

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

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**IRB Study GCRC 2475  
Consent Form Version Date:** July 28, 2006

**Title of Study:** Range of neutrophil response to 10,000 EU of Clinical Center Reference Endotoxin in Otherwise Healthy Smokers

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**Funding Source:** SCCOR Grant P50HL084934-01

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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 Phase 1 research study is to use a dose of inhaled endotoxin (obtained from the National Institutes of Health, and called Clinical Center Reference Endotoxin or CCRE) that has not caused prolonged cough, shortness of breath or other problems in a small number of healthy non-smoking individuals, but causes changes in certain cells in airways that the scientists can measure in your sputum. Changes in these cells may suggest the beginning of a mild response to endotoxin. Endotoxins are a product of a bacteria and are a component of cigarette smoke, and we are interested in seeing whether active smokers' cells respond to an inhaled endotoxin challenge. Eventually, these types of studies will be used to examine why some people are more sensitive to endotoxin than others. Endotoxin is also a component of outdoor air pollution, and is found in high levels in a number of different workplaces (cotton mills, poultry farms), and is even found in homes. You will inhale a dose of 10,000 EU (endotoxin units). In our previous studies with healthy non-smoking people, CCRE endotoxin at 10,000 EU produced no significant health problems.

You are being asked to be in the study because you are an otherwise healthy current cigarette smoker.

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

You should not be in this study if you:

- Use daily medications or supplements that would preclude participation in the protocol per the study doctor
- Have asthma or other lung disease
- Have a medical history or underlying health problems that preclude participation in the protocol per the study doctor
- Are allergic to albuterol, acetaminophen, aspirin-like drugs or any other medication that may be used in the study
- Have had any viral or "flu-like" illness in the past 2 weeks
- Are pregnant as determined by menstrual history or urine pregnancy test
- Have worked on a pig farm, or in a grain or cotton storage site in the last 6 months

### **How many people will take part in this study?**

If you decide to be in this study, you will be one of approximately 15 people in this research study.

### **How long will your part in this study last?**

You will be in the study for 2 weeks. You will need to come by the study center to review and sign the consent form. This will take about 30 minutes, and may be done on the first day, or at a separate visit. After you sign the consent form, it will take about 3 hours to complete the first study day. This will occur in the morning. You will come back the next day for your exposure. This visit will last all day, and you should be discharged home at about 4:30 in the

evening. However, if you have unexpected problems with the study we will ask you to spend the night in the General Clinic Research Unit at UNC Hospitals. You will return to the research lab the next morning for about an hour. We will give you diaries to complete each day at noon for 4 days, and we will give you a phone call on the 3<sup>rd</sup> or 4<sup>th</sup> day after your exposure. You will return to the research lab 5 to 10 days after your exposure for a checkout visit. This visit will last about an hour.

### **What will happen if you take part in the study?**

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

You will have participated in our Screening and Database study, 98-CEMALB-293. The skin test results, sputum sample and methacholine challenge results from that study determine that you are eligible for this study, and we will put a copy of those results in your study binder.

#### Study Day 1:

- Your **medical history** will be reviewed;
- A brief **physical examination** will be performed to ensure general good health, including vital signs;
- A urine **pregnancy test** for all females with child-bearing potential;
- **Spirometry** or **pulmonary function testing (PFT's)** – This breathing test is measure how much air you blow out and how quickly you blow it out. You will need to have normal lung function to be able to continue in the study.
- **Blood draw:** 4 tubes of blood (approximately 6 teaspoon) will be drawn
- **Induced sputum collection:** You will inhale 3% saline solution for 7 minutes, and then be asked to produce a sputum sample. We will repeat the PFT's, and ask you to inhale 4% saline. After you give us a sputum sample, we will repeat the procedure and ask you to inhale 5% saline. This procedure should take about 30 minutes.
- **Discharge PFT's and vital signs:** You will be discharged from the lab when your vital signs and lung function are at your baseline measurements, and you are comfortable.

#### Study Day 2:

- **Arrival in lab:** We will ask you about your general health since discharge, and collect vital signs;
- **PFT's:** You will do a breathing test for us, and then every hour for 6 hours after the LPS challenge;
- **Endotoxin (LPS) Challenge:** You will be asked to breathe 10,000 endotoxin units. The endotoxin used will be Clinical Center Reference Endotoxin (CCRE), prepared from the bacterial strain *E. Coli* and supplied by the NIH. It will be placed into 5 ml of sterile water. You will inhale this preparation using a DeVilbiss ultrasonic nebulizer which delivers the endotoxin as an inhaled mist in similar way to the saline administration during the sputum induction. This procedure will take approximately 10 minutes to complete.

- **Vital Signs:** We will measure your vital signs, including heart rate, blood pressure, temperature, and oxygen saturation (amount of oxygen in your blood) every hour.
- **Sputum Induction:** Approximately 6 hours after you inhale the LPS, we will obtain a sputum induction. The procedure is identical to the one done on study day 1.
- **Blood draw:** We will draw 6 tubes (approximately 6 teaspoons) of blood
- **Symptom Scoring Sheet:** You will be given a sheet to record your symptoms after your challenge, just like you did during the day immediately after the challenge, and instructions on when and how to call us.
- **Discharge:** You will be sent home at the end of the study day. You will have contact information for the study personnel on call if you need anything. If you have unexpected problems during the study day, you will be admitted to the GCRC at UNC Hospitals for overnight observation.

#### Study Day 3:

- **Return to Lab:** You will need to come back to the study lab in the morning
- **Vital Signs:** We will collect your vital signs;
- **PFT's:** You will do a breathing test;
- **Symptom Scoring Sheet:** We will ask you to complete a symptom scoring sheet;
- **Discharge:** You will be discharged from the study lab;

Telephone follow up: A member of the study team will contact you by phone 3 to 4 days after your challenge sessions to ask about your health.

**Final Visit (1-2 hours):** You will return to the clinic 5 to 10 days after the challenge for a final check up by the study doctor. We will collect your vital signs and ask you to do a PFT for us.

In addition, blood sputum samples that are left from this investigation will be stored until we have made all the measurements we need to for this study. Any samples that are left over will continue to be stored. **We will give you a separate consent form which discusses sample storage in the Center for Environmental Medicine, Asthma, and Lung Biology Repository for storage of coded samples (05-PED-1073). You do not have to allow us to store these samples after this study is complete to participate 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. If you are interested, we can provide some smoking cessation information, as well as suggest some smoking cessation programs.

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

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

- **Spirometry/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 PFT's to be sure your lung function returns to baseline before you are discharged from the CEMALB.

- Albuterol: If you need to use the albuterol, the most likely risks include tremor, nervousness, shakiness, headache, nausea, or lightheadedness.
- The amount of endotoxin used in this study is based on that which has been previously used for studies of the effect of inhaled LPS in asthmatic and normal subjects. The 10,000 units dose of endotoxin is approximately equal to the amount of endotoxin a person would inhale over an eight hour period in many job settings, such as working on an industrial pig farm. Immediate adverse effects of endotoxin might include shortness of breath, cough, wheeze, headache and flu-like symptoms. Such doses are observed at doses of inhaled endotoxin of approximately 60,000 EU. Doses of endotoxin of 20,000 EU or less rarely cause noticeable side effects, as determined from studies in this laboratory as well as others. Nonetheless, there can be no guarantee that a given person may not be unusually sensitive to the effect of endotoxin.
- **Blood sampling** –will be performed by well-trained personnel, and entails only a risk of mild discomfort with the infrequent possibility of hematoma formation. A small risk of infection also exists.
- **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 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 because you are recovering from an upper respiratory infection. Second, all endotoxin 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.

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 at the start of the study. This is part of the study, so you will not have to pay for the test.

Men should not father children while in the study.

If you or your partner becomes pregnant during the study you should notify the researcher right away.

**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 records will be kept on file at the Center for Environmental Medicine, Asthma and Lung Biology. Access to your information is only granted to the study team. A copy of this consent form will be placed in your medical record and your lab values will become part of your medical record. The study staff may contact you by email to schedule or remind you of study visits, however no specific medical information, such as your lab results, will be included in the emails.

This research may be reviewed by the FDA.

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. If you have received your exposure to endotoxin, we will ask you to allow us to be sure your lung function and vital signs are normal before you leave the study area.

**Will you receive anything for being in this study?**

You will receive \$425 for your participation in this study if you complete all study procedures. This sum is not intended to coerce completion or participation, but to emphasize the importance of all the visits, and to signify the importance of your time and commitment to the research study. You will be compensated for the visits completed as follows:

### COMPENSATION FOR THE SESSION

Completion of Day 1:	\$ 75
Completion of Day 2:	175
Completion of Day 3:	<u>75</u>
	\$325

Completion of Discharge Visit: \$25

Protocol Completion Bonus	\$ <u>75</u>
TOTAL:	\$425

If you are scheduled for a session and arrive in the lab, and that session is cancelled for any reason, but rescheduled, you will be paid \$50. If you withdrawal from the study, you will be reimbursed for completed visits. If the study doctor stops testing due to concerns for health and safety, you will receive full compensation in the amount of \$350.00.

We will give you parking coupons to cover the cost of parking in the UNC parking lot, and we will provide lunch for you on the exposure day. We will provide reimbursement if you drive more than 30 miles one way from your home to be in the study.

#### **Will it cost you anything to be in this study?**

It will not cost you anything to participate in this study.

#### **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 sponsored by a grant for the National Heart, Lung and Blood Institute (NHLBI).

#### **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](mailto:IRB_subjects@unc.edu).