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

IRB Study # 98-0799
Consent Form Version Date: December 13, 2006

Title of Study: Database and Screening Protocol for Research Studies of the Center for Environmental Medicine & Lung Biology

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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 screen a number of subjects for eligibility in future and ongoing lung function research studies. You will not be committed to participate in a specific research study by completing this protocol. Some of the screening data we collect may be used to determine whether you qualify for other research studies. We may also analyze your screening data to obtain information that will help us answer other research questions related to lung disease.

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

You should not participate in this study if…

- you are younger than 2 or older than 50
- you use daily medications or supplements that would preclude participation in the protocol per the investigator.
- your medical history or underlying health problems preclude participation in the protocol per the investigator.
- you are pregnant, as determined by menstrual history or urine pregnancy test, or if you are nursing a baby.
- if you have needed to visit an emergency room in the last 4 weeks for asthma
- if your screening spirometry results are less than 70% of the predicted FEV1 values, you may not participate in all parts of the study.
- if you use certain medicines for your asthma (either an inhaler or pills) you will not perform the methacholine challenge, but at the discretion of the investigator you can participate in other components of the screening protocol.

How many people will take part in this study?

If you decide to be in this study, you will be one of an unlimited number of people in this research study.

How long will your part in this study last?

Your participation in this study will take approximately 4 hours to complete all testing procedures. Although you may choose to schedule one or more testing components at a time, you should plan on completing the screening protocol in a timely fashion (within 6 weeks). Your name and information will remain in the database forever unless you choose to withdraw. We will make our measurements of the samples we collect from you today, and then we will ask you to allow us to store those samples indefinitely in our repository for use in other research projects. The repository is study number 05-2528 and is a separate consent form and study. You do not have to allow us to store those samples in the repository in order to participate in this study.

What will happen if you take part in the study?

During the course of this study, the following will occur:

- Detailed **medical history** will be obtained and reviewed by a licensed health care facilitator prior to additional participation;
- A brief **physical examination** will be performed to ensure general good health;

- A urine **pregnancy test** for all females with child-bearing potential;
- Allergy **skin testing** - This test measures the subject's sensitivity to common aeroallergens. Commercially available antigen preparations for skin testing will be administered using a Multi-Test device. The skin is not broken with this procedure, but redness and itching at positive antigen sites is expected. If you are using an antihistamine, we will either perform this testing when you are not using the medication, or we may ask you to withhold the medication for 3 to 5 days and then return to the clinic for testing. At any time while you are withholding the medication for testing purposes, if your symptoms increase, please resume the medicine and notify the study coordinator.
- **Nitric oxide measurement:** this measures the amount of nitric oxide (NO) present in expired air. An increased concentration of NO in exhaled air may be found in normal persons with acute inflammation during upper respiratory tract infections and in association with symptoms in patients with allergic rhinitis. It is also increased in asthmatics. Thus, measurement of the concentration of NO in expired air may be useful as an indirect assessment of airway inflammation in asthmatics. Lung production of NO will be measured by collection of a sample of exhaled gas. Nasal production of NO will be measured directly by connecting a NO analyzer sampling line to one nostril with the other nostril open to ambient air. During both measurements, you will be asked to close the soft palate at the back of the mouth to prevent cross-contamination of samples. We will demonstrate how to do the maneuver. The entire procedure should be completed in less than 10 minutes.
- **Spirometry or Pulmonary Function Testing (PFT's):** This test measures the volume of air that can be exhaled and the rate of airflow during exhalation after a maximal inhalation. You will inhale as deeply as possible, then exhale as rapidly and completely as possible into the spirometer. Measurements obtained from each maneuver include the forced vital capacity (FVC), the forced expiratory volume in the first second (FEV1), the maximal mid-expiratory flow rate (FEF 25-75%) and the peak flow (PF). The largest FVC and FEV1, from at least 3 acceptable trials, are selected for analysis; the flow rates are selected from the trial with the largest sum of FVC.
- **Methacholine Bronchial Provocation Challenge:** This test measures the responsiveness of the airways to a standard cholinergic bronchoconstriction agent (non-specific airway reactivity). Methacholine challenge testing is a standard clinical procedure to determine airway reactivity in patients with known or suspected asthma. We will ask you to abstain from caffeine the morning of your test to make the results more accurate. You will inhale 5 breaths from the nebulizer at each concentration starting with saline control. Each breath is started from resting end-expiratory lung volume (FRC) and continued until a maximum inhalation is reached.
  Increasing (doubling) concentrations are inhaled until your FEV1 falls by at least 20% from the post saline value, the highest concentration has been inhaled, or you experience discomfort or anxiety sufficient for the investigator or you to consider further testing unacceptable. Methacholine concentrations will be 0.075, 0.156, 0.312, 0.625, 1.25, 2.5, 5.0, and 10.0 mg/ml. If you experience symptoms that do not rapidly and spontaneously go away at the end of the procedure, you will receive 2 puffs of an inhaled bronchodilator (Albuterol) MDI. You will not be discharged until your spirometry levels return to baseline.

- **Pre and Post Bronchodilator Spirometry:** At the discretion of the investigator, we may ask you to perform a spirometry test, and then inhale 2 puffs of Albuterol, a bronchodilator. You will wait 15 to 30 minutes, and repeat the spirometry. This may be done if your breathing test or medical history suggests that your spirometry values might respond to the Albuterol, and it will give us (and you) additional information about your breathing. This will need to be done on a different day than the methacholine challenge, or it may be done instead of the methacholine challenge.
- **Induced sputum collection**: Induced sputum is a method for obtaining lower airway secretions. This procedure provides a non-invasive measurement of airway inflammation. We will ask you not to eat for 2 hours prior to this test as food residue in your mouth may contaminate the samples. If you are asthmatic or have a positive methacholine challenge test, you will receive pretreatment with 2 puffs of an albuterol MDI to inhibit bronchospasm. We will ask you to breathe 3% saline from an ultrasonic nebulizer through a mouthpiece for 7 minutes while seated. You will come off the mouthpiece and be asked to gargle, clear your throat, blow your nose, and then to cough samples from deep in the chest, and spit it in a cup. We will do a pulmonary function test (PFT) to check your breathing. Then you will inhale 4% saline for 7 minutes, and repeat the cough/pft procedure. Finally you will inhale 5% saline, and again perform the cough and PFT's. If your PFT's drop 20% or more from your baseline, we will stop the procedure.
- **Specimen collection for markers, including genetic markers**: You will be asked to provide a about 1 tablespoon of blood and/or a swab of the inside of your cheek to be collected and tested for the presence of markers thought to be important in the inflammatory response to exposure to environmental contaminants such as Endotoxin.

The results of these tests will determine whether you will be asked to participate in other research studies done here at the CEMALB. These results are kept in your study file, they do not become part of your UNC medical record. Neither you nor your insurance company will be billed for any of the tests done in this study.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

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

Several measures have been taken to minimize risk to you. First, you will not receive a challenge if you are having difficulty breathing due to an underlying condition such as asthma or chronic obstructive pulmonary disease; or if you are recovering from an upper respiratory infection. Second, all methacholine challenges will take place in the Center for Environmental Medicine, Asthma and Lung Biology, a facility staffed with personnel who are experienced in administering these challenges and equipped with appropriate resuscitative equipment. The professional skills and facilities of the UNC Medical Center will also be available for consultation and emergency or follow-up treatment.

This study might involve the following risks and/or discomforts to you:

- **Allergen skin testing:** Expected side effects include redness and itching at allergen skin test sites. These side effects are temporary in nature, but resolution varies from minutes to 2 days. On rare occasions, an over-the-counter antihistamine may be needed. All testing instruments are single use and do not break the skin, so infection is not an issue with this procedure.
- **Nitric oxide measurement**: None
- **Spirometry/Methacholine Challenge/Induced Sputum Collection:** Multiple testing attempts may cause **wheezing** in susceptible individuals. A **physician** is immediately available and rescue **albuterol** is on hand. You will be carefully monitored with pulmonary function testing to ensure a return to baseline prior to your discharge from the CEMALB and/or progression to methacholine challenge or induced sputum collection. Coughing and on rare occasion, fever or infection has been associated with induced sputum collection.
- **Blood sampling**: if appropriate, will be performed by well-trained personnel, and entails only a risk of mild discomfort with the infrequent possibility of bruising. A small risk of infection also exists.
- **Buccal Swab collection:** The preparation for this procedure involves rinsing your mouth and gently brushing the inside surface of both cheeks with a toothbrush, which may result in minor irritation.
- **Confidentiality:** All individuals who have been granted access to the data to perform their research-related duties will be bound by an agreement of confidentiality.

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

We do not know the effect of the study drug on babies before they are born, or on nursing children. 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 on the study day. This is done as part of the protocol and there is no charge to you.

If you or your partner is planning to become pregnant in the next couple of months, you should not participate in this study at this time.

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?
All database records will be kept at the EPA building at UNC, and access will only be allowed to the research personnel listed on this form. Paper files are kept locked in the coordinators office, and all computer databases are password protected. The paper files and the computer database used for recruitment will have your name and contact information, as well as your study number. Any information that goes to the investigators' will only have your study number.

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.

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 receive $75 for your participation in this database screening. This sum is to compensate you for your time. We will provide you with parking coupons if you parked in any UNC Hospitals parking lot.

You are free to end your participation in this database screening for any reason. Discontinuation of testing will result in a pro-rated compensation at the rate of $15/hour. If the investigator stops testing due to concerns for health and safety, you will receive full compensation in the amount of $75.00.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study. All tests and procedures are paid for by the study. Neither you nor your insurance company will be billed.

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 a grant from the National Institutes of Health. The funds are provided so that we may have a database of subjects eligible for other studies funded by both the NIH and other sponsors. The researchers do not 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.