

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

Medical IRB Study # GCRC 1983
Consent Form Version Date: July 7, 2005

Title of Study: Safety Study To Determine the Effect of a 10,000 EU Dose of Clinical Center Reference Endotoxin in Allergic and Mildly Asthmatic Adults

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Sponsor: National Institutes of Health

You are being asked to take part in a research study. The investigators listed above are in charge of the study; other professional persons may help them or act for them.

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

Research studies are designed to gain scientific knowledge that may help other people in the future. You may not receive any direct benefit from participating. There may also be risks associated with participating in research studies.

Your participation is voluntary. You may refuse to participate, or may withdraw your consent to participate in any study at any time, and for any reason, without jeopardizing your future care at this institution or your relationship with your doctor. If you are a patient with an illness, you do not have to participate in research in order to receive treatment.

Details about this particular study are discussed below. It is important that you understand this information so that you can decide in a free and informed manner whether you want to participate. You will be given a copy of this consent form. You are urged to ask the investigators 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?

Endotoxin is a component of outdoor air pollution, an air contaminant found in a number of different workplaces, and is even found in homes. The Endotoxin used for this study is obtained from the National Institutes of Health, and is called “Clinical Center Reference Endotoxin”, or CCRE. The purpose of this Phase 1 research study is to identify a dose of inhaled endotoxin that is safe (does not cause prolonged cough, shortness of breath or other problems), but causes changes in your sputum cell samples that the scientists can measure. Phase 1 research studies like this one are not intended to be a treatment, but are a scientific investigation. Eventually, these types of studies will be used to examine why some people are more sensitive to Endotoxin. Scientists at other universities have found that while most people do not have a significant lung response to endotoxin at doses as high as 60,000 EU, a few respond to as little as a total dose of 4500 EU. Our study is designed to identify very sensitive persons using a dose of 10,000 EU. In our previous studies in our lab, using an endotoxin from another source, we have used higher doses (15,000 endotoxin units) with no significant problems.

How many subjects will participate in this study?

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

How long will your participation last?

Your overall participation in this study will last about 2 weeks. Day 1 will require you to be in the CEMALB for about 2 to 3 hours in the morning. On day 2 you will come to the CEMALB in the morning, stay all day, and then you be admitted to the GCRC at UNC Hospitals to stay overnight. On Day 3, we will discharge you from the hospital, and you will come back to the CEMALB for about an hour. You will be sent home with diary cards, we ask that you fill them out at noon each day for 4 days. On the 3rd or 4th day after your exposure, a member of the study team will call you. You will need to come back to the CEMALB between 7 and 10 days after your exposure day.

What will happen if you take part in the study?

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

Study Day 1:

- We will ask you to have a light breakfast at least 2 hours prior to arrival in lab;
- 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 identical to that done during Part 1 of the screening protocol;

- **Blood draw:** 1 tube of blood (approximately one tablespoon) will be drawn to measure your complete blood count, or CBC
- **Induced sputum collection:** This procedure is identical to that done during the Database Screening protocol. You will inhale 3% saline solution for 7 minutes, and then be asked to cough up a sputum sample. We will repeat the pft's, and ask you breathe 4% saline. After you give us a sputum sample, we will repeat the procedure and ask you to breathe 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 are at your baseline, and you are comfortable.

Study Day 2:

- **Preparation:** Please eat breakfast prior to coming to the lab, however please do not consume caffeine.
- **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 until the challenge solution is completely spent. 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 1 tube (approximately 1 tablespoon) of blood to check a CBC prior to discharge.
- **Symptom Scoring Sheet:** You will be given a sheet to record your symptoms each time the nurse collects your vital signs.
- **Discharge:** You will be discharged from the lab to the GCRC to spend the night. The nursing staff will monitor your vital signs, and you will be given dinner.

Study Day 3:

- **Vital signs:** The nursing staff at the GCRC will check your vital signs;
- **Breakfast:** Will be provided in the GCRC;
- **Return to Lab:** You will be escorted back to the study lab by someone from the study staff;
- **PFT's:** You will do a breathing test;

- **Vital Signs:** We will measure your vital signs, including heart rate, blood pressure, temperature, and oxygen saturation;
- **Symptom Scoring Sheet:** You will be given a sheet to record your symptoms after your challenge, and instructions on when and how to call us.
- **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 day to ask about your health.

In addition, sputum samples that are left from this investigation will be stored indefinitely to possibly be used in research studies not yet known. You will be provided with a brochure entitled *Information About Storage and Use of Specimens With Identifying Information* that is designed to answer your questions, and given a separate consent form for these stored specimens. If you do not want to allow your samples to be stored, that will not prevent you from participating in this study.

Are there any reasons you should not participate?

You should not participate in this study if...

- You use daily medications or supplements that would preclude participation in the protocol as determined by the study doctor, such as daily use of Albuterol for asthma symptoms, theophylline, or if you or your doctor have changed your asthma medication regimen in the last month because of inadequately controlled asthma.
- You have a medical history or underlying health problems that preclude participation in the protocol as determined by the study doctor
- You are allergic to albuterol, acetaminophen, aspirin-like drugs or any other medication that may be used in the study
- You have had any viral or “flu-like” illness in the past 6 weeks
- You are pregnant as determined by menstrual history or urine pregnancy test
- You have worked on a pig farm, or in a grain or cotton storage site in the last 6 months

What are the possible risks or discomforts?

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, and coughing repeatedly may make your chest hurt. 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 endotoxin challenge or induced sputum collection.
- **Endotoxin Challenge** – 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. 10,000 units 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 in an industrial pig farm. Immediate adverse effects of endotoxin might include shortness of breath, cough, wheeze,

headache and flu-like symptoms. Such problems are observed at doses of inhaled endotoxin of approximately 60,000 EU. Doses of endotoxin of 15,000 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. A copy of this consent form will be placed in your UNC Hospitals medical record, and your blood sample results are also part of that medical record.

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 unrecognized responses to endotoxin that would be a risk we cannot foresee.

In addition, there may be uncommon or previously unrecognized risks that might occur.

What are the possible benefits?

This study is not designed to benefit you directly. **This is not a study of a new asthma medication.** The benefits to you will include a brief physical and labwork, and information about your lung function. Any abnormalities discovered will be explained. The scientific community will benefit by defining the safest dose of Endotoxin to use in future studies of the effect of endotoxin in asthma and lung function in people.

What if we learn about new risks 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?

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-CH will take all steps allowable by law to protect the

privacy of personal information. Information from this study will be submitted to the US Food and Drug Administration (FDA), and the study may be reviewed by research review groups within UNC.

Your records will be kept on file at the Center for Environmental Medicine, Asthma and Lung Biology in locked files. Access to your information is only granted to the study team.

Because you will be admitted to the hospital during your participation in this study, a copy of this consent form will be placed in your medical record. This will allow the doctors caring for you to obtain information about what drugs or procedures you are receiving in the study and treat you appropriately, if you have other health problems or needs during the study.

Will you be paid for participating?

You will receive \$375 for your participation in this study if you complete all tests. 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:	200
Completion of Day 3:	<u>75</u>
	\$350
Protocol Completion Bonus	\$100
TOTAL:	<u>\$450</u>
Completion of Discharge Visit:	\$25

If you are scheduled for a session and arrive in the lab, and that session is cancelled, but rescheduled, you will be paid for study day 1 and 2. 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 \$475.00.

Will it cost you anything to participate?

There will be no costs to you for participating.

Who is sponsoring this study?

This research is conducted by the UNC Center for Environmental Medicine, Asthma and Lung Biology, with funds provided by the National Institutes of Health.

What will happen if you are injured by this research?

All types of research involve possible risk, some including the risk of personal injury. In spite of all precautions, you might develop complications from participating in this study. If such complications arise, the researchers will assist you in obtaining appropriate medical treatment,

but any costs associated with the treatment will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to compensate you for any such complications or injuries, or for related medical care. However, by signing this form, you do not waive 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.

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 further questions, or if a research-related injury occurs, you should Dr. David Peden at 919.966.0768.

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

This research has been reviewed and approved by the Committee on the Protection of the Rights of Human Subjects (Medical IRB) at the University of North Carolina at Chapel Hill. If you have any questions or concerns regarding your rights as a research subject, you may contact the Chairman of the Committee at (919) 966-1344.
