AEROSOL GENERATION BY COUGH

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

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November 6, 2007

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Section A. Justification

A1. Circumstances Making the Collection of Information Necessary

The National Institute for Occupational Safety and Health (NIOSH) is authorized to conduct research to advance the health and safety of workers under Section 20(a) (1) of the 1970 Occupational Safety and Health Act. The relevant section of this law is in Attachment 1.

Many respiratory diseases are spread when healthy people come into contact with infectious fluids from sick individuals. The most common mode of transmission is direct contact with infected persons, or contact with items or people they have touched [1]. In addition, however, some respiratory illnesses can also spread via infectious aerosols that are generated by coughing and sneezing [2]. Riley et al. [3] established that tuberculosis is spread by inhalation of respirable particles generated by infected individuals. British studies of classrooms and offices found aerosols containing viable salivary streptococci and other oral bacteria that were thought to be created during speaking, coughing, and sneezing [4]. Severe acute respiratory syndrome (SARS) and avian influenza are known to spread through infectious aerosols [5; 6], and this may include cough-generated aerosols as well [6; 7].

The airborne transmission of disease is of great concern to the public health community because of the increasing prevalence of drug-resistant strains of tuberculosis, the epidemic potential of newly-emerging diseases like avian influenza, and the threat of bioterrorism using agents such as bubonic plague. The possible spread of infectious disease by aerosols is of particular concern among health-care workers and emergency responders who face a much greater risk of exposure to these hazards than does the general public. In 2000, NIOSH [8] reported that 3% of all tuberculosis cases in the United States occurred in health-care workers. During an outbreak of SARS in Toronto in 2003, over one-third of the victims were hospital staff; an investigation into the Toronto epidemic concluded that SARS was spread primarily through contact with respiratory droplets [9].

Cough-generated aerosols are especially important because coughing is a ubiquitous symptom of respiratory infections [10]. The explosive airflow associated with coughing exerts strong shear forces on the fluids lining the walls of the upper airways and the oropharyngeal space. These shear forces are thought to induce waves in the mucus and entrain some mucus as droplets, which helps moves the mucus to the top of the trachea where it can be swallowed [11; 12]. During this process, an aerosol of respiratory mucus and oral secretions is created and expelled from the mouth. Larger aerosol particles impact or settle quickly onto nearby surfaces where they can be transferred to

people by touch. Smaller particles dry rapidly and tend to stay airborne for an extended time, allowing them to be inhaled by individuals who are many meters away.

The ability of an illness to spread by aerosol dissemination depends primarily on two factors: (1) the quantity and virulence of infectious material within the aerosol; and (2) the quantity, size distribution, and properties of the aerosol itself. Although it is accepted that coughing can produce aerosols containing infectious materials, large gaps exist in our understanding of the generation and dispersion of these aerosols, particularly with regard to their physical properties. For example, only a few studies have examined the size distribution of cough-generated aerosols, and none have looked at aerosol particles below 0.3 μm [13-16]. This lack of information hampers the ability of health scientists to model and predict the generation of infectious aerosols by coughing and to understand whether or not cough-generated aerosols are likely to be an important means of transmission of particular diseases.

In an effort to reduce the potential for airborne transmission of SARS, tuberculosis, and influenza, the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) recommend that health care workers wear approved N95 or better respirators whenever they could potentially inhale infectious material (N95 respirators are dust masks that are certified to filter out at least 95% of airborne material during normal breathing) [1; 17]. In addition, CDC and WHO also recommend that patients with these illnesses be instructed to wear disposable respirators or surgical masks whenever they might infect others, such as during transport [17-19]. Surgical masks are a common choice, probably because they are cheaper and more comfortable than respirators. N95 respirators are known to be more effective than surgical masks at filtering out airborne particles during inhalation, but it is unclear how effective these masks or respirators actually are in reducing infectious aerosol release from such patients, particularly for smaller aerosol particles. This is especially true for cough-generated aerosols, since coughing produces much greater particle concentrations and higher air velocities than normal breathing.

The purpose of this project is to gain a better understanding of the production of aerosols by coughing. To do this, we propose to analyze the aerosols produced by people during voluntary coughing. In addition, we propose to study the effectiveness of surgical masks and N95 respirators at blocking the release of cough-generated aerosols. The results of our research will give scientists and health professionals greater insight into the airborne transmission of disease and allow them to better assess and improve the effectiveness of preventive measures.

A2. Purpose and Use of the Information Collection

The purpose of this project is to better understand some of the factors involved in the production of aerosols of airway fluids by coughing. The project has two specific aims:

Specific aim 1: Measure the quantity and size distribution of aerosol produced during human coughs. The purpose of these experiments is to measure the quantity and particle size distribution of the aerosol produced by coughing, and to determine how this aerosol changes after repeated coughs and over time. For this work, we will use a system that includes a spirometer, and two aerosol analyzers. Human respondents will exhale or cough into the system, and the aerosol produced by each respondent will be characterized to determine the quantity and size distribution of the aerosol produced by human coughs. This information will be used in modeling and predicting the spread of diseases by airborne transmission and in developing countermeasures to minimize the dissemination of infectious aerosols.

Table A2-A: Experiments to be conducted for Specific Aim 1.

	Respiratory maneuver	Repetitions	Number of respondents	Number of responses per respondent
Part 1	cough	3 coughs	20	1
Part 2	forced exhalation	1 exhalation every 2 minutes for 20 minutes	20	1
Part 3	cough	1 cough every 2 minutes for 20 minutes	20	1
Part 4	cough	1 cough every 2 minutes for 20 minutes, performed 4 weeks and 8 weeks after Part 3	20	2

Specific aim 2: Determine the effectiveness of surgical masks and N95 respirators at filtering cough-generated aerosols. The purpose of these experiments is to measure how effective standard surgical masks are at blocking the release of cough-generated aerosols in comparison to N95 respirators. For this work, we will use the same system as in Aim 1, with the addition of a mask holder to which surgical masks or disposable respirators can be attached. Human respondents will cough into the system, and the aerosol produced by each respondent will flow through a mask or respirator and then be analyzed. These experiments will allow us to determine how effective each mask or respirator is at preventing the release of cough-generated aerosols. This information will be directly applicable to developing better recommendations for

the treatment and handling of the sick and the protection of health care workers and first responders from infectious aerosols.

Table A2-B: Experiments to be conducted for specific Aim 2.

	Three coughs total, one under each of the following conditions			Number of respondents
	1	2	3	
Part 1	no mask/ no respirator	surgical mask	N95 respirator	40
Part 2	no mask/ no respirator	surgical mask	surgical mask with edge leaks	40
Part 3	no mask/ no respirator	N95 respirator	N95 respirator with edge leaks	40

A3. Use of Improved Information Technology and Burden Reduction

The pre-test and health questionnaire data will be collected using single-page forms which can be filled out in a few minutes manually. Aerosol data will be collected using computerized data acquisition systems operated 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 found that aerosol generation by repeated coughs over time has not been previously examined, nor have any studies directly quantified the ability of surgical masks or N95 respirators to intercept cough-generated aerosols. The proposed research was discussed with other researchers in this field, including Dr. David G. Frazer (NIOSH), Dr. Bean T. Chen (NIOSH), Dr. Donald Milton (University of Massachusetts), Dr. Rashida Khakoo (West Virginia University Hospital) and Dr. Melanie Fisher (West Virginia University Hospital), all of whom agreed that this work had not been performed previously and was worth pursuing. The proposed research was also presented to the CDC Working Group on Non-Pharmaceutical Interventions. During the subsequent discussion, group members indicated they were not aware of any previous research that had collected this specific information.

A5. Impact on Small Businesses or Other Small Entities

No small entities are involved in this project.

A6. Consequences of Collecting the Information Less Frequently

Respondents will be asked to fill out the pre-test questionnaire, the health questionnaire and the informed consent form once. No alternative methods are available to collect this information. There are no legal obstacles to reducing the burden.

A7. Special Circumstances Relating to the Guidelines of 5CFR 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 (on April 5, 2007, Vol. 72, No. 65, pages 16792-16793; shown in Attachment 2). Two comments were received. The first comment questioned how far airborne bacteria and viruses are able to travel and discussed the use of respirators. The second comment questioned whether or not this work had been done previously. The comments and responses are shown in Attachment 3.

2. Consultation Outside the Agency

This project was subjected to anonymous external peer review by two scientists and one statistician outside of NIOSH. Because the reviews were anonymous, the identities of the reviewers are not permitted to be released to the project officer. The review process was supervised by:

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A9. Explanation of Any Payment or Gift to Respondents

NIOSH employees volunteering for this study will not be compensated beyond their normal NIOSH salary. Non-employees of NIOSH who volunteer to participate in this study will receive an incentive of $20.00 for each session of this study in which they participate. 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 the NIOSH study "Workplace Stress Among Underground Coal Miners" (OMB No. 0920-0657), volunteers were recruited to complete a saliva test and avoid food, drink and exercise before they collected the samples. Volunteers received an incentive of $35 for completing the test. This incentive plan has proven to be a very effective technique for recruiting volunteers

A10. Assurance of Confidentiality Provided to Respondents

The Privacy Act is applicable to this data collection. The applicable System of Records Notice is 09-20-0147 - Occupational Health Epidemiogical Studies and EEOICPA Program 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 otherwise 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).

The names of participants will be recorded in order to allow the tracking of participants across multiple sessions. Participants will be assigned a code number from a master list. The participants' names will be recorded alongside each code number on the list. No other information will be included on the master list. Only the project officer and the technician who is testing the subjects will have access to the master list. When not in use, the questionnaires, consent forms and the master code list will be stored in a locked cabinet accessible only by the project officer and technician conducting the study. This information will be kept until one year after the study results are published, after which it will be shredded.

The participant's code number will be used on the health questionnaire and on computer aerosol data files instead of the participant's name. This serves two purposes. First, using code numbers provides a means to label and connect health questionnaires and data files from multiple sessions without the identity of the participant, which helps protects the privacy of the participant.

Second, because NIOSH employees are involved as test subjects, the NIOSH HSRB requires that a system be established so that the project investigators will not learn personal medical information about specific participants. In order to accomplish this second objective, the HSRB approved the following procedure: After the pre-test questionnaire has been completed and reviewed, the respondent will be given a health questionnaire and an envelope, both of which are labeled with the code number. They will be asked to fill out the questionnaire, seal it in the envelope, and give it to the project officer. The project officer will give the envelope to a technician not involved in testing and who will not know the identity of the subject. After testing of all respondents is

completed and results are being analyzed, the project officer will give the technician a list of the code numbers of all participants whose data is being used in each part of the study (if participants drop out of the study before completing testing or if their data is unusable for some reason, their results will be excluded). The technician will then tabulate the health information for these participants and provide the totals to the project officer for each part of the study. Thus, the study investigators will be told, for example, that for Specific Aim 1, five participants had asthma and four were smokers, but will not know which individuals have asthma or are smokers.

A11. Justification for Sensitive Questions

No sensitive information will be collected during this study.

A12. Estimates of Annualized Burden Hours and Costs

1. Estimated Annual Burden Hours

The study involves 140 respondents who will respond to the pre-test questionnaire, health questionnaire and consent form once. It is estimated that the pre-test questionnaire will take about 5 minutes to complete. The estimate below assumes that 5% of respondents will be excused from the study because of their responses to the pre-test questionnaire. The health questionnaire will take about 5 minutes to complete, and the consent form will require about 20 minutes to read and understand. The estimated annual burden is provided in table A12-A.

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*
All participants	Pre-test questionnaire	147	1	5/60	12
Qualified participants	Health questionnaire	140	1	5/60	12
	Consent form	140	1	20/60	47
Total					71

2. Estimated Annual Burden Cost

Estimated annual burden costs for those surveyed are shown in Table A12-B. Costs are based on the mean hourly rate for the US civilian labor force, which is $19.29 based on data from the US Bureau of Labor Statistics for June of 2006.

Table A12-B. Estimated Annual Burden Cost

Type of respondent	*Form*	*No. of respondents*	*Total burden hours*	*Mean hourly wage*	*Estimated Annual Burden Cost*
All participants	Pre-test questionnaire	147	12	$19.29	$231.48
Qualified participants	Health questionnaire	140	12	$19.29	$231.48
	Consent form	140	47	$19.29	$906.63
Total					$1369.59

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

There will be no additional cost burden.

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 two years. There will be no new overhead, support staff, or construction required for the survey administration and data analysis. The study will last two years and will not require any travel. The total cost of the project will be approximately $59,800.

Table A14. Annualized cost to the Federal Government

Personnel--1 GS-12, 20% time	$15,600
Personnel--1 GS-9, 20% time	$10,800
Supplies for aerosol measurement systems	$2,500
Gloves, masks, wipes, copies of questionnaires, etc.	$1,000
Total of Annualized estimate of federal cost	$29,900

A15. Explanation for Program Changes or Adjustments

Not applicable. These data collection efforts are new activities.

A16. Plans for Tabulation and Publication and Project Time Schedule

Table A16-A shows a proposed time schedule.

Activity	Months
Begin data collection	1 month after OMB approval
Complete data collection	13 months after OMB approval
Complete data analysis	16-20 months after OMB approval
Publication	24 months after OMB approval

Data Analysis Plan

Specific Aim 1: Measure the quantity and size distribution of aerosol produced during human coughs.

Table A2-A shows the experiments to be performed under Specific Aim 1. This table assumes that twenty respondents will participate in this part of the study, and that all respondents will participate in all parts.

Specific Aim 1 uses the quantity of aerosol produced and the aerosol size distribution as outcome measures. In addition, the volume of air produced during each cough and the humidity inside the spirometer will be recorded as possible confounding variables. The quantity of aerosol produced will be determined by grouping the particle concentration data from the aerosol analyzers into three size ranges: 0.01 to 0.1 μm; 0.1 to 1 μm; and 1 to 20 μm. The aerosol size distribution will be determined by fitting a lognormal distribution to the combined particle count data to determine the count median aerodynamic diameter (CMAD) and geometric standard deviation (GSD).

Part 1: Design and Analysis: The primary measure in Part 1 of Aim 1 is the particle amount measured after a cough at times 0, 5 and 10 minutes. The design structure of this experiment is a repeated measure consisting of the three measurements made on each of three coughs from each participant. The hypothesis is that background levels will decrease by a factor of 1000 within ten minutes. Twenty subjects will be used in order to achieve a statistical power level of 0.80. Analysis will be performed using the Mixed Procedure on the SAS platform to perform an analysis of variance with repeated measures. Results will be considered significant if $p \leq 0.05$.

Part 2: The primary measure in Part 2 of Aim 1 is the particle amount measured after a forced exhalation every two minutes for 20 minutes. The design structure of this experiment is a repeated measure structure consisting of 10 time measurements. Based on the hypothesis that background levels will decrease by a factor of 100 by the end of the 20 minutes, 20 respondents will be used in order to achieve a statistical power of 0.80. There is no previous study focusing on forced exhalations, so the power analysis for Part 2 was based on the same preliminary data as for Part 3. Analysis will be performed using the Mixed Procedure on the SAS platform to perform an analysis of variance with repeated measures. Results will be considered significant if $p \leq 0.05$.

Part 3: The primary measure in Part 3 of Aim 1 is the particle amount measured after a cough every two minutes for twenty minutes. The design structure of this experiment is a repeated measure structure consisting of 10 time measurements. Based on the hypothesis that background levels will decrease by a factor of 100 by then end of 20 minutes, 20 respondents will be used in order to achieve a statistical power of 0.80. Analysis will be performed using the Mixed Procedure on the SAS platform to perform an analysis of variance with repeated measures. Results will be considered significant if $p \leq 0.05$.

Part 4: The primary measure in Part 4 of Aim 1 is the amount of particles generated during each session. This data will be used as pilot data to run a power analysis and determine the sample size needed to detect differences. The pilot data used in the other parts of Aims 1 and 2 will not be used for this, since there is only one session in each experiment. Twenty respondents will be used in Part 4 in order to determine if further study is feasible. The Power Procedure on the SAS platform and NCSS PASS will be used to perform a power analysis to determine the sample size of future experiments.

Specific Aim 2: Determine the effectiveness of surgical masks and N95 respirators at filtering cough-generated aerosols.

Table A2-B shows the experiments to be performed under Specific Aim 2. Each respondent will be asked to make three coughs under each condition. For each session with each respondent, the order of the conditions (mask type, leaks, etc.) will be varied.

As noted earlier, it is not clear how much the cough-generated aerosol for an individual will vary from session to session. For this reason, the experiments are designed so that each respondent produces at least one cough without a mask or respirator during each session. The results from the cough without a mask will be compared to the other coughs in the session in order to estimate the fraction of the aerosol that is able to penetrate a surgical mask or N95 respirator. We also expect that the masks and respirators will affect particle penetrations differently depending on particle size. Results will be analyzed in three size ranges (0.01 to 0.1 μm; 0.1 to 1 μm; and 1 to 20 μm).

Part 1: Design and Analysis: The primary measure in Part 1 of Aim 2 is the particle amount of a cough measured with a surgical mask, an N95 respirator, and no face cover. The design structure of this experiment is a three-way treatment structure, with each respondent being measured on all three combinations of face cover. To test the hypothesis that the surgical mask keeps out 70% of particles and the respirator keeps out 95% of particles, 40 respondents will be used in order to achieve a statistical power of 0.80. Analysis will be performed using the Mixed Procedure on the SAS platform to perform a standard one-dimensional analysis of variance. Results will be considered significant if $p \leq 0.05$.

Part 2: Design and Analysis: The primary measure in Part 2 of Aim 2 is the particle amount of a cough measured with a surgical mask, a surgical mask with leaks, and no face cover. The design structure of this experiment is a three-way treatment structure, with each respondent being measured on all three combinations of face cover. Based on the hypothesis that the surgical mask will keep out 70% of particles, 40 respondents will be used in order to achieve a statistical power of 0.80. Analysis will be performed using the Mixed Procedure on the SAS platform to perform an analysis of variance. Results will be considered significant if $p \leq 0.05$.

Part 3: Design and Analysis: The primary measure in Part 3 of Aim 2 is the particle amount of a cough measured with an N95 respirator, the respirator with leaks, and no face cover. The design structure of this experiment is a three-way treatment structure, with each respondent being measured on all three combinations of face cover. Based on the hypothesis that the respirator will keep out 95% of particles, 40 respondents will be used in order to achieve a statistical power of 0.80. Analysis will be performed using the Mixed Procedure on the SAS platform to perform an analysis of variance. Results will be considered significant if $p \leq 0.05$.

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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