

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

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**IRB Study # 06-0528 (formerly GCRC #2537)**

**Consent Form Version Date:** January 22, 2007

**Title of Study:** Phase 1 Study of *Dermatophagoides farinae* inhalation in humans

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Asthma and Lung Biology

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**Study staff:** Hazel Shepherd RN, MSN; Lynne Newlin-Clapp; Sally Ivins, BA; Martha Almond, RRT, RPFT, Carole Robinette, MS.

**Funding Source:** National Institutes of Health (NHLBI-RO1 HL080337)

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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?**

Allergen extracts, including dust mite allergen extract (also known as *Dermatophagoides Farinae* or *D Farinae*) are FDA approved therapies for injection immunotherapy for inflammation and irritation of the nose caused by allergies. Likewise, such extracts have been used in research studies involving oral or nasal inhalation to evaluate inflammatory and immune processes involved in allergic inflammation.

The purpose of this research study is to learn more about the effect of inhaled dust mite allergen extract on airway responses in allergic individuals with mild asthma. Information learned from this study will be used to identify a safe dose range of *D Farinae* extract for use in inhalation challenge studies. Challenge studies are used to evaluate the body's response (such as changes in markers of inflammation found in sputum) to an inhaled allergen, irritant or various types of air pollution. This study will also help determine how inhalation of the allergen affects mucociliary clearance (MCC) which is a measure of how quickly mucus clears from the airway.

You are being asked to be in the study because you have mild asthma and are allergic to dust mites.

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

You should not be in this study if you have any of the following:

- History of immunologic disease, or are undergoing therapeutic immune suppression for cancer or other diseases.
- If you have received emergency treatment from a physician for an asthma exacerbation within the past 12 months or if you have had any oral or intravenous steroid treatment in the past 12 months except for use of steroid cream on your skin.
- Inability to withhold inhaled or oral bronchodilating medications (such as albuterol) for 12 hours prior to allergen challenge.
- If you are pregnant or nursing a baby
- If you are a woman of child bearing potential who is not using dependable contraception (such as birth control pill, IUD, estrogen patches) or completely abstinent.
- If you have smoked more than ½ pack of cigarettes per week within the past 12 months.
- If you have had a viral upper respiratory tract infection within 4 weeks of the scheduled challenge.
- If you have had any acute infection requiring antibiotics within 2 weeks of challenge (or 4 weeks in the case of azithromycin).
- If you are participating in any study using an investigational agent within 4 weeks of this study.

**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?**

The initial baseline visit will take 4-5 hours, and the following day you will return for additional procedures that will take up to approximately 2 hours. The day after the follow-up day, you will

be contacted by phone and this call will last about 5 minutes. At least 2 days later, you will return for 3 sequential days for the challenge procedure. The day prior to the challenge (Day 1) you will have a 1 hour visit and the next day you will return for the allergen challenge. The challenge and post challenge testing (Day 2) will take approximately 8-9 hours and you will then be admitted to the UNC Hospital General Clinical Research Center (GCRC) for an overnight stay. The next morning (Day 3) you will have 1-2 hours of follow-up testing and you will receive a 24 hour follow-up phone call which will last about 5 minutes. Within the following 10 days you will return for a brief (less than 1 hour) final visit.

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

You will be asked to complete the following visits. A table summarizing the visits and procedures for each is below as well as detailed explanations of the procedures and evaluations to be performed.

#### **Baseline visit**

1. The study will be discussed and you will sign this consent form.
2. Your medical history and current medications will be reviewed
3. Vital sign measurements will be obtained (temperature, pulse, respiratory rate, blood pressure), symptom scoring and oxygen saturation (blood oxygen level which is noninvasively measured by briefly putting a painless clip onto your finger)
4. Urine pregnancy test for women of child bearing potential will be performed
5. Spirometry will be performed as described on page 5 of this document
6. Physical exam of the ears, nose, throat and chest will be done
7. Venipuncture (blood draw)
8. Xenon equilibrium gas scan as described on page 6
9. MCC (mucociliary clearance) procedure as described on page 6

#### **24 hours post baseline visit**

1. We will review any change in your medical status over prior 24 hours
2. Vital signs, oxygen saturation and symptom score will be measured
3. Follow up MCC scan
4. Collection of exhaled breath for measurement of nitric oxide level.
5. Sputum induction (inhalation of saline designed to produce cough) will be performed preceded by albuterol as described on page 5.

#### **Post Challenge Observations/Reporting**

You will be contacted by phone 24 hours after sputum induction for follow-up

#### **24-48 hours prior to challenge visit (at least 2 days after the baseline visit)**

1. We will review any change in medical status since your last visit
2. Vital signs, oxygen saturation, and symptom score will be evaluated
3. Spirometry will be measured
4. Physical exam of the ears, nose, throat and chest will be performed

### **Allergen challenge day**

1. We will review any change in medical status since your last visit
2. Vital signs, oxygen saturation, and symptom score will be measured
3. Urine pregnancy test for women of child bearing potential will be performed
4. Spirometry
5. If above measures are acceptable, allergen challenge will be performed as described below
6. Post-challenge monitoring will occur throughout the remainder of the morning and afternoon
7. Post challenge venipuncture (blood draw)
8. Four hours post challenge, you will have another MCC scan
9. You will be admitted to the GCRC for an overnight stay in the UNC General Clinical Research Center (GCRC). You will be asked to perform either spirometry with a personal spirometer or peak flow assessments on an every other hourly basis until at least 9 PM and up to 11 pm if you are awake.

### **24 hours post challenge**

1. You will be discharged from GCRC, and accompanied by a study staff member, proceed directly to the Center for Environmental Medicine, Asthma and Lung Biology (CEMALB).
2. Vital signs, oxygen saturation, and symptom score will be measured
3. Collection of exhaled breath for measurement of nitric oxide level.
4. Spirometry will be evaluated
5. Venipuncture (blood draw)
6. Follow-up MCC scan will be performed
7. Sputum induction will be completed preceded by albuterol

### **Post Challenge Observations/Reporting**

1. You will be contacted for phone call follow-up 24 hours after the post-challenge sputum induction
2. You will be given a symptom scoring sheet for each day up to 96 hours (4 days) after challenge which you will need to bring with you at the final visit

### **Study discontinuation visit within 10 days of the final challenge dose:**

1. Vital signs, oxygen saturation, and symptom score will be measured
2. Your symptom scoring sheets for the 4 days after the challenge will be collected
3. Spirometry will be performed
4. If any findings are abnormal, medical evaluation as directed by the study physician will be undertaken prior to study discontinuation

**Table of Study Procedures**

Procedures to be performed at various time points are listed in the following table.

	base- line	study visit 24 hrs post- baseline	24-48 hrs pre- challen ge	allergen challenge day	24 hrs post- challenge	discontinua tion visit
consent	X					
review history/AE's	X	X	X	X	X	X
urine HCG (prior to challenge and MCC)	X			X		
vital signs	X	X	X	X	X	X
spirometry	X	X	X	X	X	X
physical exam	X		X			
Xenon equilibrium scan	X					
MCC*	X			X		
follow-up scan		X			X	
sputum induction		X			X	
symptom score	X	X	X	X	X	X
allergen challenge				X		
overnight in GCRC				X		
24 hrs post sputum phone follow-up		X			X	
Venipuncture	X			X	X	
Exhaled nitric oxide		X			X	

\*MCC: mucociliary clearance measurements

**Additional information regarding procedures and measurements to be performed****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. We will be using the standard method recommended by the American Thoracic Society guidelines for measurement of spirometry throughout this study.

**Sputum induction:**

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. 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 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 FEV<sub>1</sub> drops 20% or more from your baseline, we will stop the procedure.

Allergen challenge procedure:

Your baseline lung function will be evaluated with spirometry testing to be sure it is safe for you to undergo the allergen challenge procedure

Doses of *D. Farinae* extract will be administered from an ultrasonic nebulizer connected to a mouthpiece which will deliver the allergen solution as a fine mist. You will inhale 5 breaths from the nebulizer at each concentration starting with saline control (salt water at the same concentration found normally in the body). After administration of the saline, concentrations of allergen will be administered starting with solutions of 0.25, 0.50, 1.0, 2.0, 4.0, 8.0, 16, 32, 64, 125, 250, 500, 1000, and 2000 AU/ml using the nebulizer. During the inhalation challenge you will be under direct observation of a physician experienced in treating asthma. The challenges will be performed in either the UNC General Clinical Research Center (GCRC) or the Pulmonary Function Laboratory of UNC Hospitals. Full emergency equipment and nursing personnel are immediately available at both locations.

The FEV<sub>1</sub> (the volume of air you forcibly exhale in the first second during spirometry evaluations) will be measured prior to and 10 minutes after each dose of allergen extract is inhaled. Starting with the saline solution, increasing concentrations allergen will be inhaled at 10 minute intervals starting with 0.25 AU/ml. The FEV<sub>1</sub> prior to the first dose of antigen will be considered the baseline value. If the FEV<sub>1</sub> has declined by less than 10% after a given concentration of allergen has been inhaled, the next higher concentration will be given. If the decline in FEV<sub>1</sub> is between 10% and 15%, spirometry will be repeated each 5 minutes for 15 minutes or until a clear low point (nadir) has been reached. If the nadir after 15 minutes is a decline in FEV<sub>1</sub> of less than a 10 %, the next higher concentration will be administered, and if it is a decline of 10-15%, the challenge will be stopped. Once the challenge is stopped, spirometry will be evaluated at pre-determined intervals for the next 6 hours. Oxygen saturation by pulse oximeter will be also be measured during the challenge. Continued monitoring of your lung function will be done during your overnight stay in the GCRC using a peak flow meter or portable hand-held spirometer. The physician responsible for the study will determine if any medication is necessary based on your lung function and symptoms.

Xenon and Mucociliary Clearance scans:

You will sit in front of the gamma camera to get a baseline measurement of the background radiation. You will inhale a small amount of radioactive xenon gas through a breathing circuit until the amount of xenon in your lungs is stable. This should take about 5 minutes. Then you will inhale an amount of radioactive particles, and sit in front of the camera for about 2 hours. This allows us to see how the mucus in your lungs moves out of the airway. You will need to return the day after this test for approximately 1/2 hour for a repeat scan.

Venipuncture (Blood draw):

Blood will be drawn to evaluate cell surface markers (such as those related to inflammation) and also to determine what genes may play a role in a person's response to allergen challenge. Using a small needle, blood will be drawn from a vein in your arm or hand. At the time of each venipuncture, up to 30 cc (2 tablespoons) will be drawn and the total for the study will be less

than 100 cc (less than ½ cup). In comparison, at the time of a typical Red Cross blood donation, approximately 500 cc is drawn.

*Exhaled nitric oxide measurement:*

We will measure the amount of nitric oxide (NO) present in orally expired air (air which you breathe out normally). An increased concentration of NO in exhaled air may be found in normal persons with acute inflammation. Thus, measurement of the concentration of NO in expired air may be useful as an indirect assessment of airway inflammation. Lung production of NO will be measured by asking you to exhale for briefly into a mouthpiece.

*Excess sample storage:*

Sputum samples that are left over from this investigation will be stored in the UNC Center for Environmental Medicine, Asthma and Lung Biology (CEMALB) repository indefinitely to possibly be used in research studies not yet known. You will be asked to review and sign 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.

**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 a better understanding of the effect of exposure to dust mites on your lung function.

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

*Spirometry and Sputum induction*

Multiple spirometry testing attempts and sputum induction may cause cough wheezing or chest tightness in susceptible individuals. A physician is immediately available and rescue albuterol is on hand if needed. Prior to sputum induction you will receive 2 puffs of albuterol to decrease the risk of bronchoconstriction with this procedure. You will be carefully monitored with pulmonary function testing to ensure a return to baseline prior to your discharge from the CEMALB. Coughing and on rare occasion, fever or infection has been associated with induced sputum collection.

*Allergen challenge:*

At the doses proposed in this study, the most significant predictable risk as a result of allergen inhalation is development of immediate airway obstruction (bronchospasm), which would cause shortness of breath, cough or wheeze. This drop in FEV<sub>1</sub> should be short lived, reversible with medications such as beta agonists (albuterol) and is the primary endpoint of the study. This effect is similar to the effect of methacholine you experienced during the separate screening protocol (98-CEMLB-293) which you previously completed since both allergen challenge and methacholine result in constriction (narrowing) of the airways as measured by your drop in FEV<sub>1</sub>. Other possible risks include development of a late phase airway response to allergen inhalation. This occurs in approximately 30% of asthmatics challenged and is characterized by more typically encountered at much higher doses, include development of systemic symptoms, including headache, fever, chills, fatigue, malaise and “flu-like” symptoms. During the inhalation challenge you will be under direct observation of a physician experienced in treating asthma. Epinephrine and diphenhydramine hydrochloride (Benadryl®) for intramuscular

administration and albuterol for inhalation will be immediately available. The challenges will be performed in either the UNC General Clinical Research Center (GCRC) or the Pulmonary Function Laboratory of UNC Hospitals. Full emergency equipment and nursing personnel are immediately available at both locations. Since a late phase response may be possible, you will be monitored overnight in the GCRC after the challenge, and additional spirometric and/or peak flow measurements will be performed during your GCRC stay. The physician responsible for the study will determine if any medication is necessary based on your lung function and symptoms.

*Xenon and Mucociliary Clearance scans:*

The lung scan, and lung clearance studies (2) all entail exposure to some radiation. Since radiation can be especially harmful to a developing fetus, it is important that pregnancy be avoided during this study by using effective birth control measures (either hormonal contraceptives, like birth control pills; or a barrier method, like condoms). The radiation dose you will receive in this study is 90 mRem. This dose is 25% of the amount of radiation you would normally receive from your usual environment in one year. You must inform one of the investigators if you have had any x-rays or other radiation exposure within the past year so that we do not exceed the yearly dose limits. If you wish, Dr. Bennett will provide you with additional information and answer any questions you may have. If desired, additional information can be obtained from Marija Ivanovic, Ph.D, Chairman of the Radiation Safety Subcommittee of UNC Hospitals at 843-0717. Although it is best to avoid radiation exposure, this is a small amount of radiation and is considered acceptable to experience on a limited basis. You should take this information into consideration when agreeing to participate in this study and any future studies and avoid radiation doses of a comparable magnitude within the next 12 months unless there is a diagnostic or therapeutic necessity.

*Drawing blood (Venipuncture):*

Venipuncture may cause brief discomfort and carries a risk of developing a bruise, hematoma (collection of blood under the skin) or, very rarely, infection. Some individuals may feel lightheaded or even faint with this procedure and subjects with a history of fainting during venipuncture will not be enrolled in this study. This procedure will be performed only by trained staff members.

*Exhaled nitric oxide measurement:*

There is no risk to this measurement since you are simply asked to exhale into a mouthpiece.

*What are the risks to a pregnancy or to a nursing child?*

Since there is potential substantial risk from radiation exposure of babies before they are born, if you are a female of child-bearing potential, you will undergo urine testing for pregnancy within 48 hours prior to administration of any radioactive substances used during the Xenon and MCC scans.

We do not know the effect of the study drug on babies before they are born, or on nursing children. For this reason, female subjects of child-bearing potential will also undergo urine pregnancy testing within 48 hours prior to the allergen challenge. 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 participate in this study if you are breast feeding your child. Pregnancy tests will be done on all women who might be able to get pregnant as indicated above and the cost of these urine tests will be paid for by study funds. 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.

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?**

Risks to subject confidentiality will be minimized by storing records with personal identifiers in an office in CEMALB which is locked when unattended by the study coordinators. Records will be kept for at least 2 years after completion of data collection. All samples will be stored with codes only (no personal identifiers). The CEMALB is located in the US Environmental Protection Agency's Human Studies Facility on the UNC campus which has a security guard and limited access 24 hours/day, 7 days/week.

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?**

The total payment for completion of all study visits will be \$750 and will be divided as follows:

Baseline visit	\$125
24 hours post baseline visit	\$75
Pre challenge visit	\$25
Challenge Day/GCRC stay	\$350
24 hours post challenge visit	\$100
Discontinuation visit	\$25
<u>Completion bonus</u>	<u>\$50</u>

TOTAL \$750

Payment will be prorated for completed visits if you withdraw or if the study physician withdraws you for medical reasons. If you arrive at the study site for any scheduled session that is subsequently canceled, but can be rescheduled, such as for weather, equipment or staffing problems, you will be compensated a flat fee of \$50.00. However, in the event you arrive for the challenge day and the challenge is canceled by the study staff, you will be paid for the challenge day and the GCRC stay. Snacks (juice and crackers or granola bars) will be provided for subjects after sputum inductions. Parking vouchers will also be provided.

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

There will be no costs to you for participating

**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 National Institutes of Health. 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.

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**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