

University of North Carolina-Chapel Hill
Consent to Participate in a Research Study
Adult Subjects
Biomedical Form

IRB Study #05-2547 (formerly 05-PED-1094)
Consent Form Version Date: August 27, 2007

Title of Study: Second hand smoke and influenza-induced responses in nasal epithelium

Principal Investigator: Terry L. Noah, MD
UNC-Chapel Hill Department: Pediatrics
UNC-Chapel Hill Phone number: (919) 966-1055
Email Address: terry_noah@med.unc.edu

Co-Investigators: Ilona Jaspers, PhD; Jean Handy, PhD; Bradford Harris, MD; David Peden, MD, MS; Marianne Muhlebach, MD; Michelle Hernandez, MD.

Funding Source: Flight Attendants Medical Research Institute (FAMRI)

Study Contact telephone number: Margaret (Peg) Herbst, RN, MSN at 919-966-2879

Study Contact email: margaret_herbst@med.unc.edu

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary. You may refuse to join, or you may withdraw your consent to be in the study, for any reason.

Research studies are designed to obtain new knowledge that may help other people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to learn about how influenza virus affects nasal inflammation in people who smoke or who are passively exposed to cigarette smoke. During the study, you will be given a dose of an approved influenza vaccine called FluMist. This vaccine is a spray that is sprayed into your nose. It has been shown to effectively prevent the “flu” in

healthy young adults. It does so by creating a limited viral infection in your nose, which does not spread to your lungs or give you the “flu.” The aims of the research study are to compare how much inflammation occurs in reaction to the vaccine in people who smoke vs. those who are commonly exposed to tobacco smoke, vs. people who are not exposed to tobacco smoke. This will be done by obtaining a series of “nasal lavages” or rinses of your nose with salt water, as well as 2 superficial biopsies of the inside lining of your nose, during the period just before and for several weeks after receiving the vaccine. Using these samples, we will measure the amount of virus and the amount of inflammation in your nose. We will assess how much smoke you are exposed to using a questionnaire, and by measuring the amount of a tobacco smoke by-product in your urine.

You are being asked to be in the study because you are a healthy young adult who smokes or who is either commonly exposed to passive tobacco smoke, or who is almost never exposed to passive tobacco smoke.

Are there any reasons you should not be in this study?

You should not be in this study if you are pregnant or nursing; if you have a history of egg allergy; if you take aspirin regularly; if you have asthma; if you have immunodeficiency (HIV or other); if you are on immunosuppressive drugs including corticosteroids; if you have a past history of Guillain-Barre Syndrome; if you have any chronic medical condition; or if you have a fever or respiratory illness within the past 3 weeks prior to entry into study.

In addition, the study investigators will check your blood for antibodies against influenza, and if you have a high level of these (suggesting that you have been recently infected with influenza), you may not be included in the study. Subjects with a confirmed positive HIV test may not stay in the study.

How many people will take part in this study?

If you decide to be in this study, you will be one of approximately 75 people in this research study.

How long will your part in this study last?

Your participation will last about 1 ½ -2 months. This consists of a 1-day screening visit followed about 3-6 weeks later by entry into study for 21 days.

What will happen if you take part in the study?

Screening visit: Your first visit will last 2 to 3 hours. You will come to the research facility where you will go over the consent form with the study coordinator. The study coordinator will obtain a history, and one of the study doctors will do a physical examination. If you are a smoker, you will be asked to perform spirometry and must demonstrate normal pulmonary function with an FVC and FEV₁ of > 80% of predicted in order to continue in the study. In order to collect this information, you will be asked to inhale as deeply as possible, then exhale as rapidly and completely as possible into a mouthpiece which is connected to a computer which measures various lung volumes and which will tell us if your lung function is normal. A sample of blood will be drawn from a hand or arm vein, to test for HIV, and recent influenza exposure, and you will be asked to give a urine sample. A “nasal lavage” will be done, which involves the

researcher spraying some salt water into your nose repeatedly then having you blow your nose into a cup. A nasal biopsy will be done, in which the researcher gently scrapes the inside lining of your nose with a plastic stick. You will be scheduled for the remainder of the study visits before your leave. *The remaining visits should last between 1 and 2 hours.*

Day (-3): About 3-6 weeks later, you will come to the research facility 3 days before you are scheduled to get FluMist. A urine pregnancy test will be performed on all female volunteers. A nasal lavage will be done at this visit.

Day (0): At this visit, you will have another nasal lavage done, and then you will get a dose of FluMist which is given by spraying into your nose.

Days 1,2,3: Each of these visits will be short visits and you will have a nasal lavage done, and you will give a urine specimen.

Day 4. You will also have nasal lavage and give a urine specimen, but you will also have another nasal biopsy done.

Day 9. You will again have a nasal lavage and give a urine specimen.

Day 21. This is the last study visit. At this visit you will have nasal lavage and give a urine specimen, but you will also have blood drawn (about 10 ml or 2 tablespoons) for the researchers to check whether you have had an immune response to the vaccine.

Visit	Procedures
Screening visit (3-6 weeks prior to Day 0)	Informed consent, history (including smoke exposure questionnaire), physical examination, blood draw for anti-influenza antibody titer, urine for cotinine, nasal lavage (NL), nasal epithelial biopsy (NBx) #1 , HIV, pregnancy test, spirometry for smokers. Subjects will be assigned to based on history and urine cotinine
Day -3 (Friday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine pregnancy test on all female volunteers
Day 0 (Monday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine) Administer FluMist
Day 1 (Tuesday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine)
Day 2 (Wednesday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine)
Day 3 (Thursday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine)
Day 4 (Friday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine) NBx #2
Day 9 (Wednesday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine)
Day 21 (Monday)	NL (Differential cell count, viral culture and Ag detection, cytokine panel) Urine (cotinine) Blood draw (HAI titer – post infection)

As indicated previously, we will collect blood, urine, nasal lavage and nasal epithelial tissue samples from you during the study. We will store these samples until we have made all the analysis we need to for the study. Excess samples which remain after all analyses for this study are completed will be stored in the CEMALB Repository for Storage of Coded Samples (IRB approved study # 05-PED-1073). You will be asked to sign a separate consent for storage of these samples. If you do not want us to store the samples after this study is complete, please let us know. This will not affect your participation in this study.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. The benefits to you from being in this study may be that by receiving an FDA-approved vaccine against influenza, this may help you avoid significant illness due to influenza virus.

What are the possible risks or discomforts involved with being in this study?

Risks of FluMist. There is a small risk of transmission of the modified influenza virus contained in the vaccine, to people around you who have problems with their immune systems. This can occur for up to 3 weeks after receiving vaccine, and the risk for this is estimated at 0.5-2.5% based on studies of transmission in group settings. We are excluding from the study any individuals who are known to have contact with immunocompromised people, and we will advise you to avoid contact with such individuals for 3 weeks after receiving LAIV. Mild “flu”-like symptoms may occur in the 7 days following vaccine, including cough, runny nose, sore throat, chills, sinusitis, and tiredness or weakness. You may take Tylenol for these symptoms if they occur.

Nasal biopsy can cause mild temporary bleeding from the nose. This can be treated if it occurs by squeezing the tip of the nose for 5-10 minutes. Nasal biopsy also is transiently painful.

Blood drawing (venipuncture) can be associated with bruising and in some individuals with fainting. Bruising will be minimized by applying pressure for several minutes after the blood drawing.

Spirometry, also know as pulmonary function testing (PFT) can be associated with wheezing in individuals with lung disease. Individuals with known lung disease are excluded from the study. In the event you have unknown lung disease, albuterol (a quick acting bronchodilator which will reverse wheezing caused by constriction) and a physician are always available.

If you are a woman and you are planning to get pregnant, you should not be in the study. Many drugs can get into the mother's milk. You should not breast feed your child while taking the study drug. Pregnancy tests will be done on all women who might be able to get pregnant at the start of the study.

In addition, there may be uncommon or previously unknown risks that might occur. You should report any problems to the researchers.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will your privacy be protected?

Your privacy will be protected by encoding samples with access to your identity limited to the investigators. Medical charts generated as part of these studies will be kept in locked files and databases accessible only to investigators and your name will not be used in any publications. Research data will be identified only by study identification numbers. This study will conform to HIPAA guidelines for clinical research. No subjects will be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies for purposes such as quality control or safety.

North Carolina law requires that certain communicable diseases, including sexually transmitted diseases (STD), be reported to local health departments. Reportable STDs include human immunodeficiency virus (HIV) infection, and acquired immunodeficiency syndrome (AIDS). Although testing is supposed to be private, this cannot be guaranteed. The principal investigator will notify any volunteer with a confirmed positive HIV test and will advise them of care services available to all HIV-infected persons living in North Carolina (N.C. Division of Public Health's [HIV/STD Prevention & Care Branch](#).)

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury

from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. However, by signing this form, you do not give up any of your legal rights.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?

You will be compensated according to the following schedule:

- Nasal biopsy = \$25 each (x 2)
- Nasal lavage = \$15 each (x 9)
- Venipuncture = \$15 each (x 2)
- Urine specimen = \$15 each (x 8)
- Completion bonus=\$25

Thus if you complete all procedures you will be paid \$360 plus compensation for parking. If you do not complete the study, you will be paid for all the procedures your have completed. You will also receive FluMist (\$60 value).

Will it cost you anything to be in this study?

You will be responsible for the cost of transportation to the research facility, but we will pay for your parking.

What if you are a UNC student?

You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?

Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?

This research is funded by the Flight Attendants Medical Research Institute. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

What if you have questions about your rights as a research subject?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject you may contact, anonymously if you wish, the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Subject's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

Signature of Research Subject

Date

Printed Name of Research Subject

Signature of Person Obtaining Consent

Date

Printed Name of Person Obtaining Consent