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University of North Carolina at Chapel Hill
Consent for Genotype Screening With Identifying Information

IRB Study #06-0548
Consent Form Version Date: September 10, 2009

Title of Study: Mechanisms by which air pollution particles exacerbate asthma in older adults with mild asthma

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EX.6

Funding Source: US Environmental Protection Agency

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What are some general things you should know about this research study?

Research studies are designed to gain scientific information 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.

Research with blood, tissue and/or body fluids (specimens) can help researchers understand how the human body works. Research using specimens can also answer other questions. Many different kinds of studies use specimens. Some researchers may develop new tests to find diseases. Others may develop new ways to treat diseases. In the future, some research may help to develop new products, such as drugs.

You may refuse to allow us to have or store your specimen. If you are a patient with an illness, you do not have to be in the research study in order to receive treatment.

Details are discussed below. It is important that you understand this information so that you can make an informed choice. 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.

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What is the purpose of this study?
Recent reports have suggested that people with a particular gene, known as the GSTM1-null gene, are more susceptible to air pollutants such as diesel exhaust. The purpose of this screening session is to determine your genotype for the GSTM1 gene. We are recruiting equal numbers of GSTM1-null and GSTM1-sufficient subjects for each group of the main study. In the main study, we will look at the cardiovascular and respiratory effects of breathing air pollution particles in older subjects with asthma, and to see if there are differences in those who are GSTM1 null and those that are GSTM1-sufficient.

How many subjects will participate in this study?
If you participate, you will be one of approximately 32 subjects who will complete the study.

How long will your participation last?
Participation in this genetic screening session of the study will last for approximately 30 minutes.

What will happen if you participate in this study?
We will briefly review your medical history and any medical conditions that you have or medications that you are currently taking. You will sign 2 copies of the study consent form. We will measure your vital signs and draw about 50 ml of blood for genotyping and blood analysis. If you are re-contacted from a previous study, you will not need genotype screening but you will need to get blood drawn for other blood analysis. At the end, we will give you a copy of the Medical History Form and please hold the form until you hear from us that you are qualified for the study, and then fill it out and mail it back to the Westat recruitment office.

How will the blood sample be collected?
You will have about 50 ml (about 3 1/3 tablespoon) of blood taken by our trained nursing staff.

What will happen to the blood?
The blood sample collected will be used to look at the GSTM1 gene. If there are excess samples left over after use for the purposes of this specific study, they will be stored at the U.S. Environmental Protection Agency Human Studies Facility located in Chapel Hill North Carolina. Only project members of the study will have access to the samples.

During the course of this research, other researchers may request access to specimens for as-of-yet unspecified research that may or may not be related to the original research from which the specimens were derived. In these cases, provided appropriate IRB approved consent has been obtained from subjects, these specimens will be provided without identifiers to these other researchers by employing a data use agreement.

Are there any reasons you should not participate?
You should not participate in this portion of the study if you are not a candidate for the subsequent portions. The inclusion and exclusion criteria will be described.

You should have mild asthma, and you asthma symptoms should be well-controlled on current medications.

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You cannot be in this study if you have been diagnosed as a moderate to severe asthmatic as defined by physician-directed emergency treatment for an asthma exacerbation within the preceding 12 months, use of systemic steroid therapy within the preceding 12 months, nighttime symptoms of cough or wheeze greater than 2 times per month, asthma symptoms (cough, wheeze, chest tightness) more than 2 times per week, requirement for albuterol due to asthma symptoms more than 2 times per week, (not including prophylactic use of albuterol prior to exercise), have chronic, continuous allergic rhinitis.

You should not have chronic diseases including diabetes, need for a heart pacemaker, a previous chest pain and heart attack or coronary bypass surgery and uncontrolled high blood pressure. You need to be non-smoker for at least 1 year prior to the study or smoked no greater than 5 packs during your life. The investigators and medical staff will explain other potential exclusionary conditions in detail to you.

You should not participate if you are unable to comply with the following requirements:

- No over the counter pain medications such as aspirin (aspirin $\leq$ 81 mg/day is allowed), Advil, Aleve or other non-steroidal anti-inflammatory medications for 7 days prior to all visits. Tylenol (acetaminophen) is permitted.
- No vitamin C or E (or multivitamins which contain Vitamins C or E) for 7 days prior to all visits.
- Avoid smoke and fumes for 24 hours before all visits.
- Avoid drinking alcohol 24 hours before all visits.
- Avoid strenuous exercise for 24 hours prior to and after all visits.
- Avoid use of antihistamines for one week prior to exposures.

You should not be in this study if you're pregnant or planning to get pregnant during the time you would be in the study, nor should you breast feed your child while being in this study. If you or your partner becomes pregnant during the study you should notify the researcher right away.

What are the possible benefits to you?

There are no direct benefits to you for completing this portion of the study. However, you will know your blood cholesterol levels and you will know your genotype of GSTM1 gene and this information will determine if you will be qualified for the further air pollution exposure study.

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

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

1. The risks associated with taking blood samples are considered minimal. A well-trained member of the staff will draw the blood. Drawing blood could cause some bruising or minor pain, which usually resolves quickly. Also, a rare complication is skin infection or an infection of the vein in which the blood has been drawn. The risk of getting and infection is minimized by the use of sterile technique. If you do have signs of infection ant the site (redness, warmth, painful skin, and swelling) after completion of the procedure, you will need to contact the EPA medical station.

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2. Risk of breach of confidentiality is minimal. You will be assigned a study number which will be used for data – not your name. The study number is all that will be entered into computer databases. All paper files which may contain your name or screening number are secure in the EPA building which has limited access 24 hours/day. A numeric coding system will be used to ensure that you cannot be directly identified from the samples alone.

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

Will there be any cost to you to participate?
The U.S. EPA will pay the costs of this research. You will not be billed for any procedures.

Will you receive anything for being in this study?
You will be paid $30 for completing this screening procedure. We will give you parking coupons to cover the cost of parking. If you live more than 30 miles outside of the Chapel Hill/Carrboro area, you will be reimbursed for mileage at the current government rate. Money received by participants in research studies is normally treated as ordinary income by taxing authorities and we will report payments made to you to the Internal Revenue Service as required by law.

Who owns the blood samples?
Any blood samples obtained for the purpose of this study become the exclusive property of The U.S. Environmental Protection Agency. The researchers may retain, preserve or dispose of these specimens and may use these specimens for research that may result in commercial applications. There are no plans to compensate you for any future commercial use of these specimens.

How will your privacy be protected?
You will be given a study code number. All electronic documents will only have that number. The paper records that the coordinators and medical doctors use may have your name. Your information can be linked to your personal information by the study number, however only study personnel have access to your personal information. Paper records which use your name are kept in a locked file cabinet in the EPA Medical Station of the Human Studies Facility. The Medical Station is locked when not attended by study staff, and the EPA Human Studies Facility has limited access to authorized individuals only, 24 hours/day for 7 days/week. Samples used for genetic analysis will be stored at the EPA Human Studies Facility.

Research studies may be done at many places at the same time. Your personal identifying information will not be sent to outside researchers.

No one 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

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reviewed by representatives of the University, research sponsors, or government agencies for purposes such as quality control or safety.

Will researchers seek approval from you to do future studies involving the blood samples?
By signing this consent form, you are giving your permission for researchers to use your specimens as described above. Current and future research is overseen by a committee called the Institutional Review Board (IRB). The role of the IRB is to protect the rights and welfare of research participants.

In some cases, the IRB may require that you be re-contacted and asked for your consent to use your specimens in a specific research study. You have the right, at that future time, not to participate in any research study for which your consent is sought. Refusal to participate will not affect your medical care or result in loss of benefits to which you are entitled.

Will you receive study results of future research involving your blood samples?
Most research with your specimens is not expected to yield new information that would be meaningful to share with you individually. In rare cases, you may be offered the opportunity to receive information about the results of research in which the specimens were used (for example, findings that would affect your medical care).

Can you withdraw the blood samples from the research study?
If you decide that you no longer wish for the specimens to be stored, you should contact the researchers on the front page of this form. You may also contact the Institutional Review Board, University of North Carolina at Chapel Hill, 919-966-3113, Medical School Building 52, CB 7097, Chapel Hill, NC 27599, or by email at IRB_subjects@unc.edu. It is best to make your request in writing.

Any analysis in progress at the time of your request or already performed prior to your request being received by the researcher will continue to be used as part of the research study. Once the researchers have been notified, your specimens would be destroyed. If you do not make such a request, the specimens may be stored forever. The researchers may choose to destroy the specimens at any time.

What will happen if you are injured by this research?
All forms of medical research, diagnosis, and treatment involve some risk of injury or illness. Despite our high level of precaution, you may develop an injury or illness due to participating in this study. If you develop an injury or illness determined by the on duty physician to be due to your participation in this research, the EPA will reimburse your medical expenses to treat the injury or illness up to $5000. If you believe your injury or illness was due to a lack of reasonable care or other negligent action, you have the right to pursue legal remedy. The Federal Tort Claims Act, 28 U.S.C. 2671 et. seq., provides for money damages against the United Sates when personal injury or property loss results from the negligent or wrongful act or omission of any employee of the EPA while acting within the scope of his or her employment. Signing this consent form does not waive any of your legal rights or release the investigator, the sponsor, the institution, or its agents from liability for negligence. If a research related injury or illness occurs, you should contact the Director of the EPA NHEERL Human Research Protocol Office at 919.966.6217.

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Who is sponsoring this study?
This research is funded by The U.S. Environmental Protection Agency. 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, you should contact the researchers listed on the first page of this form or the EPA Director of the National Health and Environmental Effects Human Research Laboratory Protocol Office at 919-966-6217.

What if you have questions about your rights as a research subject?
All research on human subjects 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 and/or the EPA Director of the National Health and Environmental Effects Human Research Laboratory Protocol Office at 919-966-6217.

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Principle investigator: Martha Sue Carraway, MD

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

Initial/Date _____