene Observation Forms

**Study is projected to last 20 weeks during the height of viral respiratory season, as determined by surveillance/incidence of RPI, but may be modified according to incidence rates. Intervention Period could be shorter than 16 weeks, but will be at least a minimum of 12 weeks.**

## Table2 **Case Definition* of Acute Respiratory Illness**

| | |
|---|---|
| | **Signs** |
| | Fever (T > 37.8° C) |
| | Tachypnea (Respiratory Rate ≥ 25) |
| | Coryza |
| Lymphadenopathy | |
| | **Symptoms** |
| | Vomiting/Nausea |
| | Diarrhea |
| | Cough |
| | Sputum Production |
| | Fatigue |
| | Malaise |
| | Headache |
| | Sore Throat |
| | Dyspnea |
| | Chills |
| | Sweats |
| | Arthralgias/Myalgias/Body Aches |
| | Other Gastrointestinal Symptoms |

*An acute respiratory illness is defined as:
The presence of any sign(s) OR two symptom(s) listed above.
Positives must represent a *change from baseline*

## Table3 **List of potential ILI pathogens**

□ Influenza A □
Influenza B
□ Respiratory Syncytial Virus Type A □
Respiratory Syncytial Virus Type B
□ Parainfluenza virus Type 1
□ Parainfluenza virus Type 2
□ Parainfluenza virus Type 3
□ Parainfluenza virus Type 4(a)
□ Parainfluenza virus Type 4 (b)
□ Human Metapneumovirus
□ Adenoviruses
□ Coronavirus OC43
□ Coronavirus NL63
□ Coronavirus 229E
□ Coronavirus HKU1
□ Human Rhinovirus
□ Cocksackie/echoviruses
□ Bocavirus
□ Bordetella pertussis
□ Streptococcus pneumonia
□ Steptococcus pyogenes
□ Staphylococcus aureus
□ Hemophilus influenza
□ Other microbial respiratory organisms of interest in the future

## Table4 **Power analysis of the sensitivity to the 4-year attack rate:**

Power analysis of the sensitivity to the 4-year attack rate for the primary outcome (laboratory confirmed influenza) and secondary outcomes (ILI, ARI). The power to detect a relative-risk of 0.75 between the N95 group and the medical mask group and the relative-risk that can be detected with 80% power are shown for scenarios representing the low and high end of reasonable attack rates in the medical mask (i.e., the control) group. For all calculations the twosided Type I error probability is 0.05.

| | Low Attack Rate Scenario | | | High Attack Rate Scenario | | |
|---|---|---|---|---|---|---|
| *Outcome* | *S.M. Attack Rate* | *Power (RR=0.75)* | *Detectable RR (80% Power)* | *S.M. Attack Rate* | *Power (RR=0.75)* | *Detectable RR (80% Power)* |
| Primary | 0.2 | 43% | 0.62 | 0.5 | 93% | 0.80 |
| ILI | 0.15 | 33% | 0.56 | 0.4 | 82% | 0.76 |
| ARI | 0.5 | 93% | 0.80 | 0.95 | 100% | 0.94 |
| LCRI | 0.3 | 91% | 0.79 | 0.7 | 100% | 0.90 |

Table5 **Sample size and power calculations for primary and secondary outcome.**

This table shows the total person-seasons of observation required for the primary outcome (LCI) and a secondary outcome (LCRI), assuming a four-year study. The annual attack rate for the medical mask (MM) group is calculated for LCI based on assumed vaccination rates and efficacy.

| | M.1.a.i.1.1.1.1.1 | LCI | M.1.a.i.1.1.1.1.2 | LCRI |
|---|---|---|---|---|
| **M.1.a.i.1.1.1.1.3 Annual attack rate, SM group** | M.1.a.i.1.1.1.1.4 | 0.12 | M.1.a.i.1.1.1.1.5 | 0.25 |
| **M.1.a.i.1.1.1.1.6 Cumulative 4-year attack rate, SM group** | M.1.a.i.1.1.1.1.7 | 0.39 | M.1.a.i.1.1.1.1.8 | 0.68 |
| **M.1.a.i.1.1.1.1.9 Detectable relative risk** | M.1.a.i.1.1.1.1.10 | 0.75 | M.1.a.i.1.1.1.1.11 | 0.75 |
| **M.1.a.i.1.1.1.1.12 Median cluster size** | M.1.a.i.1.1.1.1.13 | 16 | M.1.a.i.1.1.1.1.14 | 16 |
| **M.1.a.i.1.1.1.1.15 ICC** | M.1.a.i.1.1.1.1.16 | 0.1 | M.1.a.i.1.1.1.1.17 | 0.1 |
| **M.1.a.i.1.1.1.1.18 Total personseasons of observation** | M.1.a.i.1.1.1.1.19 | 10,024 | M.1.a.i.1.1.1.1.20 | 5,104 |

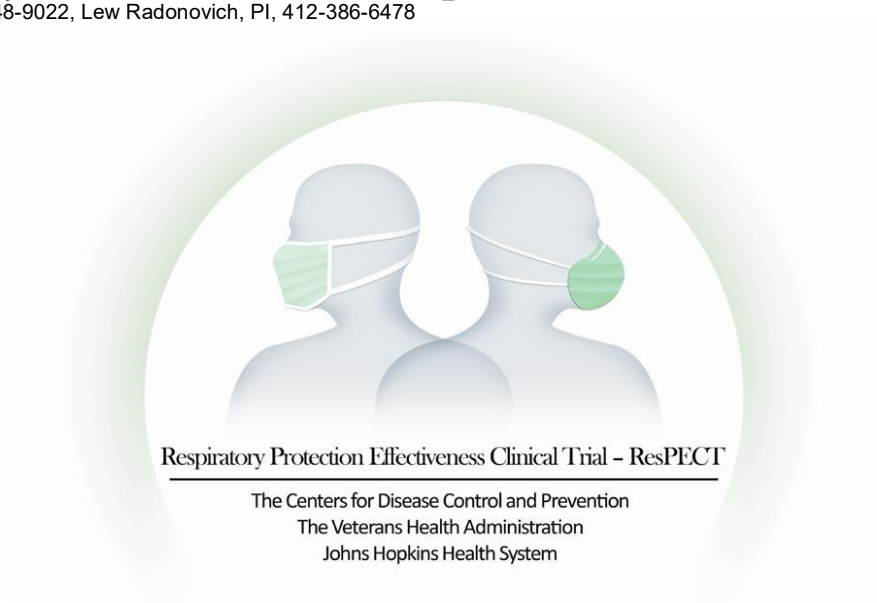
## *M2 Appendices*

### *Appendix A* Cluster Randomization Scheme

| M.2.a.i.1.1.1.1.1 | **Cluster A FPE** | **Cluster B FPE** |
|---|---|---|
| M.2.a.i.1.1.1.1.2 Week 1 | M.2.a.i.1.1.1.1.3 Not yet randomized | M.2.a.i.1.1.1.1.4 Not yet randomized |
| M.2.a.i.1.1.1.1.5 Week 2 | M.2.a.i.1.1.1.1.6 N95 Respirator | M.2.a.i.1.1.1.1.7 Medical Mask |
| M.2.a.i.1.1.1.1.8 Week 3 | M.2.a.i.1.1.1.1.9 N95 Respirator | M.2.a.i.1.1.1.1.10 Medical Mask |
| M.2.a.i.1.1.1.1.11 Week 4 | M.2.a.i.1.1.1.1.12 N95 Respirator | Medical Mask |
| M.2.a.i.1.1.1.1.13 Week 5 | M.2.a.i.1.1.1.1.14 N95 Respirator | M.2.a.i.1.1.1.1.15 Medical Mask |
| M.2.a.i.1.1.1.1.16 Week 6 | M.2.a.i.1.1.1.1.17 N95 Respirator | M.2.a.i.1.1.1.1.18 Medical Mask |
| M.2.a.i.1.1.1.1.19 Week 7 | M.2.a.i.1.1.1.1.20 N95 Respirator | M.2.a.i.1.1.1.1.21 Medical Mask |
| M.2.a.i.1.1.1.1.22 Week 8 | M.2.a.i.1.1.1.1.23 N95 Respirator | M.2.a.i.1.1.1.1.24 Medical Mask |
| M.2.a.i.1.1.1.1.25 Week 9 | M.2.a.i.1.1.1.1.26 N95 Respirator | M.2.a.i.1.1.1.1.27 Medical Mask |
| M.2.a.i.1.1.1.1.28 Week 10 | M.2.a.i.1.1.1.1.29 N95 Respirator | M.2.a.i.1.1.1.1.30 Medical Mask |
| M.2.a.i.1.1.1.1.31 Week 11 | M.2.a.i.1.1.1.1.32 N95 Respirator | M.2.a.i.1.1.1.1.33 Medical Mask |
| M.2.a.i.1.1.1.1.34 Week 12-16 | M.2.a.i.1.1.1.1.35 N95 Respirator | M.2.a.i.1.1.1.1.36 Medical Mask |

## Appendix B Recruitment Flyer

## The Respiratory Protection Effectiveness Clinical Trial (ResPECT)




In the face of a respiratory disease epidemic, what kind of respiratory protection works best? We are investigating what type of facial protective equipment is more effective in preventing flu and other respiratory pathogen transmission. Help us find the answer! Earn up to $599 for your time and participation in our research study!

Open to outpatient healthcare workers over the age of 18. We will be visiting your clinic for enrollment soon.

**Questions?**

Please call the ResPECT Team at 410.614.6206/pager 410.434.0821
OR
email us at respect@jhmi.edu

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 0.614.6206, 410.614.6206, 410.614.6206, 410.614.6206, 410.614.6206, 410.614.6206, 410.614.6206, 410.614.6206, 410.614.6206, 410.434.0821 | | | | | | | | |
| ResPECT Study Res | PECT Study Res | PECT Study Res | PECT Study Res | PECT Study Res | PECT Study Res | PECT Study Res | PECT Study Res | PECT Study |
| 0 1 | 3 4 | 6 7 | 9 0 | 2 3 | 5 6 | 8 9 | | |

Name: _____

## *Appendix C* Inclusion/Exclusion Screening

### Inclusion/Exclusion Screening

Inclusion/Exclusion Screening Form

| | Yes | No |
|---|---|---|
| 1. Are you 18 years or older? | □ | □ |
| 2. Do you have daily face-to-face (within 6 feet) contact with patients during work shifts? | □ | □ |
| 3. Are you willing to wear either an N95 respirator or a medical/surgical mask when coming into contact with patients with suspected/confirmed respiratory infection for the duration of the study period? | □ | □ |
| 4. On average, do you work at least 24 hours per week in a clinic setting? | □ | □ |
| a. **If yes**, on average, how many hours per week do you have patient contact (within 6 feet of patients) at this clinic? _____<br>b. **If no**, on average, how many hours a week do you work in the clinic in which you were recruited for this study? _____ | | |
| 5. During the intervention period (flu-season), will you be working at only one clinic or emergency department?<br><br>(If no, ask details, record in notes, and report to PI) _____ | □ | □ |
| 6. (N/A for women): If you have facial hair, are you willing to shave it off and keep it off, so that you can be fit tested for and wear a mask or respirator for the 16-week study period? | □ | □ |
| 7. Can you wear a respirator or medical mask for an extended period of time? | □ | □ |
| 8. Are you able to walk (or minimally exert yourself) for 10 minutes without becoming short of breath or needing to rest? | □ | □ |
| 9. (N/A for men): Are you currently pregnant or attempting to become pregnant? | □ | □ |

Exclusion based on PI reasoning: _____

Notes:

_____

_____

_____

Name: _____

## Appendix D Baseline Survey

This information will be kept confidential. We are collecting this information for your participant payments and to contact you in regards to the study.

**Contact Information**

1. **What is your first name?** _____
2. **What is your last name?** _____
3. **What is your date of birth?** _____
4. **What is your address?**

   _____

   _____ _____

5. **What is your daytime phone number?** _____
6. **What is your evening phone number?** _____
7. **What is your email address?** _____
   (It is important that you use the same email for all documents related to the study)
8. **What is the best way to contact you (day/evening phone, pager, email, text, social media etc.)?**

   _____
9. **Have you been a participant in the ResPECT Study in the past?** □Yes □ No

   **If yes, please choose the year(s) where you have participated:**

   **Johns Hopkins**

   □ 2010-2011
   □ 2011-2012
   □ 2012-2013

   □ **Other (site and year):**_____
   _____
   _____

□ 2013-2014

**10. At which clinic or Emergency Department are you employed?**

_____

Name: _____

**11. Has your name changed since you last participated?** □Yes □ No

If yes, what was your name previously? _____

**12. Do you anticipate any changes that could affect your eligibility for the ResPECT Study over the next year? (i.e. third trimester of pregnancy, change in work location, etc.)** □Yes □ No

If yes, explain (this information is completely confidential and will not be shared with your employer or other staff members):

_____

_____

**Demographic Information 13.**

**What is your gender?**

□ Female □ Male

**14. What is your ethnicity?**

□ Hispanic or Latino

□ Non-Hispanic or non-Latino

**15. What is your race? (Check all that apply)**

□ Black or African American □ Caucasian/White □ American Indian/Alaskan Native

□ Asian □Native Hawaiian or other Pacific Islander □ More than one race □ Other (please list) _____

**16. What is your job/role at this institution?**

□ MD/DO – House Staff □ MD/DO - Fellow or Faculty

□ Dentist □ Physician Assistant/Nurse Practitioner

□ Nursing Staff □ Clinical Technician (ED, Dental, Dialysis, Radiology, etc.)

□ Medical Student □ Clinical Support (CMA, CNA, Dental, etc.)

□ Nursing Student □ Patient Support Assistant/Care Worker/Care Assistant

□ Administrative/Clerical □ Environmental Services/Housekeeping

□ Registration/Reception □ Respiratory/Physical/Occupational Therapist

□ Social Worker/Pastoral Care □ Paramedic

□ Other_____

**17. Not including yourself, please provide the following information about the members of your household. If none, please enter "0".**

| **Age of household members** | **# of household members** | **# of immunocompromised household members** | **# of household members who received seasonal** | **# of household members** |
|---|---|---|---|---|
| | **(does not include you!)** | **(chemotherapy, transplant, steroids, etc.)** | **flu vaccine** (since July 2014) | **diagnosed with influenza A** (since July 2014) |
| 0–5 years | | | | |
| 6-24 years | | | | |
| 25-64 years | | | | |
| 65+ years | | | | |

| **The following questions pertain to you.** | Yes | No |
|---|---|---|
| **18. Do you smoke tobacco?** | | |
| a. If yes, how many times do you smoke tobacco (cigarettes, pipe, cigars) in a day? □ <5 □ 5-10 □ 11-20 □ >20 | | |
| **19. Do you have any of the following conditions?** | | |
| a. COPD (Chronic obstructive pulmonary disease) | | |
| b. Asthma | | |
| c. Other respiratory disease | | |
| i. If yes, please specify _____ | | |
| d. Heart disease (i.e. severe congestive heart failure, angina) | | |
| ii. If yes, please specify _____ | | |
| e. Neurologic disease (i.e. stroke, MS) | | |
| iii. If yes, please specify _____ | | |
| f. Other systemic disease (i.e. rheumatoid arthritis, lupus) iv. If yes, please specify _____ | | |
| **20. Do you use any of the following medications regularly?** | | |
| a. Albuterol/ventolin | | |
| b. Inhaled medication | | |
| c. Antipyretics (i.e. Tylenol, Ibuprofen, Aspirin) | | |
| d. Immunosuppressants (i.e. oral corticosteroids, antibodies) | | |

Today's Date: ____/___/____
(MM/DD/YEAR)
Study Subject ID: _____

| | | |
|---|---|---|
| e. Steroid nasal sprays | | |
| **21. Do you wear or use any of the following?** | | |
| a. Glasses (prescription or non-prescription) | | |
| b. Contacts | | |
| **22. (N/A for men) Are you currently pregnant or are you attempting to become pregnant ?** | | |
| a. If currently pregnant, what trimester? _____ | | |

## *Appendix E* Pre-Study Survey

**Vaccination**

1) **Have you had a lab-confirmed or physician-diagnosed case of influenza between July 2014 and today?**
   a) If yes, approximately when? Date:
2) **Did you receive a vaccination for influenza between July 2014 and today?**
   a) If yes, approximately when? Date:
   b) If yes, what type of vaccine did you receive?
   □ Injectable (killed) vaccine □ Inhaled/nasal (live, attenuated) vaccine 3) **Did you receive a vaccination for pertussis (often included with vaccinations for diphtheria and tetanus, also known as the DTaP or Tdap) between July 2014 and today?**
   a) If yes, approximately when? Date:

**Knowledge**

1. **If a patient came in with the following symptoms, I would use the following personal protective equipment (PPE)…** (Check all that apply)

| | |
|---|---|
| | |

| Symptoms | Hand hygiene | Gowns | Gloves | Eye protection/ face shield | Medical/ surgical masks | N95 respirator | Don't know |
|---|---|---|---|---|---|---|---|
| Fever, cough, sore throat | □ | □ | □ | □ | □ | □ | □ |
| Bloody/ productive cough, chest pain, fever, weight loss | □ | □ | □ | □ | □ | □ | □ |
| Itchy rash and blisters | □ | □ | □ | □ | □ | □ | □ |
| Sore throat, runny nose, sneezing, mild cough | □ | □ | □ | □ | □ | □ | □ |
| Diarrhea, vomiting, stomachache | □ | □ | □ | □ | □ | □ | □ |
| Dry, uncontrollable cough | □ | □ | □ | □ | □ | □ | □ |
| Immuno-compromised patient (chemotherapy, transplant patient, steroid therapy) | □ | □ | □ | □ | □ | □ | □ |

2. **If I needed to perform a nebulizer treatment on a patient with respiratory or influenza-like symptoms, I would use the following PPE…** (Check all that apply)

| Hand hygiene | Gowns | Gloves | Eye protection/ face shield | Medical/ surgical masks | N95 respirator | Don't know |
|---|---|---|---|---|---|---|
| □ | □ | □ | □ | □ | □ | □ |

**Behaviors**

**Medical/surgical mask**

**3. I wear a medical/surgical mask during my work shift…**

(If never, skip to question 6)

□ All patients □ Immunocompromised patients

□ Patients with respiratory or influenza-like illness □ Other? _____

□ Patients with confirmed influenza A □ I never plan to wear medical/surgical mask

**4. I wear a surgical/medical mask when required by policy…**

**(i.e. when in contact with a patient on droplet isolation)**

□ Never □ With some patient contacts □ With every patient contact

**5. When I do wear a medical mask, I do so…**

Please rank the following reasons in order of importance:

(1 = most important, 2 = important, 3 = less important, 4 = least important):

____ To avoid getting a respiratory infection

____ To keep from spreading respiratory pathogens among patients

____ To keep from spreading respiratory pathogens to my family or those I live with

____ Because I am required to wear mask by supervisor, Occupational Health, or clinic policy

**6. The following reasons may deter me from wearing a surgical/medical mask…**

(Check all that apply)

□ Uncomfortable
□ Interferes with communication
□ Masks don't protect from infection
□ Wear N95 instead
□ Difficulty breathing
□ Masks are unavailable
□ No need to wear a mask
□ Other _____


**N95 Respirator**

**7. I wear an N95 respirator during my work shift…**

(If never, skip to question 10)

□ All patients
□ Patients with respiratory or influenza-like illness
□ Patients with confirmed influenza A
□ Immunocompromised patients
□ Other? _____
□ I never plan to wear medical/surgical mask

**8. I wear an N95 respirator when required by policy…**

**(i.e. when in contact with a patient on droplet isolation)**

□ Never □ With some patient contacts □ With every patient contact

**9. When I do wear an N95 respirator, I do so…**

Please rank the following reasons in order of importance

(1 = most important, 2 = important, 3 = less important, 4 = least important):

____ To avoid getting a respiratory infection
____ To keep from spreading respiratory pathogens among patients
____ To keep from spreading respiratory pathogens to my family or those I live with
____ Because I am required to wear respirator by supervisor, Occupational Health, or clinic policy

**10. The following reasons may deter me from wearing an N95 respirator…**

(Check all that apply)

□ Uncomfortable
□ Interferes with communication
□ Respirators don't protect from infection
□ Wear masks instead
□ Difficulty breathing
□ Respirators are unavailable
□ No need to wear a respirator
□ Other _____

**11. When were you last fit-tested to wear an N95 respirator in a healthcare setting?**

□ Within 1 year (12 months) □ Within 2-5 years □ Greater than 5 years □ Never
□ Don't know

**Attitudes/Beliefs**

12. **Do you think medical/surgical masks or N95 respirators are effective and necessary for preventing the transmission of influenza?** (Check all that apply)

| | Mask | N95 |
|---|---|---|
| Effective | □ | □ |
| Necessary | □ | □ |
| Not effective or necessary | □ | □ |
| Other measures (hand hygiene, cough etiquette) are more important | □ | □ |

13. **Wearing a medical/surgical mask or an N95 respirator has the following effect(s) on patient interaction:** (Check all that apply)

| | Mask | N95 |
|---|---|---|
| Makes communicating difficult | □ | □ |
| Increases patients' fear of infection | □ | □ |
| Increases patients' concern/confusion about lack of FPE consistency | □ | □ |
| Decreases patients' fear of infection | □ | □ |
| Has little or no effect on patient interaction | □ | □ |

## Appendix F Daily Exposure Form (Monday, Tues, etc.)

**If you have developed respiratory/flu-like symptoms today, please contact the ResPECT Study Staff as soon as possible:**

**Phone: xxx-xxx-xxxx**
**Email: email@domain.edu**
**Pager: xxx-xxx-xxxx**

Please complete the Daily Form each day **regardless** of whether you work.

**REMINDER:** Individuals with facial hair must continue to shave any facial hair during the study period.

FPE = facial protective equipment (medical/surgical mask or N95 respirator)
Please refer to the Symptomatic Event Report Form, Weekly Diary, or ResPECT business card for list of respiratory/flu-like symptoms.

1. This form is for XXX (date range) – did you work today or have a shift that started on this date?
   □ Yes □ No
2. What shift is this in your work week starting Monday? (Please select one.)
   □ First Work Day
   □ Second Work Day
   □ Third Work Day
   □ Fourth Work Day
   □ Fifth Work Day
   □ Sixth Work Day
   □ Seventh Work Day
3. Did you feel sick or have any respiratory or influenza-like symptoms on this work date?
   □ Yes □ No

a. If yes, did you contact the ResPECT Study Staff? □ Yes □ No

b. If yes, did you remember to fill out a Symptomatic Event Form? □ Yes □ No

4. Were you in contact with any patients or coworkers with confirmed influenza or who appeared to have a respiratory or influenza-like illness on this work date?

□ Yes □ No

a. If yes, what was the estimated duration ( in minutes) of contact over the whole work shift?

□ <15 minutes □ 15-29 minutes □ 30-44 minutes

□ 45-59 minutes □ 1-2 hours □ >2 hours

b. If yes, the contact(s) occurred: (select all that apply)

□ Within 6 feet □ Further than 6 feet □ In direct contact (e.g., touching)

c. If yes, I wore Facial Protective Equipment (FPE):

□ None of the time □ Part of the time □ All of the time □ Don't know

d. If yes, what type of FPE?

□ **N95** □**Medical/surgical mask**

4. Estimate how often you performed hand hygiene before and after seeing each patient on this date:

□ Never □ Some patient encounters □ Most patient encounters

□ All patient encounters □ Don't remember □ No patient encounters

5: Estimate how often you wore a **medical/surgical mask** on this date:

□ Never □ Some patient contacts □ Most patient contacts □ All patient contacts □ Don't remember

6: Estimate approximately how many total hours you wore a **medical/surgical mask** on this date:

□ Never □ <15 minutes □ 15-29 minutes □ 30-44 minutes □ 45-59 minutes □ 1-2 hours □ >2hours

7: Estimate how often you wore an **N95 respirator** on this date:

□ Never □ Some patient contacts □ Most patient contacts □ All patient contacts □ Don't remember

8: Estimate approximately how many total hours you wore an **N95 respirator** on this date:

□ Never □ <15 minutes □ 15-29 minutes □ 30-44 minutes □ 45-59 minutes □ 1-2 hours □ >2hours

9: On this work date, did you perform any of the following procedures? If yes, write in the number of times performed and mark the type of protection worn during the procedure.

| # of times | | **N95** | **Surgical Mask** | Other PPE | None |
|---|---|---|---|---|---|
| | Intubation* | | | | |
| | Respiratory/airway suctioning** | | | | |
| | Nebulizer treatments*** | | | | |
| | Nasopharyngeal aspiration**** | | | | |

*placement of a flexible plastic tube into the trachea (windpipe) to maintain an open airway or to serve as a conduit through which to administer certain drugs

**removal of airway secretions by inserting a suction catheter into the patient's oral airway and/or trachea

***a drug delivery device used to administer medication in the form of a mist inhaled into the lungs

****insertion of catheter or tube to suction mucus from patient's nasal cavity, sometimes in addition to saline wash

Today's Date: _____/__/_____
(MM/DD/YEAR)
Study Subject ID: _____

## *Appendix G* Weekly Diary

**Phone: 410-614-6206**
**Email: respect@jhmi.edu**
**Pager: 410-434-0821**

1. **In the week from Monday, DATE to Sunday, DATE, have you experienced any of the following symptoms? (Please check all that apply.)**

| | **Yes** | **No** | **Unsure** | **Date of Onset** (MM/DD/YEAR) |
|---|---|---|---|---|
| Fever (greater than 37.8°C or 100.1°F) | □ | □ | □ | __/__/____ |
| Nasal congestion/runny nose(Coryza) | □ | □ | □ | __/__/___ |
| Headache | □ | □ | □ | __/__/____ |
| Sneezing | □ | □ | □ | __/__/____ |
| Fatigue | □ | □ | □ | __/__/____ |
| Dry cough | □ | □ | □ | __/__/____ |
| Body aches (myalgias or arthralgias) | □ | □ | □ | __/__/____ |
| General feeling of being sick (malaise) | □ | □ | □ | __/__/____ |
| Sore throat | □ | □ | □ | __/__/____ |
| Sputum production | □ | □ | □ | __/__/____ |
| Diarrhea | □ | □ | □ | __/__/____ |
| Bloody sputum | □ | □ | □ | __/__/____ |
| Chills | □ | □ | □ | __/__/____ |
| Nausea/vomiting | □ | □ | □ | __/__/____ |

| | | | | |
|---|---|---|---|---|
| Abnormal sweating | □ | □ | □ | __/__/____ |
| Rapid breathing/shortness of breath (tachypnea ≥25) | □ | □ | □ | __/__/____ |
| Swollen lymph nodes (lymphadenopathy) | □ | □ | □ | __/__/____ |
| Other Gastrointestinal symptoms (please specify) | □ | □ | □ | __/__/____ |
| Other (please specify) | □ | □ | □ | __/__/____ |

**2. <u>If you developed any of the above symptoms:</u>**

Did you call the study coordinator? □ Yes □ No

If NO, please contact the ResPECT Study Staff as soon as possible.

Did you receive an upper respiratory swab? □ Yes □ No

**3. In the last week, have you: (Please check all that apply)**

| | **Yes** | **No** | **Don't remember** |
|---|---|---|---|
| Had any problems with seasonal or chronic allergies? | □ | □ | □ |
| Used any nasal sprays? *If yes, please specify:*_____ | □ | □ | □ |
| Taken any antihistamines or decongestants? *If yes, please specify:*_____ | □ | □ | □ |
| Taken any fever-reducing medication (Tylenol, Ibuprofen, Aleve, aspirin)? *If yes, please specify:*_____ | □ | □ | □ |
| Taken any immune-suppressing drugs? *If yes, please specify:*_____ | □ | □ | □ |
| Been exposed to anyone with symptoms of a respiratory illness (please refer to list of symptoms above) | □ | □ | □ |

**4: Were you in contact with any household members with respiratory or influenza-like illness this week?**

□ Yes □ No

**a. If yes, how many? _____**

a. **If yes, what was the total duration** of **contact with all household members with respiratory or influenza- like illness?**

□ Never □ <15 minutes □ 15-29 minutes
□ 30-44 minutes □ 45-59 minutes □ 1-2 hours □ >2 hours

b. **If yes, the contact (or most of the contacts) were (select all that apply):**

□ Within 6 feet □ Further than 6 feet away

□ In direct contact (i.e. touched) the family member

c. **If yes, I wore FPE**

□ None of the time □ Part of the time □All of the time □Don't know

□ If yes, what type of FPE? □ **N95** □**Medical/surgical mask**

**5. Do you remember a significant exposure to a person with respiratory or influenza-like symptoms on any day of this week?**

| Monday (M/DD) | Tuesday (M/DD) | Wednesday (M/DD) | Thursday (M/DD) | Friday (M/DD) | Saturday (M/DD) | Sunday (M/DD) |
|---|---|---|---|---|---|---|
| | | | | | | |

**6. Did you receive a vaccination for influenza this week?**

□ Yes □No

a) If yes, approximately when? Date: ____/____ /_____
(MM/DD/YEAR)

b) If yes, which type of vaccine did you receive?

□ Injectable (killed) vaccine □ Inhaled/nasal (live, attenuated) vaccine

**7. Did you receive a vaccination for pertussis (DTaP or Tdap) this week?**

□ Yes □No

a) If yes, approximately when? Date: ____/____ /_____
(MM/DD/YEAR)

**8.** If you were absent from work this week as a result of any of the symptoms you experienced, how many days were you absent?

□ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7

Today's Date: ____/___/____
(MM/DD/YEAR)
Study Subject ID: _____

## Appendix H Post-Study Survey

**Medical/surgical mask**

**1: In the future, I plan to use a medical/surgical mask when delivering healthcare to the following patients: (Check all that apply)**

□ All patients
□ Patients with respiratory or influenza-like illness
□ Patients with confirmed influenza A
□ Immunocompromised patients
□ Other? _____
□ I never plan to wear a medical/surgical mask

**2: If you plan on wearing a medical/surgical mask in the future, please rank the following reasons in order of importance (1 = most important, 2 = important, 3 = less important, 4 = least important):**

**____** To avoid getting a respiratory infection
____ To keep from spreading respiratory pathogens among patients
____ To keep from spreading respiratory pathogens to my family or those I live with
____ Required to wear mask by supervisor, Occupational Health, or clinic policy

**3: Which of the following statements most reflects your future plans for medical/surgical mask use?**

□ I will wear a mask more often than before
□ I will wear a mask as often as before
□ I will wear a mask less often than before
□ Don't know

**4: If you will not use a medical/surgical mask in the future, check all the reasons that apply**

□ Uncomfortable
□ Interferes with communication
□ Masks don't protect from infection
□ Wear N95 instead
□ Difficulty breathing
□ Masks are unavailable
□ No need to wear a mask
□ Other _____

**5: How often during the course of the study were you unable to wear the medical/surgical mask due to discomfort?**

□ Always □ Often □ Rarely □ Never


**N95 respirator**

**6: In the future, I plan to use an N95 respirator when delivering healthcare to the following patients:**

□ All patients □ Immunocompromised patients
□ Patients with respiratory or influenza-like illness □ Other _____ □
Patients with confirmed influenza A □ I never wear a respirator

**7: If you plan on wearing an N95 respirator in the future, please rank the following reasons in order of importance (1 = most important, 2 = important, 3 = less important, 4 = least important):**

____ To avoid getting a respiratory infection
____ To keep from spreading respiratory pathogens among patients
____ To keep from spreading respiratory pathogens to my family or those I live with
____ Required to wear mask by supervisor, Occupational Health, or clinic policy

**8: Which of the following statements most reflects your future plans for N95 respirator use?**
□ I will wear a respirator more often than before
□ I will wear a respirator as often as before
□ I will wear a respirator less often than before □
Don't know

**9: If you will not use an N95 respirator in the future, check all the reasons that apply.**

□ Uncomfortable □ Difficulty breathing
□ Interferes with communication □ Respirators are unavailable
□ No need to wear a mask □ Respirators don't protect from infection
□ Wear mask instead □ Other _____

**10: How often were you unable to wear the N95 respirator due to discomfort?**

□ Always □ Often □ Rarely □ Never

**11: Did you receive a vaccination for influenza between July 2012 and today?**

□ Yes □No

a. If yes, approximately when? Date: ____/____ /____
(month) (day) (year)

b. If yes, which type of vaccine did you receive?

□ Injectable (killed) vaccine □ Inhaled/nasal (live, attenuated) vaccine

**12: Did you receive a vaccination for pertussis (often included with vaccinations for diphtheria and tetanus, also known as the DTaP or Tdap) between July 2014 and today?**

□ Yes □No

a) If yes, approximately when? Date: _____

## Appendix I Hand Hygiene and FPE Observation Form

**ResPECT: HandyAudit Paper Observation Form**

Date: _____ Time: _____ Clinic: _____ Observer:_____

| Observation | Job Title | Participant? | Start in pt environment? | Respiratory patient? | Observation Actions | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Yes/No | | | Action 1 | Action 2 | Action 3 | Action 4 | Action 5 | Action 6 | Action 7 | Comments |
| 1 | | | | | | | | | | | | |
| 2 | | | | | | | | | | | | |
| 3 | | | | | | | | | | | | |
| 4 | | | | | | | | | | | | |
| 5 | | | | | | | | | | | | |
| 6 | | | | | | | | | | | | |
| 7 | | | | | | | | | | | | |
| 8 | | | | | | | | | | | | |
| 9 | | | | | | | | | | | | |
| 10 | | | | | | | | | | | | |

Observation Action Codes (OACs)

***Enter OACs chronologically into Observation Actions columns above, for each observed encounter*

- SAN (seconds)
- HW (seconds)
- T Ext Env
- T PT
- T PT Env
- Mask on (S or N95)
- Mask off
- ENTER pt Env
- EXIT to PT
- EXIT to Ext
- Goggles
- Gloves on
- Gloves off
- VIS
- Not VIS
- Shield
- ASP
- BFL
- Gown

5/7/2013

**ResPECT: HandyAudit Paper Observation Form**

Glossary: Observation Action Codes

| OAC | Definition |
|---|---|
| ASP | An aseptic procedure was performed |
| BFL | Provider had a body fluid exposure |
| ENTER pt Env | Provider entered patient environment |
| EXIT to Ext | Provider exited to external environment |
| EXIT to PT | Provider exited to new patient environment |
| Gloves off | Provider removed gloves |
| Gloves on | Provider put on gloves |
| Goggles | Provider wore goggles |
| Gown | Provider wore a gown |
| HW (seconds) | Hands washed (number of seconds spend washing) |
| Mask off | Provider removed the mask |
| Mask on (S or N95) | Provider put on a mask (surgical or N95 respirator?) |
| Not VIS | Provider was not visible |
| SAN (seconds) | Hand sanitizer (number of seconds hands rubbed) |
| Shield | Provider wore a full face shield |
| T Ext Env | Provider touched external environment |
| T PT | Provider touched patient |
| T PT Env | Provider touched patient environment |
| VIS | Provider became visible |

## *Appendix J* Explanation of exclusion from study

**The Respiratory Protection Clinical Effectiveness Trial - NA_00031266**

**Exclusion Explanation**

Thank you for your interest in the Respiratory Protection Clinical Effectiveness Trial. Unfortunately, you have been excluded from the study based on your answers to an exclusion/inclusion survey. You may have been disqualified for one or more of the following reasons: You are a part-time worker; an N95 respirator was unable to properly fit to your face based on a qualitative fit test; you are unable to wear an N95 respirator or surgical mask due to an intolerance to the masks or as suggested by occupational health or a trained clinician; you have facial hair which interferes with the efficacy of the N95 respirator; you are in your third trimester of pregnancy (due to possible changes in the shape of your face); you have a medical condition that makes you more susceptible to influenza-related complications or unable to wear a mask; a member of the study staff has deemed you unfit for the study.

Regardless of why you were excluded from the study, there are a number of precautions you can take, as a healthcare worker, to greatly reduce the risk of infection.

- Wash your hands frequently, especially before and after having contact with a patient. If soap and water are not immediately available, use an alcohol-based hand rub such as Purell.

- Get the flu vaccine, as well as the H1N1 vaccine, if possible. Both vaccines come in an inactivated shot form and a live, attenuated nasal mist.

- Cover your mouth and nose when sneezing or coughing. This should ideally be done into a tissue, but if one is not available, use the bend in your arm.

- Use personal protective equipment such as gloves and appropriate facial or respiratory protection.

- Consult the Occupational Health department for any additional information about how to protect yourself from influenza and respiratory infections

If you become infected with influenza, it is important that, if possible, you wear appropriate facial or respiratory protection because you are susceptible to complications. An N95 respirator is recommended. If you are unable to wear an N95 respirator, you should consult the Occupational Health

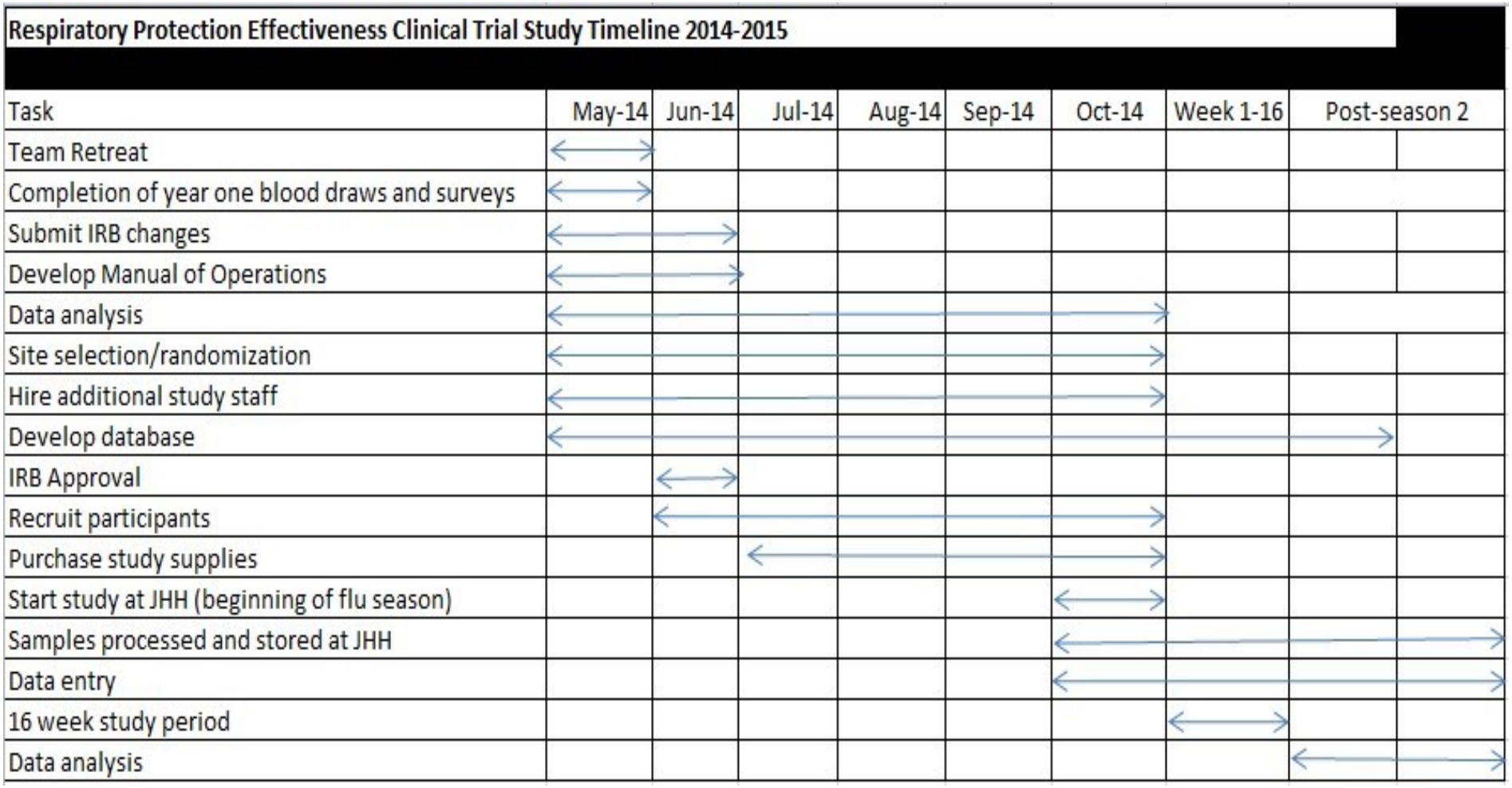
department; you may be able to use a medical mask or other form of FPE. It is extremely important that you are vaccinated with the seasonal vaccine, which includes the pandemic H1N1 strain. If you are concerned about the risks of being vaccinated, please call Johns Hopkins Infection Control at 410-9558384. The risks due to vaccination are minimal compared to the risks of complications should you become infected with H1N1 or seasonal influenza. You should also conduct a thorough hand hygiene regimen to minimize your exposure to influenza. If you feel feverish and have a sore throat or cough, it is recommended that you see a clinician immediately.

Those with chronic respiratory or systemic disease were excluded from the study due to a higher risk for influenza-related complications, such as pneumonia. For this reason, protecting yourself from seasonal influenza and H1N1 is important. You should follow the standard procedures listed above, and if you have a fever with a cough or a sore throat, you should immediately see a clinician. If you have a respiratory or systemic illness, and you are in frequent patient contact, it is recommended that you receive the seasonal vaccine.

## Appendix K Certification Criteria for Study Sites

- Minimum of 24 clinics/clusters employing a median of at least 16 full-time HCPs. May also have fewer clinics that are easily divisible into 24 separate work environments, with 16 or more people working in each environment
- History of collaboration with other sites on large clinical trials
- Research infrastructure experience with clinical studies
- Active research staff to conduct the study
- High interest level and enthusiasm of HCP participants
- High number of patients who present for healthcare with a diagnosable respiratory illness
- Outpatient/primary care facilities
- Track record of collaborative research
- Site is preferred to have a track record of clinical trials
- Site is preferred to have a pediatric component in their set of possible study locations (because the incidence of infectious diseases is highest in these settings). This criterion would not apply to VA study sites.
- Active respiratory protection program including training and annual fit testing in place

**Appendix L Study Timeline**



Today's Date: ____/___/____

(MM/DD/YEAR)

Study Subject ID: _____ Study Site: _____

## *Appendix M* Amended Fit Testing Medical Questionnaire

**Reference: Appendix C to Sec. 1910.134: OSHA Respirator Medical Evaluation Questionnaire (Mandatory)**

**ResPECT Study Questionnaire**

Please answer the following questions.

1. Have you been fit tested within the past 6 months? Yes _____ No _____
2. If you have been fit tested within the past 6 months, have you either lost or gained 10% or more of your total body weight after the fit test? Yes _____ No _____

To the employer: Answers to questions in Section 1, and to question 9 in Section 2 of Part A, do not require a medical examination.

To the employee:

Can you read (circle one): Yes/No

Your employer must allow you to answer this questionnaire during normal working hours, or at a time and place that is convenient to you. To maintain your confidentiality, your employer or supervisor must not look at or review your answers, and your employer must tell you how to deliver or send this questionnaire to the health care professional who will review it.

Part A. Section 1. (Mandatory) The following information must be provided by every employee who has been selected to use any type of respirator (please print).

1. Today's date: _____
2. Your name: _____
3. Your age (to nearest year):_____
4. Sex (circle one): Male/Female
5. Your height: _____ ft. _____ in.

6. Your weight: _____ lbs.

7. Your job title: _____

8. A phone number where you can be reached by the health care professional who reviews this questionnaire (include the Area Code): _____

9. The best time to phone you at this number: _____

10. Has your employer told you how to contact the health care professional who will review this questionnaire (circle one): Yes No

11. Have you worn a respirator (circle one): Yes No

If "yes," what type(s):_____
_____

Part A. Section 2. (Mandatory) Questions 1 through 9 below must be answered by every employee who has been selected to use any type of respirator (please circle "yes" or "no").

1. Do you ***currently*** smoke tobacco, or have you smoked tobacco in the last month: Yes No

2. Have you ***ever had*** any of the following conditions?

a. Seizures (fits): Yes No
b. Diabetes (sugar disease): Yes No
c. Allergic reactions that interfere with your breathing: Yes No
d. Claustrophobia (fear of closed-in places): Yes No
e. Trouble smelling odors: Yes No

3. Have you ***ever had*** any of the following pulmonary or lung problems?

a. Asbestosis: Yes No
b. Asthma: Yes No
c. Chronic bronchitis: Yes No
d. Emphysema: Yes No
e. Pneumonia: Yes No
f. Tuberculosis: Yes No

g. Silicosis: Yes No
h. Pneumothorax (collapsed lung): Yes No
i. Lung cancer: Yes No
j. Broken ribs: Yes No
k. Any chest injuries or surgeries: Yes No
l. Any other lung problem that you've been told about: Yes No

4. Do you ***currently*** have any of the following symptoms of pulmonary or lung illness?

a. Shortness of breath: Yes No
b. Shortness of breath when walking fast on level ground or walking up a slight hill or incline: Yes No
c. Shortness of breath when walking with other people at an ordinary pace on level ground: Yes No
d. Have to stop for breath when walking at your own pace on level ground: Yes No e.
Shortness of breath when washing or dressing yourself: Yes No
f. Shortness of breath that interferes with your job: Yes No
g. Coughing that produces phlegm (thick sputum): Yes No
h. Coughing that wakes you early in the morning: Yes No
i. Coughing that occurs mostly when you are lying down: Yes No
j. Coughing up blood in the last month: Yes No
k. Wheezing: Yes No
l. Wheezing that interferes with your job: Yes No
m. Chest pain when you breathe deeply: Yes No
n. Any other symptoms that you think may be related to lung problems: Yes No

5. Have you ***ever had*** any of the following cardiovascular or heart problems?

a. Heart attack: Yes No
b. Stroke: Yes No
c. Angina: Yes No
d. Heart failure: Yes No
e. Swelling in your legs or feet (not caused by walking): Yes No
f. Heart arrhythmia (heart beating irregularly): Yes No
g. High blood pressure: Yes No
h. Any other heart problem that you've been told about: Yes No

6. Have you ***ever had*** any of the following cardiovascular or heart symptoms?

a. Frequent pain or tightness in your chest: Yes No
b. Pain or tightness in your chest during physical activity: Yes No
c. Pain or tightness in your chest that interferes with your job: Yes No
d. In the past two years, have you noticed your

heart skipping or missing a beat: Yes No e.
Heartburn or indigestion that is not related to eating: Yes No

f. Any other symptoms that you think may be related
g. to heart or circulation problems: Yes No

7. Do you ***currently*** take medication for any of the following problems?

a. Breathing or lung problems: Yes No
b. Heart trouble: Yes No
c. Blood pressure: Yes No
d. Seizures (fits): Yes No

8. If you've used a respirator, have you ***ever had*** any of the following problems? (If you've never used a respirator, check the following space and go to question 9:)

a. Eye irritation: Yes No
b. Skin allergies or rashes: Yes No
c. Anxiety: Yes No
d. General weakness or fatigue: Yes No
e. Any other problem that interferes with your use of a respirator: Yes No

9. Would you like to talk to the health care professional who will review this questionnaire about your answers to this questionnaire: Yes No

## Appendix N Symptomatic Event Report Form

If you have developed any respiratory or influenza-like symptoms today, please contact the ResPECT Study Staff as soon as possible.

Phone: 410-614-6206
Email: respect@jhmi.edu
Pager: 410-434-0821

Study Subject ID: _____
Study Site: _____

Today's date: _____/___/____
(MM/DD/YEAR)

Complete the Symptomatic Event Report Form and Remember to contact the ResPECT Study Staff if you develop one of the following symptoms:

1. Please complete the following table if you have experienced anyone of the following symptoms? (Please check all that apply.)

| | Yes | No | Unsure | Date of Onset (MM/DD/YEAR) |
|---|---|---|---|---|
| Fever (greater than 37.8°C or 100.1°F) | ☐ | ☐ | ☐ | __/__/____ |
| Nasal congestion/runny nose(Coryza) | ☐ | ☐ | ☐ | __/__/___ |
| Headache | ☐ | ☐ | ☐ | __/__/____ |
| Sneezing | ☐ | ☐ | ☐ | __/__/____ |
| Fatigue | ☐ | ☐ | ☐ | __/__/____ |
| Dry cough | ☐ | ☐ | ☐ | __/__/____ |
| Body aches (myalgias or arthralgias) | ☐ | ☐ | ☐ | __/__/____ |
| General feeling of being sick (malaise) | ☐ | ☐ | ☐ | __/__/____ |
| Sore throat | ☐ | ☐ | ☐ | __/__/____ |
| Sputum production | ☐ | ☐ | ☐ | __/__/____ |
| Diarrhea | ☐ | ☐ | ☐ | __/__/____ |
| Bloody sputum | ☐ | ☐ | ☐ | __/__/____ |
| Chills | ☐ | ☐ | ☐ | __/__/____ |

| | | | | |
|---|---|---|---|---|
| Nausea/vomiting | ☐ | ☐ | ☐ | __/__/____ |
| Abnormal sweating | ☐ | ☐ | ☐ | __/__/____ |
| Rapid Breathing/shortness of breath (tachypnea≥25) | ☐ | ☐ | ☐ | __/__/____ |
| Swollen lymph nodes (lymphadenopathy) | ☐ | ☐ | ☐ | __/__/____ |
| Other Gastrointestinal symptoms (please specify) | ☐ | ☐ | ☐ | __/__/____ |
| Other (please specify) | ☐ | ☐ | ☐ | __/__/____ |

2.) If you answered yes to any one of the above symptoms, did you take any of the following actions?

a) Seek medical help from a

MD/Provider □ Yes □No
Emergency Department □ Yes □No
Occupational Health Services □ Yes □No

b) Take medication

Tylenol □ Yes □No

Ibuprofen □ Yes □No

Aleve □ Yes □No

Aspirin □ Yes □No

Oseltamivir □ Yes □No

3.) If you answered YES to any of the above symptoms, are your symptoms still present?

□ Yes □No

If no, when did your symptoms end? __/__/____

## Appendix O Adverse Event Submission Form

*The Principal Investigator must promptly report to the IRB, in writing, any unanticipated side effects, hazards, or other problems involving risks to subjects or others. Promptly report all adverse events considered to be related to research procedures to the Steering Committee. Please fax to Jenna Los at 410-614-6207.*

M.2.a.i.1.1.1.1.61 Date:

M.2.a.i.1.1.1.1.62 Principal Investigator: Perl, Trish

M.2.a.i.1.1.1.1.63 Protocol#: NA_00031266

M.2.a.i.1.1.1.1.64 Protocol Title: The Respiratory Protection Clinical Effectiveness Trial

| M.2.a.i.1.1.1.1.65 Research Coordinator(s): | M.2.a.i.1.1.1.1.66 Phone: | M.2.a.i.1.1.1.1.67 Fax: |
|---|---|---|
| Jenna Los | 410-614-6206 | 410-614-6207 |

Report Type: ☐ Initial ☐ Follow-up

Subject Identifier # (study ID number, do not list medical record number or other personal identifier): AE

Date:

AE Description (brief):

Is the adverse event a previously described complication that is listed in the "Risk" section of the Investigator's Brochure ☐ Yes ☐ No

| **This is a (an):** | **The opinion of the Principal Investigator is that the relationship of the research procedure is:** |
|---|---|
| M.2.a.i.1.1.1.1.68 ☐ **Unanticipated/Unexpected Event**<br><br>M.2.a.i.1.1.1.1.69 (Any untoward event that is not identified with the current | ☐ M.2.a.i.1.1.1.1.72 Unrelated<br>☐ M.2.a.i.1.1.1.1.73 Probably related<br>☐ Possibly related not related<br><br>M.2.a.i.1.1.1.1.74 Probably related |
| investigator brochure or study protocol)<br><br>M.2.a.i.1.1.1.1.70 ☐ **Serious Adverse Event**<br><br>M.2.a.i.1.1.1.1.71 (Any untoward medical occurrence that results in death, is life-threatening, requires patient hospitalization, prolongs existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital abnormality) | M.2.a.i.1.1.1.1.75 ☐ Related<br><br>M.2.a.i.1.1.1.1.76 ☐ Other: |
| _____ | _____ |
| INVESTIGATOR SIGNATURE | DATE |

*(Sub-investigator may sign if the investigator is unavailable (i.e. out of the country)*

## Appendix P Participant File Checklist

Study ID: _____ Study Site: _____

- **Consent obtained:** ☐ Yes ☐ No Date of consent: ___/____/_____ (MM/DD/YEAR)
- **Reviewed & entered in RedCap:**
  - Baseline survey: Yes ☐ No ☐
  - Inclusion/exclusion criteria: ☐ Yes ☐ No

○ Eligible? Yes No ○

➢ **If eligible, date enrolled (date emailed by RedCap):** ____/_____/_____

- Site assignment: ☐ N95 ☐ Medical Mask
- *If N95, complete Amended Fit Test Questionnaire.*

○ *Fit test qx reviewed (signed & dated) by licensed MD or RN: Yes ☐ No ○ ☐ Fit testing:*

- ☐ *Qualitative* ☐ *Quantitative*
- ☐ *Pass* ☐ *Fail Date of testing:* ___/____/_____ *(MM/DD/YEAR)*

○ *Successfully fit-tested for the following respirator:* _____

- Vendor form reviewed and submitted: ☐ Yes ☐ No ☐ On file from prior year

○ Initial payment: $_____.00 & Date Submitted: ___/____/_____

- *[If only submitting final payment] Emailed participant earning status:* ____/_____/_____

○ Final payment: $_____.00 & Date submitted: ___/____/_____ ➢ **Withdrawn?**

- If yes, date withdrawn: ____/_____/_____ (MM/DD/YEAR)
- If yes, reason withdrawn (list option #): _____

Option 1: No longer eligible due to change in work location
Option 2: Lack of time/schedule conflicts
Option 3: Swab discomfort
Option 4: Can't Keep up with Surveys
Option 5: Mask Discomfort
Option 6: Does not believe seeing enough flu to be helpful
Option 7: No reason given
Option 8: Other (please describe):
Option 9: *Administrative Withdrawal* - Team removed due to lack of completion

## Appendix Q HSE Qualitative Fit Test Evaluation Form

NAME_____ DATE_____

(PLEASE PRINT CLEARLY)

CLINIC NAME_____

HAS SUBJECT EATEN WITHIN THE LAST 15 MINUTES? (CIRCLE ONE) YES NO

COULD THE SUBJECT TASTE SACCHARIN? (CIRCLE ONE) YES NO*

* IF NO, REFER FOR QUANTITATIVE TESTING

RESPIRATOR ASSESSMENT

RESPIRATOR TYPE: N95 ELASTOMERIC (OTHER SPECIFY)_____

MANUFACTURER 3M KIMBERLY CLARK (OTHER SPECIFY)_____

STYLE: 1870 1860 (OTHER SPECIFY)_____

SIZE: SMALL MEDIUM LARGE N/A

ADEQUACY OF RESPIRATOR FIT NOTES

ROOM FOR EYE PROTECTION? (CIRCLE ONE) YES NO MASK POSITIONED PROPERLY?

-FIT ACROSS NOSE BRIDGE? (CIRCLE ONE) YES NO -CHIN PROPERLY PLACED? (CIRCLE ONE) YES NO STRAPS POSITIONED PROPERLY?

-LOWER AROUND NECK? (CIRCLE ONE) YES NO

-UPPER AT CROWN OF HEAD? (CIRCLE ONE) YES NO

| CHALLENGE EXERCISES | PASS | FAIL |
|---|---|---|
| 2ND MODEL: PASS FAIL | | |
| NORMAL BREATHING | | |
| DEEP BREATHING | | |
| TURNING HEAD (SIDE TO SIDE) | | |
| MOVING HEAD (UP & DOWN) | | |
| TALKING | | |
| BENDING (AT WAIST/KNEE BENDS) | | |
| NORMAL BREATHING | | |

FIT TEST RESULTS: (CIRCLE ONE) PASS FAIL

**NOTES:** _____

**HSE STAFF:** _____**DATE**_____

## Appendix R Supplies for Take-Home Kits

In order to comply with Dangerous Goods and Hazardous Materials Shipping Regulations, the kits will include materials for specimen collection, triple packaging and proper labeling, and instructions to complete collection and shipping:

1. Specimen Tubes (Primary Packaging)
    a. UTM Tube and 2 regular flocked swabs
2. Biohazard Bags (for Secondary Packaging)
3. Absorbent Sheets (for Secondary Packaging)
4. FedEx Padded Envelope (for Outer Packaging)
    a. FedEx Small Pak
    b. Inside Dimensions: 12-3/4" x 10-1/4"
5. FedEx Box (for Outer Packaging)
    a. FedEx Small Box
    b. Inside Dimensions: 12-1/4" x 10-7/8" x 1-1/2"
6. FedEx UN3373 Pak (for Outer-Outer Packaging)
    a. UN 3373 Pak
    b. Inside Dimensions: 18" x 13-1/2"
7. Barcode identifier labels (tracking purposes)
8. 'Shipping Dangerous Goods and Hazardous Materials' instructions (Appendix S)
9. 'At-Home Symptomatic Upper Respiratory Swab Directions' (Appendix T)
10. 'Take-Home Kit Packaging Information' (Appendix U)
11. 'For Any Questions Regarding This Package Or Its Contents' contact information insert
12. 12. Swab Delivery Form and separate envelope with line indicated "For Personnel Use Only" for lab to indicate date and time of receipt (Appendix X).

## Appendix S Shipping Dangerous Goods and Hazardous Materials

**What are dangerous goods?** Articles or substances which are capable of posing a significant risk to health, safety or to property when transported by air.
**What are hazardous materials?** A substance or material that has been determined by the Secretary of DOT to be capable of posing an unreasonable risk to health, safety, and property.

- Hazardous materials are organized into nine primary hazard classes, however, this study will be dealing solely with Class 6.2 (Infectious Substances.) ○ Class 6.2 includes two sub-categories: Category A are the most virulent agents and Category

B are potentially pathogenic substances. Take-home kits will be shipped under a Category B classification with the label UN3373.

***There are steep penalties for non-compliance with hazardous materials regulations.***

**Packaging:**

- Triple Packaging is used in sending <u>any</u> biological substance. Triple packaging contains: primary receptacle leak-proof (liquids), leak-proof secondary packaging and durable outer packaging. Triple packaging must always be used whether shipping Category A, B, or Exempt substances.
- Marking and labeling for Category B biological substances requires a diamond-on-point label with UN3373 with the words "Biological substance, category B" adjacent. It must also include the name, address, and phone number of a responsible person, either on the package or the waybill.

**Category B Infectious Substances:**

- Can <u>never</u> be taken aboard an aircraft in carry-on or checked baggage, nor on your person.
- May be transported in your private vehicle or in any other private motor vehicle, provided they meet the appropriate packaging requirements.

**Specific Security Procedures:**

- All packages of hazardous materials intended for shipment should be kept in a secure area until collection by the shipper.
- Do not leave a package unattended in an unlocked area.
- If left in a locked area where others have access, sure they are known to you and reliable.

# Appendix T <u>At-Home Symptomatic Upper Respiratory Swab Directions</u>

**Be sure to complete <u>both</u> the nasal and throat swab procedures.**

## At-Home Symptomatic <u>NASAL</u> Swab Directions

<u>Considerations</u>:

When possible, do your swab before starting antibiotic therapy or use of antihistamines. Antibiotics may suppress growth of infecting agent, causing a false negative culture.

**<u>Swab Directions:</u>**

1. Blow your nose to remove excess mucous.
2. Remove cap from the tube & place cap upside down on a clean surface.

   a. Open plastic swab package at the end nearest to the handle (Photo Companion 1, Figure 1).

3. Take swab by the handle (be sure not to touch any part of the swab below the breakpoint). Tilt head back slightly & insert swab approximately 2 cm (¾ inches) into one naris, rotate against the anterior nasal mucosa.

   a. Rotate for 3 seconds to ensure swab contains both cells, as well as mucosa (Photo companion 1, Figure 2, & 3).

4. Place the swab inside the tube until the end touches the bottom.

   a. Bend the swab shaft against the side of the tube to remove the handle at the breaking point (Photo companion 1, Figure 4).

5. Cap specimen swab collection tube and continue to Throat Swab Directions.

## **Photo Companion 1:** At-Home Symptomatic Nasal Swab Directions

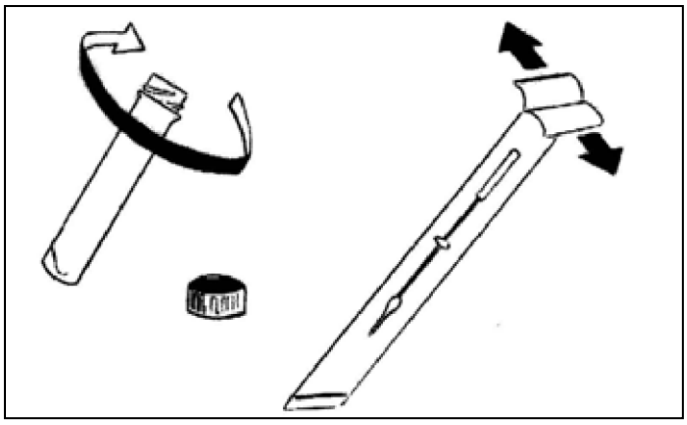


**Figure 1:**

**Figure 2**:

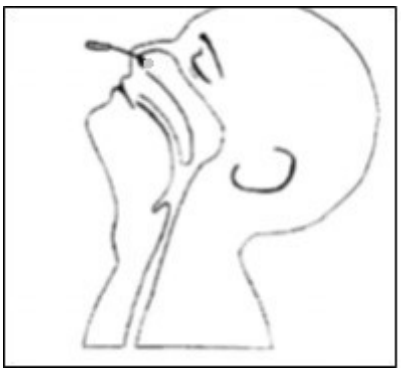


**Figure 3**:

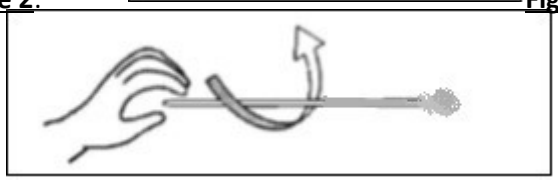
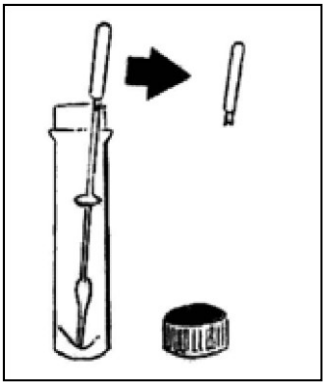


**Figure 4**:



## At-Home Symptomatic THROAT Swab Directions

Swab Directions:

1. Position yourself in front of a well-light mirror so that your oral cavity (mouth & throat) is well defined.

2. Remove cap from the tube & place cap upside down on a clean surface.

3. Open plastic swab package at the end nearest to the handle (Photo companion 1, Figure 1).

4. Take one (unused) swab by the handle (be sure not to touch any part of the swab below the breakpoint).

5. Breathe deeply and flex tongue towards the bottom of your mouth (to avoid contact with the swab).

    a. Guide the swab to the posterior pharynx (back of throat), taking care not to touch tongue, cheeks, and uvula (Photo companion 2, Figures 1 & 2).

    b. Swab vigorously while saying "Ah." (This lifts the uvula and decreases the gag reflex.) Swab area from right tonsillar area across posterior pharynx (back of throat) to left tonsillar area and across to right tonsillar area.

    c. In addition, areas of inflammation, ulceration, exudation, or with white patches should be touched. Rub vigorously, not gently, to remove organisms adhering to the mucosal membrane.

6. Do not touch swab tip after removal.

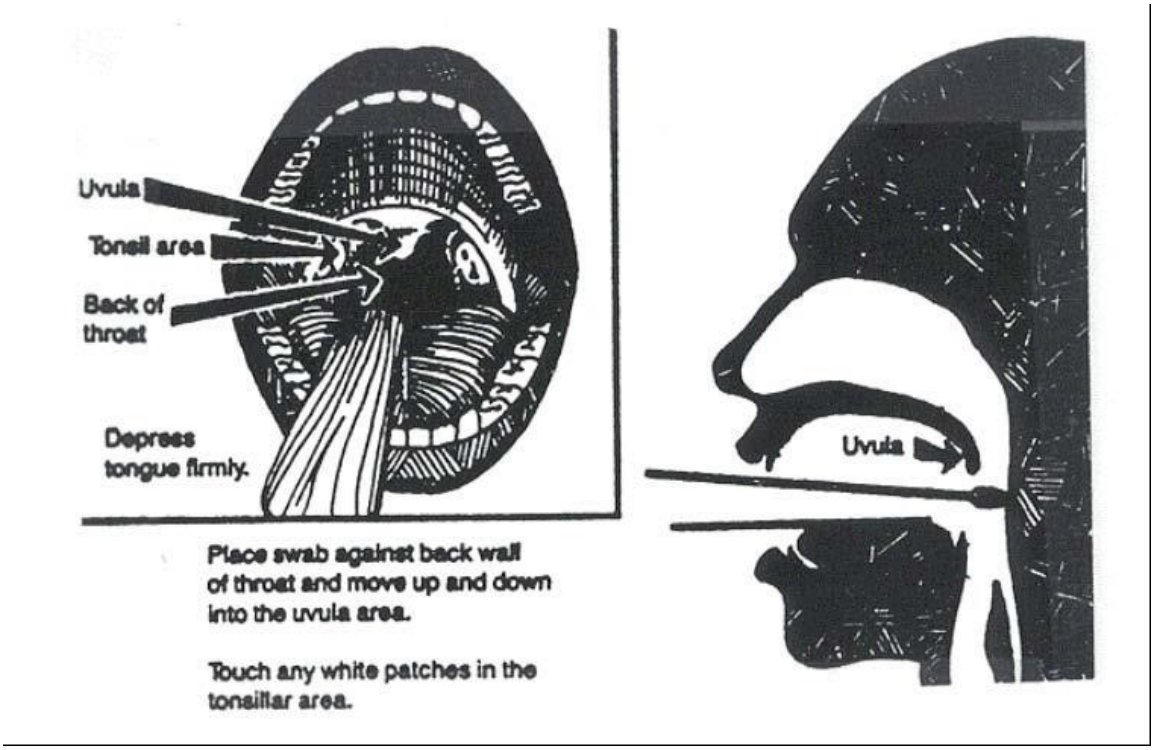
7. Place the swab inside <u>the same tube</u> until the end touches the bottom
    a. Bend the swab shaft against the side of the tube to remove the handle at the breaking point (Photo companion 1, Figure 4)

8. Cap the specimen swab collection tube tightly.

9. Peel off **<u>one</u>** barcode and place it on tube.

10. Read "Shipping Dangerous Goods and Hazardous Materials" handout.

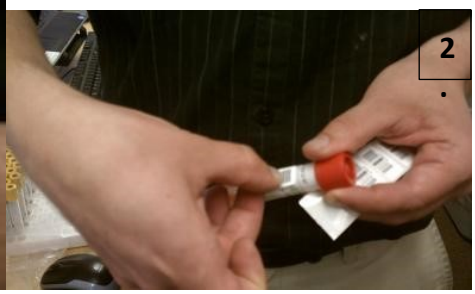
## **Photo Companion 2:** At-Home Symptomatic Throat Swab Directions

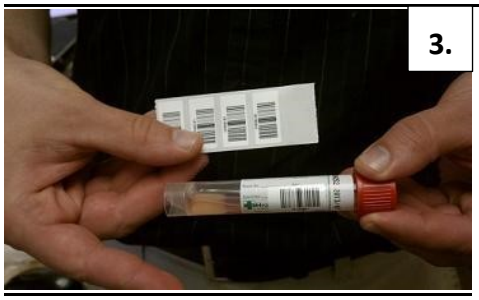



**Great job taking your own throat swab!**

## Appendix U Take-Home Kit Packaging Information

**Please follow the instructions below to ship your collected nose and throat swabs.**




Return THESE unused labels to us in the biohazard bag along with the specimen swab collection tube
See Step 4

**1.) Insert swabs into specimen tube.**

Specimen tube with screw-top containing nose and throat swabs, labeled with your barcode ID, is your "primary packaging". **Proper labeling of swab tube:**

Remaining labels should be included in bag with tube, but not peeled off backing.

Swab Delivery Form should be completed from the link in your weekly email.

**2.) Place the specimen tube inside the biohazard bag with absorbent sheet.**


Biohazard bag with absorbent sheet is your "secondary packaging

**3.) Place the remaining 4 (not peeled off the backing) specimen barcode ID labels in biohazard bag with specimen tube.**

**4.) Place biohazard bag ("secondary packaging") into FedEx padded envelope. Then place this envelope into FedEx box.**

The padded envelope provides protection.


The FedEx box will be your "outer packaging".

**5.) Insert the 'For Any Questions' contact information sheet between the FedEx box and the padded envelope.**

**6.)** Seal the FedEx® corrugated cardboard box with its contents.

**7.) Seal the orange FedEx UN 3373 Pak.**


FedEx® UN 3373 Pak [intended for Biological Substance, Category B (UN 3373) specimens] is an extra layer, an "outer-outer packaging," used because it already comes with the required hazardous materials labels.

**8.)** Keep your prepared FedEx® package in a secure area until collection by shipper.

**9.)** Call 1.800.463.3339 to schedule a FedEx Express pick up from your home. In case needed by FedEx agent, the account number is xxx-xxx-x (located on the pre-printed waybill).

**10.)** Complete online your "Swab Delivery Form."

## Biological samples cannot be put into a FedEx Drop Box.

### Appendix V Participant Correspondence Email Templates

**Mass ResPECT Recruitment Email**

Greetings from the ResPECT study!

We are recruiting healthcare workers from your place of work for a 19 week study researching the effectiveness of surgical masks vs. N95 respirators in preventing the transmission of flu and other respiratory pathogen illnesses (RPI). If you choose to participate in this study, you will be randomly assigned to wear either a surgical mask or an N95 respirator during all close contact with patients with suspected RPI. Your experiences will be shared with us via weekly surveys as well as randomized anonymous compliance observations made by our research assistants.

Participants will:

- complete a baseline and pre-study survey
- submit to 2 blood draws (at the beginning and end of study) as well as 2 combined nasal and throat swabs
- be fit-tested if necessary (if working at an N95-assigned site)
- be expected to wear their assigned facial protective equipment (FPE) when in close contact with patients with suspected RPI
- Surveys:
  - **Weekly Diary** for each week of the study
  - **Daily (Monday, Tuesday, etc.) Forms** for each day of the week
  - **Symptomatic Event Report** Form if you become ill
- be randomly observed by study staff to assess adherence to FPE use as well as hand hygiene
- be asked to inform study staff if you are on vacation, are sick, or are otherwise unavailable during a week of the study
- be asked to complete a post-study survey after the end of the study

Participation in the study is open to any healthcare worker with regular close patient contact who works a minimum of 24 hours per week at the assigned study site and is willing and able to comply with the study requirements, as outlined above.

Participants can receive a maximum of $599.00 compensation for partaking in the study. The rate of compensation is based directly on the participant's completion of study requirements (surveys, diaries, blood draws and specimen collections.)

Please call or e-mail us if you are interested in participating in our study, or if you have any questions. Also, be sure not to miss our first recruitment/information session at your site on [*date for that site*]!

For more information, please see our Facebook page at www.facebook.com/RespectStudy

Sincerely,
[see signature line information at end of templates]

**ResPECT Ineligible Email Template:**

Dear [First Name of Participant; automatically generated by secure RedCAP],

Thank you for your interest in the ResPECT Study! Unfortunately, you are ineligible to join our study so we won't be able to include you at this time. If you have any questions, please feel free to contact your local ResPECT Team.

Thank you,
[See Signature Info]

**ResPECT Initial Welcome E-mail**

Dear [First Name of Participant; automatically generated by secure RedCAP],

Thank you for agreeing to participate in the ResPECT Study! You will fill out a series of surveys throughout the intervention period. Links for the new surveys will be emailed to you each week, as well as any surveys that were left incomplete from the previous week.

Please click the link below to access your Pre-Study Survey so that we can get some information about you before the intervention period of the study begins:

LINK HERE

Thank you,
[Signature Line Info]

**Respect Week [week number] Survey Email Template**

Dear ____,

Welcome to Week 2 of ResPECT!

Please use the links below to complete the appropriate forms for this week.
These links are unique to YOU and should not be forwarded to others.
If you are unable to open these links or have questions, please notify the ResPECT team in your area.

Week 2 Forms:

Monday (Week 2) [Required regardless of days worked ]
Tuesday (Week 2) [Required regardless of days worked]
Wednesday (Week 2) [Required regardless of days worked]
Thursday (Week 2) [Required regardless of days worked]
Friday (Week 2) [Required regardless of days worked]
Saturday (Week 2) [Required regardless of days worked]
Sunday (Week 2) [Required regardless of days worked]

Weekly Diary (Week 2) [Required regardless of days worked]

Symptomatic Event Report Form 1 (Week 2) [only if you have symptoms]
Symptomatic Event Report Form 2 (Week 2) [only if you have symptoms]

Swab Delivery Form – Take-Home Kit [only if instructed to use your take-home kit]

**********
In this section, you will find your INCOMPLETE forms from last week (Week 1); they will not be available again, so please complete them as soon as possible:

Monday (Week 1) [Required regardless of days worked]
Tuesday (Week 1) [Required regardless of days worked]
Wednesday (Week 1) [Required regardless of days worked]
Thursday (Week 1) [Required regardless of days worked]
Friday (Week 1) [Required regardless of days worked]

Saturday (Week 1) [Required regardless of days worked]
Sunday (Week 1) [Required regardless of days worked]

Weekly Diary (Week 1) [**required**]

Symptomatic Event Report Form 1 (Week 1) [only if you have symptoms] Symptomatic Event Report Form 2 (Week 1) [only if you have symptoms]

Swab Delivery Form – Take-Home Kit [only if instructed to use your take-home kit]

**********
Thank you for your continued participation!
[Signature Line Info]

**Survey and Week Info to Participants**

Hello ResPECT Study Participants!

Now that we have started our study, we realize there is some confusion about filling out the surveys and what a "survey week" consists of. Please note that you will be emailed survey links late Sunday/early Monday that will be for the week **beginning** on that Monday. For example, the links sent late last night are for the work week starting today through Sunday (**Week 1 = Date – Date**).

There are 3 categories of Forms sent in each weekly email:

- You should fill out your Daily Exposure Form at the end of every day whether or not you work..
- A Symptomatic Event Form should be filled out whenever you feel sick and may need to be swabbed, as soon as possible after feeling sick (so if you feel sick today, please do not wait until Friday to fill out this form or contact us directly).
- The Weekly Diary should only be filled out **after** you have finished all your work shifts for that week. It will cover the time period from when you receive the email until your last work shift that week or Sunday evening, whichever comes first. We are working on resetting the surveys that were submitted today in error.

For your convenience, here are all the time periods (Mon-Sun) covered by Study Week:

- **Week 1**: date - date

[…..]

- **Week 16**: date - date
- **FINAL STUDY ITEMS (after intervention period ends)**: post-study survey, blood draw #2

[Signature Line Info]

**Study Activation to Champions**

Hello ResPECT Study Site Champions!

The ResPECT Study is activating on **<day, date>** and you can expect to see more staff than usual wearing masks. We are asking that all participants wear masks anytime they are within 6 feet of patients with respiratory symptoms, so please feel free to remind staff you know to be participating (or any of your staff as it is good infection control practice!) to wear their masks at the appropriate time.

You can also expect to see us periodically during the 16 weeks – we will be there doing compliance checks, swabs, and replenishing masks. On the week when your site is chosen for swabs, we will let you know in advance when you expect us.

Thank you again for agreeing to assist the study this flu season!!!

[Signature Line Info]

**Study Activation to Participants**

Hello ResPECT Study Participants!

It is time to start wearing masks – we are activating the study on **<day, date>!!!** Please remember to wear your masks when within 6 feet of patients with respiratory symptoms and make sure to do your daily and weekly surveys! You will receive a weekly email with a link to that week's surveys.

A couple reminders about the take-home swab kits:

- Please call us if you plan to use a take-home kit and/or submit a symptomatic event form. We will then determine if we would like you to take a sample at home.
- There are 2 swabs required for each sample: 1 nasal and 1 throat; instructions are provided in the take-home kit and you can always call us for clarification
- For the nasal swab, please make sure you insert the swab 2 -3 centimeters inside your nostrils! We realize it will be uncomfortable, but we need you to do your best to get us good samples.
- If you are sick on the weekend (Friday through Sunday) please wait until Monday to do your swab. FedEx doesn't pick up Sunday and the lab is closed through the weekend.

[Signature Line Info]

**Symptomatic and Incompletes Info to Participants**

Hello ResPECT Study Participants!

Now that we are in Week 2, we have noticed some additional confusion over the surveys. Please recall from previous email that you will be emailed survey links late Sunday/early Monday that will be for the week **beginning** on that Monday. You should not complete your **Weekly Diary** until you have stopped working for that week.

In addition, the **Symptomatic Event Forms** are only if you feel sick and may need to be swabbed. If you don't feel sick, you don't need to fill it out. We gave you 2 each week in case you feel sick more than once that week. You may also call the office or email us if you feel sick and want to know if you should swab yourself (or have a Research Assistant come take one).

You will now notice some "**Incompletes**" at the bottom of your list of Weekly Surveys. These will only appear for the previous week (you get 2 weeks to complete your surveys and then they disappear). Also make sure to complete 7 Daily Exposure Forms each week – this year you're required to do all 7!!

Thank you so much for your continued help,

[Signature Line Info]

**Question #2 Clarification to Participants**

Hello ResPECT Study Participants!

The flu season has arrived and we have been following up on everyone's submissions! Many of you have seen us recently for a swab because you're ill, and many more of you have been confused when we ask about your symptoms.

The problem across the board is on the Daily Exposure form, Question #2 – which asks if you feel sick. Please be careful here; the question is **not** about the patients you were exposed to – it only wants to know about **you.** Question #3 is about your patients and coworkers.

We love hearing from everyone, but whenever you say "Yes you're having symptoms" (of any sort, including a headache) we get an automated notification. And then we worry that you're

sick! So please be extra careful on this form – it'll save you the hassle of explaining yourself to us every week.

Thanks so much!
[Signature Line Info]

**Swab Week to Champions**

Hello <CHAMPION NAME>!

Your site has been selected to have nose-throat swabs done the week of <DATE to DATE>. We would like your assistance to make this process as efficient as possible. If you could please send us schedules for the below participants and let us know of any schedule conflicts with site events we would greatly appreciate it! We have emailed the participants for their schedules, but your input is very valuable to us.

We appreciate your help!!

[Signature Line Info]

**Swab Week to Participants**

Hello XXXXX Site Participants!

Congratulations! Your site has been selected to have nose-throat swabs done the week of <DATE to DATE>. We would like to visit your site <DATE> at <TIME>. If you will not be on site during this time, please send us your schedule as soon as possible so we can visit when you are working. It is very important that we see you this week, so please consider dropping by if you are not working so we don't miss you.

We look forward to seeing you <DATE>!!!

[Signature Line Info]

**Week 6 Survey Reminder**

Hello Respect Study Participants!

We are nearing the half-way point for the study – which means your first payment is being tallied (YAY!). However – your payment is dependent on completion of surveys so in order

to maximize your payment, the following forms need to be submitted to us by **<INSERT DATE>.** Please go through your email and make sure you've submitted:

1) **Pre-Study Survey**
2) **Weekly Diary –** for each week, total of 6 (even if you did not work)
3) **Daily Exposure Survey** – for each day of the week (even if you do not work)

We are re-sending the Pre-Study Survey to all participants – if you have **not** filled this out, please submit this as soon as possible!! You can check whether the survey is complete by simply clicking on the link – if you've submitted it, the link will not work.

Remember: If you don't submit all the surveys, you won't get all your money! If you can't find the emails, please let us know so we can resend them!!!

Thanks and we look forward to your participation in the second half!

[Signature Line Info]

**Final Blood Draw to Participants**

Hello XXXXX Site Participants!

You're almost finished!! Starting <date>, we will be visiting <CLINIC OR ED NAME> to collect the last blood draw from everyone. We would like to visit on <DATE> at <TIME>. If you will not be on site during this time, please send us your schedule as soon as possible so we can visit when you are working. It is very important that we see you sometime between April 30th and May 18th so you can get full participation credit for being in the study!!

Please also remember to do the Post-Study Survey by April 30th. We look forward to seeing you in the upcoming weeks!!!

[Signature Line Info]

**End of Study to Participants**

Hello XXXXX Site Participants!

You're almost finished!! Starting April 30th, we will be visiting <CLINIC OR ED NAME> to collect the last blood draw from everyone. We would like to visit on <DATE> at <TIME>. If you will not be on site during this time, please send us your schedule as soon as possible so we can visit

when you are working. It is very important that we see you sometime between April 30th and May 18th so you can get full participation credit for being in the study!!

Please also remember to do the Post-Study Survey by April 30th. We look forward to seeing you in the upcoming weeks!!!

[Signature Line Info]

**ResPECT Post-Study Email Template**

Dear ____,

We would like to thank you so much for your participation in the ResPECT Study. We would not have been successful or made any meaningful results without the participation of you and other healthcare workers like you.

In order to receive your final study payment, you need to complete a final blood draw (if you haven't already), as well as your final survey, the Post-Study Survey. Please click below to access it:

LINK HERE

Thank you,
[Signature Line Info]

**ResPECT Final Email Template**

Dear ___,

This email signifies that you have completed the ResPECT Study for this season! Once again, we would like to thank you for all of your help in this research.

We have submitted everyone's final study payments to be processed. You should receive this check (pro-rated based upon your amount of participation) in the next 2-3 weeks; if you do not receive it in 1 month, please contact your local ResPECT Team who can assist you in tracking down the problem.

Thank you again!
[Signature Line Info]

**ResPECT Supplemental Vaccination Questions Email Template**

Dear **[Participant Name]**,

Thank you again so much for your participation in the ResPECT Study. As we wind down this multi-year study, we realize that there were a couple additional questions we should have asked about other vaccinations you may have previously received.

Please use the link below to access and answer these final couple questions (at the most, depending on responses, you could have 5 questions total):

**[Participant's Link here]**

**Thank you once again for your continued support and participation in this very important study.**

Sincerely,

The ResPECT Study Team

[site specific info]

**Signature Line Information (will be tailored to which arm the participant is recruited under: Baltimore, Denver, Houston, New York, or Washington DC)**

The ResPECT Study Team
Children's Hospital Colorado: 720-777-8864; respectstudy@childrenscolorado.org
Denver Health: 303-436-4843; Amy.Irwin@dhha.org (Amy)
Denver VA: 303-399-8020 x6862; vhaechrespect@va.gov
Houston VA: 713-794-7224 or 713-791-1414 x5458; VHAHOUMCLRespectStudy@va.gov
Johns Hopkins: 410-614-6206; respect@jhmi.edu
New York: 212-686-7500 x4469 and 718-836-6600 x6588; ResPECTStudy@va.gov
Washington DV VA: 202-745-8457 DC.ResPECT@va.gov

[this part only for Weekly Emails]
Reminder: Please contact your study team if you develop any flu-like symptoms and please wear your study-assigned masks when interacting with patients with suspected influenza-like illness.

## Appendix W Payment Schedule

| Study Requirement | Frequency | Payment Amount | Total Possible Payment |
|---|---|---|---|
| **Pre-study package:**<br>1. Pre-study attitudes, beliefs, and opinions survey (Preliminary survey)<br>2. Baseline survey (participant demographic information)<br>3. Blood draw #1 | 1x (subject to being eligible to participate) | $ 55.00 | $ 55.00 |
| **Randomized nasal and throat swab set** | 2-3x | $60.00 (1st & 2nd set)<br>$59.00 (3rd set) | $120.00-$179.00 |
| **Weekly symptom diary** | 12-16x | $ 5.00 (each) | $ 60.00-$80.00 |
| **Daily Exposure Form** | Every day during study period | $ 5.00 (weekly) | $ 60.00-$80.00 |
| **Post-study package:**<br>1. Blood draw # 2<br>2. Post-study attitudes, beliefs, and opinions survey | 1x | $ 70.00 | $ 70.00 |
| ***Study Bonus:** Prorated according to participant completion of weekly symptom diaries and daily exposure forms. | 1x | Up to $135.00 | Up to $135.00 |
| | | | |
| | | **Maximum Total Study Payment** | **$500.00** (12 wks) **or** **$599.00** (16 wks) |

**Payment Schedule:** There are two payment dates- the first payment will be distributed midway through the study period, and the second payment will be distributed at the end of the study period. The first payment has a maximum of $175 and the second payment, which will include the bonus, has a maximum of $325 if the study ends after 12 weeks and $424 if extended to 16 weeks. Payment amounts will reflect each participant's completion of study requirements. Payment is capped at $599 for tax purposes. Please contact the ResPECT Research Office with any payment questions.

**Reminder:** Please contact the ResPECT Research Office at 410-614-6206 or respect@jhmi.edu if you experience ANY of the respiratory/flu-like symptoms listed on the Symptomatic Event Form (symptoms also listed on weekly symptom diary and back of ResPECT Study business card).

## Appendix X Swab Delivery Form

# Swab Delivery Form

Participant ID: _____

1.) When did symptoms begin? (date and time)

2.) When is pick-up scheduled? (date and time)

   a. What is the FedEx tracking number? (16-digit field)

Please remember to complete your Symptomatic Event Form online! Please contact us at XXXXX@domain.com or XXX-XXX-XXXX with any questions or concerns.

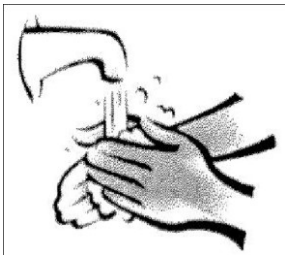
## Appendix Y Patient-Based Observation Form

**Please let us know…**

Were **you** given a face mask to wear today? Yes_____ No_____

Did you see your doctor, nurse, or other healthcare professional wear a **face mask** during your visit today? If yes, please circle the mask that most closely resembles what they wore.

| | | | |
|---|---|---|---|
| ***N95 Masks*** |  |  |  |
| ***Medical Masks*** |  |  | |
| ***Other*** | Mask unlike those above.<br>Please describe mask: | | |



Did you see your doctor, nurse, or other healthcare professional clean their hands during your visit today?

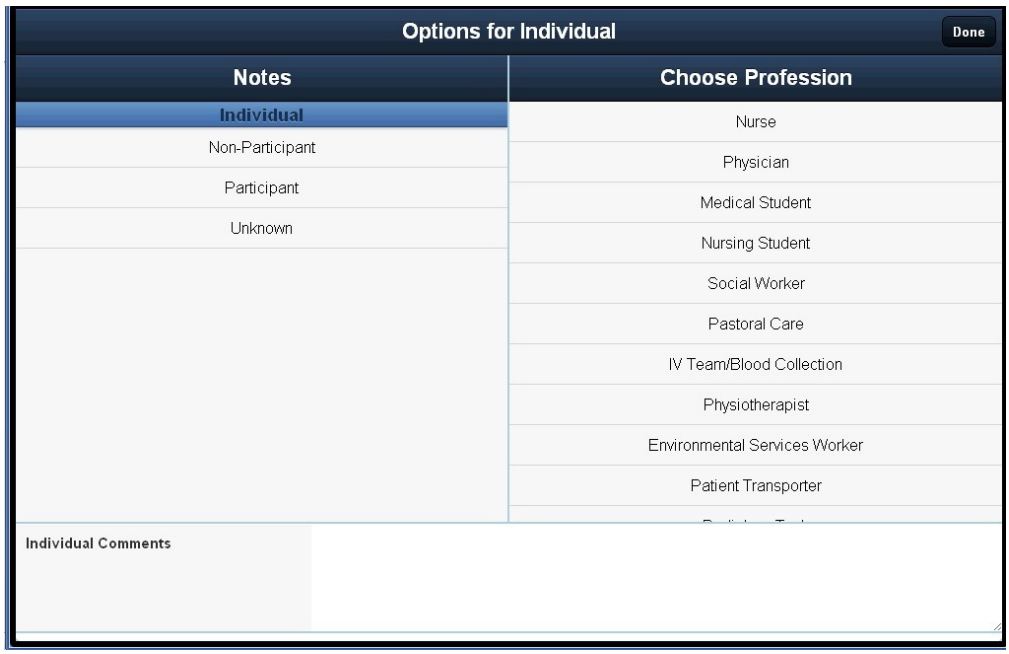
Yes _____ No _____

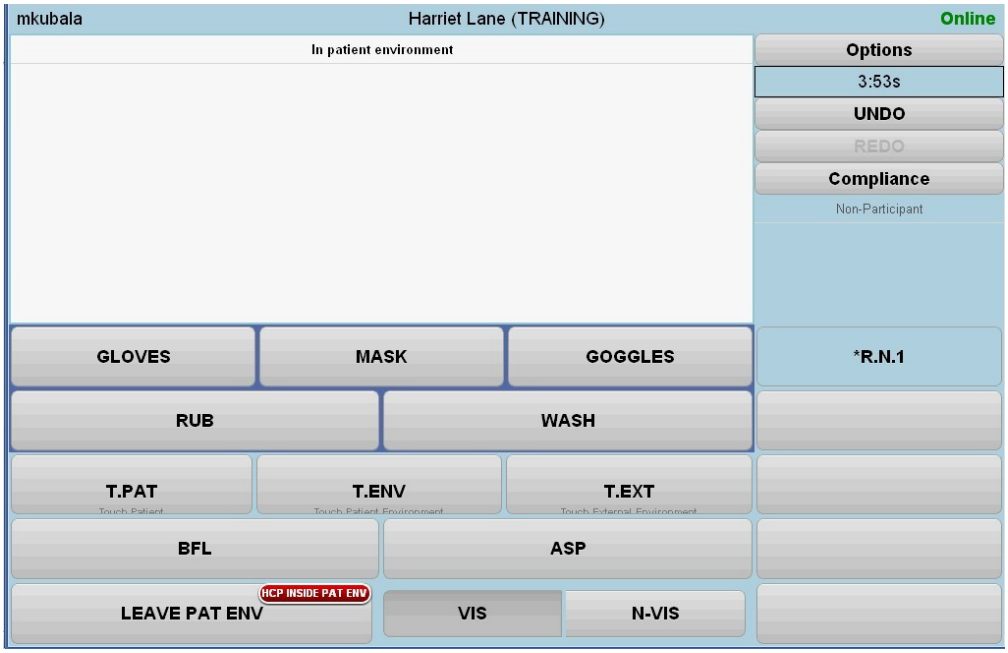
If yes, what did they use? Please indicate **when** they used this method.

| | BEFORE your exam | AFTER your exam |
|---|---|---|
| Sanitizing Gel | | |
| Sanitizing Foam | | |
| Soap and Water | | |

Thank you for answering our survey!

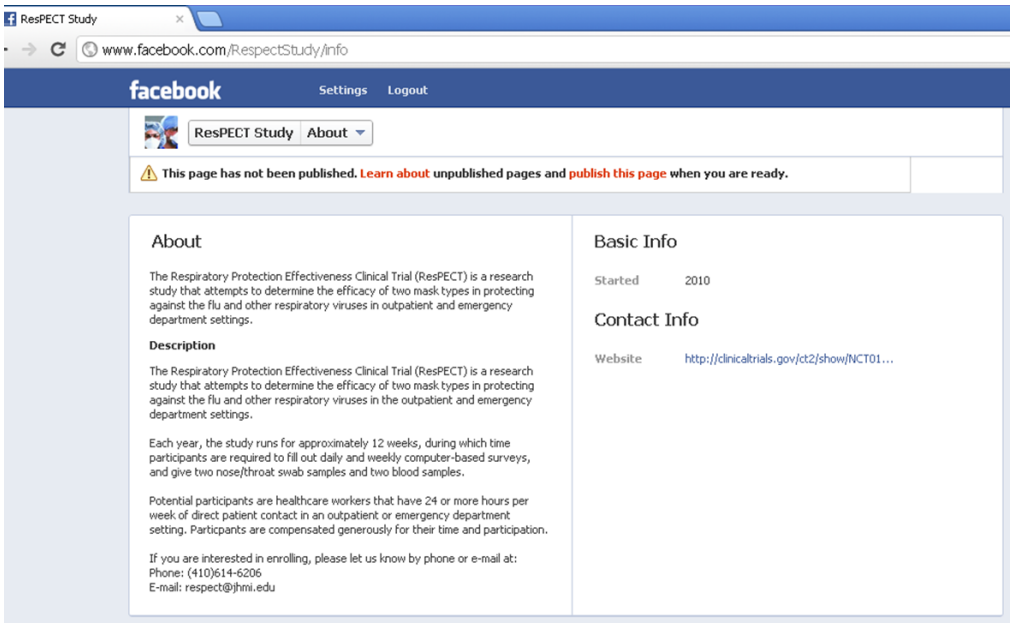
## Appendix Z HandyAudit Compliance Monitoring






## Appendix AA Respect Study Facebook Page


ResPECT Study
www.facebook.com/RespectStudy
facebook
Settings
Logout
This page has not been published. Learn about unpublished pages and publish this page when you are ready.
Admin Panel
Help us make this study a huge success by becoming a participant!
If you have any questions, or would like more information please don't hesitate to call, e-mail, or message the Baltimore team:
Phone: (410)614-6206
E-mail: respect@jhmi.edu
or hit"message" below to message us!
Respiratory Protection Effectiveness Clinical Trial - ResPECT
The Centers for Disease Control and Prevention
The Veterans Health Administration
Johns Hopkins Health System
Edit Profile Picture
ResPECT Study
5 likes · 6 talking about this
Community
The Respiratory Protection Effectiveness Clinical Trial (ResPECT) is a research study that attempts to determine the efficacy of two mask types in protecting against the flu and other respiratory viruses in outpatient and emergency department settings.
About
Photos
Events
Likes
5
Highlights
Status
Photo / Video
Event, Milestone +
Write something...
Activity
Recent
ResPECT Study created the event FINAL BLOOD DRAWS!
ResPECT Study updated their cover photo.
7 minutes ago
ResPECT Study updated their cover photo.
12 minutes ago


ResPECT Study
www.facebook.com/RespectStudy/info
facebook
Settings
Logout
ResPECT Study
About
This page has not been published. Learn about unpublished pages and publish this page when you are ready.
About
The Respiratory Protection Effectiveness Clinical Trial (ResPECT) is a research study that attempts to determine the efficacy of two mask types in protecting against the flu and other respiratory viruses in outpatient and emergency department settings.
Description
The Respiratory Protection Effectiveness Clinical Trial (ResPECT) is a research study that attempts to determine the efficacy of two mask types in protecting against the flu and other respiratory viruses in the outpatient and emergency department settings.
Each year, the study runs for approximately 12 weeks, during which time participants are required to fill out daily and weekly computer-based surveys, and give two nose/throat swab samples and two blood samples.
Potential participants are healthcare workers that have 24 or more hours per week of direct patient contact in an outpatient or emergency department setting. Particpants are compensated generously for their time and participation.
If you are interested in enrolling, please let us know by phone or e-mail at:
Phone: (410)614-6206
E-mail: respect@jhmi.edu
Basic Info
Started
2010
Contact Info
Website
http://clinicaltrials.gov/ct2/show/NCT01...

Appendix BB Mask Up Sample Poster

# WE WANT YOU TO MASK UP!

Today's Date: ____/___/____
(MM/DD/YEAR)
Study Subject ID: _____

Appendix CC **Supplemental Vaccination Questions**

**1) Have you ever had measles?**
a) If yes, approximately when? Date:

**2) Have you ever had varicella (aka chicken pox)?** a) If yes, approximately when? Date:

**3) If you have <u>not</u> had measles or varicella (chicken pox) or you are unsure, have you ever received a vaccination for measles (often included with vaccinations for mumps, rubella, and sometimes varicella/chicken pox, known as MMR or MMRV)?**
a) If yes, what type of vaccine did you receive?

☐ 2 doses as a child ☐ 2 doses as an adult

☐ 1 dose as a child ☐ 1 dose as an adult

☐ 0 doses as a child ☐ 0 doses as an adult

b) If yes, approximately when did you receive your dose(s)?
Year of 1st dose:
Year of 2nd dose:

**4) Have you ever received a pneumococcal vaccination (pneumonia)?** a) If yes, approximately when? Date:

**5) Have you ever received a tuberculosis vaccination (this is <u>not</u> the same as the "TB skin test")?**
a) If yes, approximately when? Date: