Persistence of Viable Influenza Virus in Aerosols

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

Section A

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Section A. Justification

A1. Circumstances Making the Collection of Information Necessary

Background: This OMB request is for a new data collection project that will examine the viability of influenza virus in cough-generated aerosols. Initial OMB approval is requested for the maximum of three years. This ICR is not related to the American Recovery and Reinvestment Act of 2009.

Under Section 20(a) (1) of the 1970 Occupational Safety and Health Act (Attachment 1), 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 lead 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 continues to be a major public health concern because of the substantial health burden from seasonal influenza and the potential for a severe pandemic. Although influenza is known to be transmitted by infectious secretions, these secretions can be transferred from person to person in many different ways, and the relative importance of the different pathways is not known. The likelihood of the transmission of influenza virus by infectious airborne particles (infectious aerosols) generated during coughing, sneezing, speaking and breathing is particularly unclear, with some investigators concluding that airborne transmission is a key route (reviewed in [1-3]), while

others maintain that it rarely, if ever, occurs (reviewed in [4]). 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 by healthcare workers. 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 [5], and this recommendation was subsequently adopted by the Centers for Disease Control and Prevention (CDC). However, the IOM panel also noted that many questions about the airborne transmission of influenza are unresolved, and the issue remains controversial.

The probability of the airborne transmission of influenza virus depends in part on the amount of aerosolized virus to which people are exposed. Two recent studies have measured the amount of airborne influenza viral RNA (the genetic material of the virus) in healthcare facilities during the influenza season [6; 7]. Both studies found that the highest concentrations of influenza RNA were detected in locations where, and during times when, the number of influenza patients was highest. The studies also found that 42 to 53% of the influenza viral RNA was contained in airborne particles less than 4 μm in aerodynamic diameter (the respirable size fraction). Aerosol particles in this size range are of particular concern because they can remain airborne for an extended time and because they can be drawn down into the deepest regions of the lungs during inhalation. In addition, a few studies have examined airborne influenza virus production at the source (influenza patients). Fabian et al. [8] and Stelzer-Braid et al. [9] detected influenza viral RNA produced by influenza patients during breathing and talking. Fabian et al. [8] 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; they also reported that over 87% of the exhaled particles were less than 1 μm in diameter. Milton et al. [10] 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.

The studies described above have provided very useful information. However, all of them measured the amount of influenza RNA (genetic material) in the samples as a way of estimating the amount of virus present. This technique is sensitive and specific, but it does not show how much of the virus is able to infect cells and begin reproducing (in a sense, whether the virus is alive or dead). This distinction is important, because the virus is only a threat if it retains its infectivity.

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Privacy Impact Assessment

Overview of the Data Collection System

The population for this study is adult patients presenting with influenza-like illness at an out-patient healthcare clinic. We anticipate that the entire study will be conducted at the student health center of West Virginia University. Participation in the study is voluntary. Participants will be given a $25.00 gift card to reimburse them for their time and inconvenience. Recruitment will be done in the clinic waiting room by a test coordinator and by distribution of flyers in the waiting room to interested patients (Supplemental documents 1-3). An enlarged version of the flyer will also be posted in the hallway leading to the waiting room.

Any person presenting at the clinic who meets the following criteria is eligible to participate in the study:

- Male or female adult ages 18 to 35.
- Symptoms of influenza-like illness.
- 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.

The data collection system consists of a printed health questionnaire (Attachment 7) and a printed informed consent form (Attachments 8-10), both of which will be completed by the participant at the study site, swabs of nasopharyngeal mucus, and aerosol particles of respiratory mucus generated by the participant during coughing. All collections will be conducted in a private examination room after the patient has seen their health care provider. A summary of the study protocols for each phase are shown in Attachments 4-6.

Each study participant will be assigned a 4-digit identification number. This number will be used to relate the aerosol particle test results 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. Participant names will not be entered into any computer data files. Data will be tracked on the computers by the identification number only.

The health questionnaires and informed consent forms will be retained for three years after completion of the study as required by the NIOSH Human Subjects Review Board. After three years, the forms will be destroyed.

Items of Information to be Collected

The data to be collected from respondents consists of a health questionnaire and an informed consent form, both of which will be completed by the participant. Nasopharyngeal swabs and cough aerosol samples will also be obtained from each participant.

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

Minors will not be recruited for the study, and the project will not have a website.

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, and the size and quantity of the particles carrying the virus. 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.

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 [5]. 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.

Privacy Impact Assessment Information

Reason for collection of the information

The information collected in this study serves three primary purposes. First, we need to ensure and document that volunteers understand the study and are willing to participate in it. This is the primary reason for the informed consent form. Second, we need to verify that the volunteers are eligible for the study and determine if they have any medical conditions that would preclude their participation. Third, we need to collect health-related information in order to allow us to relate the results of the tests on the nasopharyngeal swabs and cough-generated aerosols to parameters such as duration and type of

symptoms, body size, oral temperature, etc. The second and third purposes are the reasons for the health questionnaire.

Intended use of the information

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 use to help formulate and revise these resources in order to better serve the healthcare community.

Information in Identifiable Form (IIF)

The following categories of Information in Identifiable Form (IIF) will be collected: participant's name, age, gender, height, weight, oral temperature, information about respiratory illness, information about their current illness, smoking history, results of influenza testing, and influenza vaccination status. In addition, biological specimens will be collected.

If the health care provider performed a rapid influenza test on the subject, the results of the test will be provided to us orally and noted on the health questionnaire. If the health care provider did not perform a rapid influenza test on the subject, we will administer the test and give the results to the test subject and their health care provider. Aside from this, we will not have access to any 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 Human Subjects Review Board 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 health questionnaire data and informed consent will be collected using printed forms which are completed manually. Nasopharyngeal swabs 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 no published studies examining the production of potentially infectious aerosols containing viable influenza virus. 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 [5].

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

In accordance with CFR 1320.8(d), a review of the proposed study was sought through a 60-day publication period in the Federal Register (FR Doc. 2010-22053, published Sept. 3, 2010, Vol. 75, No. 171, Pg. 54151-54152; shown in Attachment 2). No comments were received.

In accordance with CFR 1320.8(d), a review of the proposed study was sought through a 30-day publication period in the Federal Register (FR Doc. 2010-32076, published Dec. 22, 2010, Vol. 75, No. 245, Pg. 80506-80507; shown in Attachment 3). No comments were received.

2. Consultation Outside the Agency

This project was reviewed and approved by the CDC Influenza Research Agenda Working Group. 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. Oral public comments on the presentation and other presentations were taken during the workshop.

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 were not reimbursed for their time. To enhance recruitment, previous studies at NIOSH and other CDC centers have provided incentives 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 wear personal aerosol samplers or to cough into an aerosol collection system. The volunteers received an incentive of $40 to participate in the study. This incentive plan proved to be a very effective technique for recruiting volunteers. For the present study, subjects will receive $25.00 to reimburse them for the time and inconvenience needed to participate.

A10. Assurance of Confidentiality Provided to Respondents

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. NIOSH's internal Human Subject Review Board (HSRB) has reviewed and approved all instruments, informed consent materials and procedures to ensure that the rights of respondents are safeguarded (Attachment 11). 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.

IRB Approval

This study has been approved by the NIOSH HSRB and West Virginia University IRB. The most recent approval of the renewal of the protocol is shown in Attachment 11.

Privacy Impact Assessment Information:

A. 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".

B. Study data will be treated in a secure manner and will not be disclosed, unless otherwise compelled by law. Each study participant will be assigned a 4-digit identification number. This number will be used to relate the aerosol particle test results 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 health questionnaires and informed consent forms 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.

The health questionnaires and informed consent forms will be retained for three years after completion of the study as required by the NIOSH Human Subjects Review Board. After three years, the forms will be destroyed. These written forms are the only source of information linking subject's names to their identification numbers.

Participant names will not be entered into any computer data files. Data will be tracked on the computers by the identification number only.

C. 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 (Attachments 8-10). Participants are given a copy of the informed consent form to take with them.

D. 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.

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

1. Estimated Annual Burden Hours: A health questionnaire (Attachment 7) will be used once for the initial screening of participants. Forty volunteers will be recruited for each of the three phases of the study, for a total of 120 volunteers. During a previous similar study, the rejection rate for participants during screening was 1.7%. Conservatively assuming that 10% of initial participants will not qualify for the study, 132 participants will be needed to obtain 120 volunteers for the study. No more than 132 participants will be screened regardless of the number of volunteer subjects recruited.

After completing the health questionnaire, the 120 qualified subjects will respond once to the informed consent form (Attachments 8-10), have their oral temperature taken, have three nasopharyngeal swabs collected, and will participate in the cough aerosol collection experiment. The informed consent form will require about 10 minutes to read and sign, the oral temperature and nasopharyngeal swabbing will take about 5 minutes, and the cough aerosol collection will take 20 minutes. The total time burden for qualified participants will be about 35 minutes.

All eligible subjects with febrile respiratory illness who report to the study room will be allowed to participate in the study. Using a conservative estimate that 50% of the volunteers will test positive for the flu, this will provide results from 60 patients with influenza. The times for burden per response are based on our use of similar forms during a previous study.

Table A12-A. Estimated Annual Response Burden

Type of respondent	*Form*	*No. of respondents*	*No. of responses per respondent*	*Average burden per response (in hours)*	*Total burden hours*
Phase 1					
Initial participants	Health questionnaire	44	1	5/60	4
Qualified participants	Informed Consent form	40	1	10/60	7
	No form; this is the time required for testing.	40	1	25/60	17
Phase 2					
Initial participants	Health questionnaire	44	1	5/60	4
Qualified participants	Informed Consent form	40	1	10/60	7
	No form; this is the time required for testing.	40	1	25/60	17
Phase 3					
Initial participants	Health questionnaire	44	1	5/60	4
Qualified participants	Informed Consent form	40	1	10/60	7
	No form; this is the time required for testing.	40	1	25/60	17
TOTAL					**84**

2. Estimated Annual Burden Cost: Estimated annual burden costs for those surveyed are shown in Table A12-B. Wage estimates are based on the *May 2009 State Occupational Employment and Wage Estimates for West Virginia (all occupations)* from the US Bureau of Labor Statistics.

Table A12-B: Estimated Annual Burden Cost

Type of respondent	*Form*	*No. of respondents*	*Total burden hours*	*Median hourly wage*	*Total respondent costs*
Initial participants	Health questionnaire	132	12	$12.98	$155.76
Qualified participants	Informed Consent form	120	21	$12.98	$272.58
	No form; this is the time required for testing	120	51	$12.98	$661.98
TOTAL					**$1090.32**

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
Payment to study respondents per year	$1,000
Total of Annualized estimate of federal cost	**$31,226**

A15. Explanation for Program Changes or Adjustments

This is a new data collection.

A16. Plans for Tabulation and Publication and Project Time Schedule

Table A16. Proposed time schedule. Please note that 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. Thus, the timing of the study will depend on the natural occurrence of influenza in the US, and this schedule will need to be adjusted accordingly. For this reason, a full 36 months approval is requested.

Activity	*Time schedule after OMB approval*	
	Start month	*End month*
Recruit and test 40 volunteers with influenza for Phase 1 studies	0	3
Culture and analyze samples, evaluate results, and refine experimental methodologies	3	12
Recruit and test 40 volunteers with influenza for Phase 2 studies	12	15
Culture and analyze samples, evaluate results, and refine experimental methodologies	15	24
Recruit and test 40 volunteers with influenza for Phase 3 studies	24	27
Culture and analyze samples, evaluate results.	27	33
Publication	33	36
TOTAL	**36 months**	

Data Analysis Plan

This project is intended to be primarily a descriptive study of the amount of viable influenza virus expelled by patients during coughing. Data will be analyzed by determining the median total virus and median viable virus detected in nasopharyngeal swabs and in each of three airborne particle size ranges, 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.