Factors Influencing the Transmission of Influenza

Request for Office of Management and Budget Review and Approval for Federally Sponsored Data Collection

Section A. Justification

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April 11, 2014

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Section A. Justification

A1. Circumstances Making the Collection of Information Necessary

Background

This OMB request is for a revised data collection project that will examine the viability of influenza virus in cough-generated aerosols. The revision is needed for OMB # 0920-0888, expiration date 5/31/2014, "Persistence of Viable Influenza Virus in Aerosols". OMB approval is requested for three years. The following changes have been made to the original data collection project:

1) To make the recruitment process faster and easier for potential participants, the initial screening will be performed verbally rather than through the health questionnaire.
2) The number of potential participants has been increased from 132 to 360. In a previous similar study, the number of potential participants who agree to join the study was 50%, which was lower than anticipated. The increase will allow the study to recruit 180 participants.
3) The number of qualified participants has been increased from 120 to 180. This is necessary to provide a sufficient number of cough aerosol samples with detectable amounts of viable influenza and is based on a previous study, where 10% of aerosol samples had culturable virus.
4) The Informed consent form has been substantially revised to make it easier to read and understand. As a result of the revisions, the burden per response for that form has been reduced from 20 to 15 minutes.
5) Because of the increases in the number of potential and qualified participants, the total burden hours has increased from 84 to 168 hours.
6) The title of the ICR has been changed to "Factors Influencing the Transmission of Influenza" in order to reflect the new focus of the project on influenza viability and to match the title of the human subjects' protocol approved by the Institutional Review Board.

Under 29 USC 669 Section 20(a)(1) of the 1970 Occupational Safety and Health Act (Attachment 1), the National Institute for Occupational Safety and Health (NIOSH) is tasked with conducting research involving innovative methods, techniques, and approaches for dealing with occupational safety and health problems. Similarly, the Centers for Disease Control and Prevention's Health Protection Goals include a Healthy Workplace goal to "promote and protect the health and safety of people who work by preventing workplace-related fatalities, illnesses, injuries, and personal health risks." The proposed project will provide needed information for addressing both of these goals in the healthcare worker population by characterizing their exposure to potentially infectious airborne material. The availability of this information will help determine the infection control and personal protective measures needed to protect healthcare workers from this hazard.

The National Occupational Research Agenda (NORA) effort led by NIOSH established national research and activity goals for groups of industry sectors. One of these groups is the Healthcare and Social Assistance (HCSA) Sector. The proposed project will contribute to HCSA Strategic Goal 5, "Stop transmission of infectious diseases in healthcare and social assistance settings among workers, patients and visitors"; HCSA Intermediate Goal 5.1, "Understanding mechanisms and routes – Investigators across a broad range of disciplines will conduct research to understand mechanisms and determinants of routes by which infectious diseases are transmitted in the healthcare and social assistance setting" and HCSA Activity/Output Goal 5.1.3, "Conduct research to better understand characteristics associated with airborne transmission, such as quantity and size distribution of aerosols generated by coughing and sneezing, determinants of survival and infectivity in airborne droplet nuclei, and virulence after airborne transmission."

Influenza is a highly transmissible respiratory virus that is of great concern because of the potential for newly-emerging strains to cause a global pandemic. If a pandemic occurs, tremendous demands will be placed on the healthcare system. However, at the same time, healthcare workers and emergency responders will face a much greater likelihood of exposure to the virus than the general public. In the early stages of the 2009 H1N1 influenza pandemic, CDC estimated that at least half of the healthcare workers who became ill with H1N1 influenza were infected on the job [1]. For this reason, it is important to understand how the virus is transmitted from person to person so that healthcare workers can be protected while they are caring for the sick.

Although influenza is known to be transmitted by infectious secretions, these secretions can be transferred from person to person in different ways, and the relative importance of the various pathways is not known [2; 3]. In particular, the role of airborne transmission in the spread of influenza is unclear, with some investigators concluding that airborne transmission is a key route (reviewed in [4-6]), while others maintain that it rarely, if ever, occurs (reviewed in [7]). The question of airborne transmission is especially important in healthcare facilities, where influenza patients tend to congregate during influenza season, because it directly impacts the infection control and personal protective measures that should be taken. During the 2009 H1N1 pandemic, for example, an Institute of Medicine (IOM) panel recommended that healthcare workers in close contact with influenza patients wear respirators to avoid infectious aerosols [8]. This recommendation was subsequently adopted by some health authorities such as the Centers for Disease Control and Prevention (CDC), but not by others, such as the World Health Organization (WHO). The IOM panel also noted that many questions about the airborne transmission of influenza are unresolved, and the issue remains controversial.

In previous studies, we showed that influenza virus RNA could be detected in airborne particles in healthcare facilities [9; 10], and that patients with influenza produced aerosol particles while coughing that contain influenza virus RNA [11]. Similar results have been reported in other studies. Stelzer-Braid et al. [12] detected influenza viral RNA produced by influenza patients

during breathing and talking. Fabian et al. [13] showed that 60% of patients with influenza A and 14% of patients with influenza B had detectable levels of viral RNA in their exhaled breath. Milton et al. [14] collected aerosol particles exhaled by influenza patients and found that patients shed about 33 viral copies/minute in aerosol particles ≥5 µm and 187 viral copies/minute in particles <5 µm. Bischoff et al. [15] demonstrated that influenza virus RNA could be detected up to 6 feet from hospitalized patients with influenza.

Although these studies have demonstrated that influenza patients do release influenza virus in airborne particles, a frequent criticism of our work has been that polymerase chain reaction (PCR) was the primary detection method. Although PCR is very sensitive, it does not distinguish between live and dead virus, and thus the potential for the virus in the expelled aerosols to infect someone is unknown. Our group and Milton's were able to grow influenza virus from two of each set of the collected samples, but this has not been sufficient to determine what fraction of influenza patients expel infectious virus in aerosols or how much infectious virus is released. Information about how much viable influenza virus is expelled in aerosol particles by patients is needed so that the potential for influenza infections to be transmitted by airborne particles can be better understood and appropriate protective measures for healthcare workers can be implemented.

In addition to searching for viable influenza virus in cough aerosols, we will also test a unique new method that may help to predict infectious aerosol production by coughing patients. Recent work at NIOSH has shown that an analysis of the sounds produced by patients during coughing can be used to screen for obstructive and restrictive lung ailments [16; 17]. Influenza typically causes an increase in airway mucus, which may increase aerosol production and also change the sound characteristics of coughs by increasing airway resistance. If so, cough sound analysis may offer a relatively simple non-invasive means to screen for patients who are likely to release the greatest amounts of infectious aerosol particles into the air. Studies of human respiratory aerosol production have found that the amount of aerosol particles produced by people varies tremendously from person to person (reviewed in [18]). Our own work has shown that both the total number of aerosol particles and the amount of airborne virus coughed out by patients with influenza vary greatly from person to person [11; 19]. In our study of influenza virus RNA in cough aerosols, 39% of the airborne influenza we detected came from just 3 of 38 patients [11]. This raises the possibility that some influenza patients may be "superspreaders"; that is, some patients may be far more likely than others to spread the disease to other people [20]. If this is the case, it would be very useful in a pandemic to be able to identify these patients so that extra precautions could be taken to protect workers and the public.

The purpose of this study is to gain a better understanding of the production of infectious aerosols by patients with influenza, and to explore cough sound analysis as a method of predicting infectious aerosol production. To do this, cough aerosols produced by volunteer subjects with influenza will be collected and tested for viable influenza virus, and the cough sounds made by these patients will be recorded.

1.1. Privacy Impact Assessment

Volunteer participants will be recruited from adult patients presenting with influenza-like illness at out-patient healthcare clinics. We anticipate that the entire study will be conducted at the West Virginia University Health Sciences Center. Participation in the study is voluntary. Any person presenting at the clinic who meets the following criteria is eligible to participate in the study:

- Male or female adult ages 18 or older.
- Symptoms of influenza-like illness (fever with one or more of the following symptoms: headache, fatigue, cough, sore throat and/or muscle aches).
- Symptoms present for 72 hours or less.
- No other respiratory illness such as severe asthma, COPD or tuberculosis.
- Otherwise good health with no underlying illnesses such diabetes.
- Not pregnant.
- No medical condition or illness that would make it difficult or uncomfortable for them to perform the test procedure.

Volunteer adult participants will be recruited by distributing flyers at the clinic. Enlarged versions of the flyer will also be posted in the clinic. Interested potential participants will be screened verbally by a test coordinator to verify that they have influenza-like symptoms and that they do not have any medical conditions that would preclude their participation. The initial verbal screening takes about 1-3 minutes. Based on our previous studies, we anticipate that about 50% of the potential participants will be eligible and will choose to participate in the study. Qualified participants who agree to participate in the study will be escorted to a test room in the healthcare facility. They will read and sign an informed consent form (Attachment 4) and complete a short health questionnaire (Attachment 5). Based on a previous study using similar forms, we estimate that the informed consent form will take about 15 minutes to read and sign, and that the health questionnaire will take about 5 minutes. After completing the forms, a medical test (Attachment 3) will occur. Two nasopharyngeal swabs and one oropharyngeal swab will be collected from the participants. They then will be asked to cough 6 times into an aerosol particle collection system, and the airborne particles produced by the participant during coughing will be collected and tested. The sounds produced during coughing will also be recorded. The test apparatus is described in detail in Section B, Data Collection Procedures. When the testing is completed, participants will receive $25 as a token of appreciation for their participation. The entire test process, from initial verbal screening to completion will take 53 minutes.

The items of information to be collected consist of an informed consent form (Attachment 4) and a health questionnaire (Attachment 5). Medical testing involving nasopharyngeal swabs, oropharyngeal swabs, cough aerosol samples and cough sound recordings will also be obtained from each participant (Attachment 3). The information collected in this project will be retained for 20 years after completion of the study as required by NIOSH. After 20 years, the records will be destroyed.

A2. Purpose and Use of the Information Collection

The purpose of this study is to measure the amount of viable influenza virus in airborne particles that are produced by patients when they cough, determine the size and quantity of the particles carrying the virus, and record the cough sounds made by patients with influenza. A better understanding of the amount of potentially infectious material released by patients and the size of the particles carrying the virus will assist in determining the possible role of airborne transmission in the spread of influenza and in devising measures to prevent it. Cough sound analysis may provide for a quick and simple method to screen for patients who are most likely to spread influenza by airborne particles.

Each participant will be asked to provide information once for this study. Participation is voluntary. Participants will receive $25 as a token of appreciation for their participation.

Under the existing OMB approval, information has been collected from 64 participants. The results of those studies have been presented at two scientific conferences and are being used to prepare a peer-reviewed journal article. However, the information gathered thus far has not been sufficient to characterize the amount of viable influenza expelled by coughing patients, which is needed to develop appropriate infection control measures.

The positive needs for the data to be collected in this study include:

- The Institute of Medicine (part of the US National Academy of Sciences) has identified information on the modes of influenza transmission, and in particular on airborne transmission by infectious aerosols, as being a critical gap that urgently needs to be filled in order to plan for infection control procedures during an influenza pandemic. The IOM urged CDC and NIOSH to undertake research in this area [8]. The proposed study will help to better understand influenza transmission and address this need.

- The NIOSH National Occupational Research Agenda includes a goal to "Conduct research to better understand characteristics associated with airborne transmission, such as quantity and size distribution of aerosols generated by coughing and sneezing, determinants of survival and infectivity in airborne droplet nuclei, and virulence after airborne transmission." (HCSA Activity/Output Goal 5.1.3, National Occupational Research Agenda, http://www.cdc.gov/NIOSH/NORA/). The proposed research relates directly to this need for information.

- Data dissemination will occur via publications (both peer reviewed and non-peer reviewed), presentations, and fact sheets. These various methods will reach people concerned with infection control and pandemic planning, providing them with needed information to develop informed and targeted prevention methods. Dissemination of the results will also be targeted to healthcare-providing organizations, healthcare workers and worker organizations to help them make appropriate informed decisions about infection control procedures and the use of personal protective equipment.

The negative consequences of not collecting this data include:

- The modes of transmission of influenza will continue to be poorly understood, which will hamper the ability to determine which infection controls procedures are vital and which are unnecessary.

- Healthcare-providing organizations and healthcare workers will lack the information they need to confidently decide whether or not personal protective equipment such as masks, face shields and respirators are needed during periods of seasonal influenza or in an influenza pandemic.

2.1. Privacy Impact Assessment Information

The information collected in this study serves the following purposes:

- The informed consent form ensures and documents that volunteers understand the study and are willing to participate in it.
- The health questionnaire allows us to verify that the volunteers are eligible for the study and determine if they have any medical conditions that would preclude their participation. The health questionnaire also allows us to relate the results of the tests on the nasopharyngeal swabs, oropharyngeal swabs, cough-generated aerosols and cough sounds to patient characteristics such as duration and type of symptoms, body size, and oral temperature.

The data collected in this project will be used to produce publications (both peer reviewed and non-peer reviewed), presentations, guidelines and recommended practices for dissemination among healthcare workers, their employers, and persons tasked with protecting the health and safety of healthcare workers. Dissemination of this information is expected to enable people concerned with infection control and pandemic planning to develop informed and targeted prevention methods. The CDC maintains an extensive catalog of guidelines, recommended practices and information resources for healthcare professionals, including information on infection control in general and influenza in particular. The information learned in this project will be used to help formulate and revise these resources in order to better serve the healthcare community.

The following categories of Information in Identifiable Form (IIF) will be collected: participant's name, age, gender, height, weight, information about respiratory illnesses, pregnancy status, information about their current illness, influenza vaccination status, flu medications taken, smoking history, and oral temperature. In addition, biological specimens and cough sound recordings will be collected. We will not have access to information from the health care provider.

The collection of IIF and other data for this project will have little to no effect on the respondent's privacy. NIOSH takes extensive safeguards to protect against any release of individual level data. The project staff will notify their supervisors immediately upon: (1)

discovering any breach or suspected breach of security, (2) discovering any unauthorized disclosure of the confidential information or (3) receipt of any legal, investigatory, or other demand for access to the confidential information in any form. Should any of these issues occur, project progress will be halted until approval is received from NIOSH supervisors to resume project activities. In addition, the NIOSH Institutional Review Board (IRB) will be informally notified of any potential breach of confidentiality within two working days of an incident and formally notified within two weeks of an incident. Proven violation of confidential information related to or obtained from the data is cause for immediate termination of access to any data and additional sanctions.

A3. Use of Improved Information Technology and Burden Reduction

The informed consent, health questionnaire and receipt data and will be collected using printed forms which are completed manually. Swabs, cough sound recordings and cough aerosol samples will be collected by the researchers; this will require no effort by the participant.

A4. Efforts to Identify Duplication and Use of Similar Information

This study does not duplicate previous research. An extensive search of the biomedical literature and discussions with other researchers in this field found only two studies that measured the production of potentially infectious aerosols containing viable influenza virus by patients, and both were too limited to draw meaningful conclusions [11; 14]. No published studies have related infectious aerosol production to cough sounds. A report by the Institute of Medicine stated that insufficient information was available to assess the potential risk from infectious aerosols produced by influenza patients, and that such research was urgently needed [8].

A5. Impact on Small Businesses or Other Small Entities

No small businesses or other small entities will be involved in this data collection.

A6. Consequences of Collecting the Information Less Frequently

Respondents will be asked to provide information one time only. No alternative methods are available to obtain the needed health information and informed consent from the participants. There are no legal obstacles to reduce the burden.

A7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances for this data collection.

A8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

1. Federal Register Notice

The 60 day Notice for this study was published in the Federal Register, Vol. 78, No. 217, on Friday, November 8, 2013 (Attachment 2). One non-substantive comment was received, and CDC's standard response was sent in response. The response acknowledged and thanked the commenter and referred them to CDC's website (Attachment 7).

2. Consultation Outside the Agency

This project was reviewed and approved by the CDC Influenza Research Agenda Working Group in 2010. The project and preliminary results from previous related work were presented at a public workshop at the US Institute of Medicine titled "Workshop on Personal Protective Equipment for Healthcare Workers in the Workplace Against Novel H1N1 Influenza A" on August 12, 2010; at a public meeting titled "Personal Protective Technology Program Healthcare Stakeholder Meeting", conducted by the CDC on June 18, 2013; and at a workshop titled "Influenza Transmission and the Built Environment–understanding modes of transmission in a sustainable future", conducted by the National Socio-Environmental Synthesis Center on March 6-7, 2014. Oral public comments on the presentations were taken during the workshops and the meeting. There were no major problems identified by these consultations that could not be resolved.

A9. Explanation of Any Payment or Gift to Respondents

Previous NIOSH studies have experienced difficulties recruiting respondents when the studies involved clinical tests and the respondents did not receive a token of appreciation for their participation. This is especially true when subjects are not feeling well and thus are less inclined to participate. To enhance recruitment, previous studies at NIOSH and other CDC centers have provided these tokens to respondents in clinical studies. For example, in a previous NIOSH study of influenza, "Experimental and Theoretical Study of Early Detection and Isolation of Influenza" (OMB No. 0920-0777), volunteers were recruited to cough into an aerosol collection system. These volunteers were offered $25 as a token of appreciation for their participation in the study, and about 50% of them agreed to participate. For these reasons, the subjects in the present study will receive $25 to thank them for their participation.

A10. Assurance of Confidentiality Provided to Respondents

This submission has been reviewed by ICRO, who determined that the Privacy Act does apply. The applicable System of Records Notice is 09-20-0147, "Occupational Health Epidemiological Studies and EEOICPA Records".

Respondents will be informed that participation in the study is voluntary and that the data supplied to NIOSH will be kept in a secure manner**,** unless compelled by law. The NIOSH IRB has reviewed and approved all instruments, informed consent materials and procedures to ensure that the rights of respondents are safeguarded (Attachment 6). Only authorized NIOSH project staff will have access to respondent names and identifiers. Personal identifying information (the participant's name) will be removed from all data before distribution or publication of results. This study has been approved by the NIOSH IRB (Attachment 6).

10.1. Privacy Impact Assessment Information:

1. Participation in the study is completely voluntary, and all respondents will be free to depart the study at any time. The study will be explained to all respondents at the beginning of their participation, and they will be asked to review and sign a written informed consent form which

explains the purpose of the study and how their information will be used and shared (Attachment 4). Participants are given a copy of the informed consent form to take with them.

2. Participants are informed at the time of recruitment that their participation is completely voluntary, and that participating or not participating in the study will not have any effect on them. The informed consent form explains the purpose of the study and how their information will be used and shared.

3. Study data will be treated in a secure manner and will not be disclosed, unless otherwise compelled by law. Information will be maintained as outlined in the CDC Privacy Act System, 09-20-0147, "Occupational Health Epidemiological Studies and EEOICPA Records" which includes safeguards such as physical safeguards for hardcopies (controlled building access, security guard service, locked rooms) and electronic safeguards for electronic copies (password-protected LAN, time-limited log-ins, file access limited to authorized users).

Each study participant will be assigned a unique identification code. This code will be used to relate the aerosol particle test results, the cough sound analysis results, the analysis of the swabs and the health questionnaire responses. The name of the test subjects or any other facts that might point to their identity will not appear anywhere in the published results. The information entered into the health questionnaire (excluding participant names) may be released as part of the publication and dissemination of the information gained in the study; however, the information is not sufficient to allow individuals to be identified.

All completed informed consent forms, health questionnaires and gift card receipts will be kept in a locked file cabinet in the Morgantown NIOSH facility (1095 Willowdale Road, Morgantown, West Virginia). Access to the facility is controlled by guards and badge-operated locks on all doors. Only the investigators of the study will have access to records that include test subject names or other data that might allow identification.

Electronic data files will use the subject ID codes only and will not include the subjects' names or other information that would allow them to be identified. All computer data files will be maintained on a password-protected LAN with time-limited log-ins and file access limited to authorized users (research staff assigned to this project). Information on laptop computers will be encrypted and secured by password protection.

The informed consent forms and health questionnaires will be retained for 20 years after completion of the study as required by NIOSH. After 20 years, the forms will be destroyed. The health questionnaire is the only source of information linking subject's names to their identification numbers.

4. A System of Records is not being created under the Privacy Act. The applicable System of Records Notice is 09-20-0147, "Occupational Health Epidemiological Studies and EEOICPA Records".

A11. Justification for Sensitive Questions

No sensitive information will be collected during this study. Social Security numbers will not be collected.

A12. Estimates of Annualized Burden Hours and Costs

A. Estimated Annual Burden Hours

The estimated annual response burden is shown is Table A12-A. Sixty participants will be needed in each year of the study for a total of 180 participants over 3 years. During previous similar studies, we found that about 50% of the potential participants declined to participate or weren't eligible for the study. Thus, we estimate that we will need to verbally screen about 360 potential participants to reach our goal of 180. In the previous studies, no participants dropped out of the study once they had decided to participate.

The informed consent form will require about 15 minutes to read and sign, and the health questionnaire will require about 5 minutes. These times for burden per response are based on our previous studies. The swabs, cough aerosol collection, and cough sound recordings will take about 30 minutes. The total time taken from the informed consent to completion will be 50 minutes. The burden for the 180 participants to respond to the informed consent form and the health questionnaire and participate in the medical testing will be a total burden of 150 hours.

Table A12-A. Estimated Annual Response Burden

Type of Respondents	*Form Name*	*No. of Respondents*	*No. of Responses per Respondent*	*Avg. Burden per Response (in hrs.)*	*Total Burden (in hrs.)*
Qualified participant	Informed consent form	180	1	15/60	45
Qualified participant	Health questionnaire	180	1	5/60	15
Qualified participant	Medical testing	180	1	30/60	90
	Total				**150**

B. Estimated Annual Burden Cost

Estimated annual burden costs for those surveyed are shown in Table A12-B. Wage estimates are based on the *May 2012 State Occupational Employment and Wage Estimates for West Virginia (all occupations)* from the US Bureau of Labor Statistics, which is the most recent data available.

Table A12-B: Estimated Annual Burden Cost

Type of Respondents	*Form Name*	*No. of Respondents*	*Total Burden (in hrs.)*	*Median hourly wage*	*Total respondent costs*
Qualified participant	Informed consent form	180	45	$13.73	$617.85
Qualified participant	Health questionnaire	180	15	$13.73	$205.95
Qualified participant	Medical testing	180	90	$13.73	$1235.70
	Total				**$2059.50**

A13. Estimates of Other Total Annual Cost Burden to Respondents and Record Keepers

There will be no additional cost burden to respondents and record keepers.

A14. Annualized Cost to the Federal Government

Costs for conducting the survey are summarized in Table A14. The total cost for this project is annualized over three years. There will be no new overhead, support staff, or construction required for the survey administration and data analysis. The study will last three years and will not require any funds for travel.

Table A14. Annualized cost to the Federal Government

Personnel--1 GS-12, 20% time per year	$17,890
Personnel--1 GS-9, 20% time per year	$12,336
Tokens of appreciation given to respondents for study participation (per year)	$1,500
Total annualized estimate of federal cost	**$31,726**

A15. Explanation for Program Changes or Adjustments

This is a revision to a previously-approved data collection (OMB # 0920-0888, "Persistence of Viable Influenza Virus in Aerosols"). The following changes have been made:

1) To make the recruitment process faster and easier for potential participants, the initial screening will be performed verbally rather than through the health questionnaire.
2) The number of potential participants has been increased from 132 to 360. In a previous similar study, the number of potential participants who agree to join the study was 50%,

which was lower than anticipated. The increase will allow the study to recruit 180 participants.

3) The number of qualified participants has been increased from 120 to 180. This is necessary to provide a sufficient number of cough aerosol samples with detectable amounts of viable influenza and is based on a previous study, where 10% of aerosol samples had culturable virus.
4) The Informed consent form has been substantially revised to make it easier to read and understand. As a result of the revisions, the burden per response for that form has been reduced from 20 to 15 minutes.
5) Because of the increases in the number of potential and qualified participants, the total burden hours has increased from 84 to 168 hours.
6) The title of the ICR has been changed to "Factors Influencing the Transmission of Influenza" in order to reflect the new focus of the project on influenza viability and to match the title of the human subjects protocol approved by the Institutional Review Board.

A16. Plans for Tabulation and Publication and Project Time Schedule

Volunteers can only be recruited and tested during influenza season, which typically lasts 1 to 3 months each year but is unpredictable and can vary significantly in time and intensity. Because of time, space and personnel constraints and the need to refine the methodology for the detection of viable influenza in cough aerosol particles, a maximum of about 60 subjects can be tested each year. Thus, we anticipate that three years will be required to complete the study.

Table A16. Proposed time schedule.

Activity	*Time schedule after OMB approval*	
	Start month	*End month*
Recruit and test 60 volunteers with influenza during first influenza season	0	3
Culture and analyze samples, evaluate results, and refine experimental methodologies	3	12
Recruit and test 60 volunteers with influenza during second influenza season	12	15
Culture and analyze samples, evaluate results, and refine experimental methodologies	15	24
Recruit and test 60 volunteers with influenza during third influenza	24	27
Culture and analyze samples, evaluate results.	27	33
Publication	33	36
TOTAL	**36 months**	

This project is intended to be primarily a descriptive study of the amount of viable influenza virus expelled by patients during coughing and of any correlations between the amount of virus expelled and the different features of the cough sounds. Data will be analyzed by determining the median total virus and median viable virus detected in the swabs and in the airborne particles, and the mean volume and flow rate of each cough. The different experiment parameters and health questionnaire information (symptoms, length of illness and vaccine status) will be tested for correlations between variables.

A17. Reason(s) Display of OMB Expiration Date is Inappropriate

No expiration date display exemption is sought.

A18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions to certification are sought.

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