TEMPLATE

INFORMED CONSENT FORM FOR RESEARCH WITH HUMAN SUBJECTS

Protocol Title: Genetic Epidemiology of Chronic Obstructive Pulmonary Disease: The COPDGene® Study

Principal Investigator: _____

Introduction

You are being invited to participate in a research study. Research studies include only people who choose to take part. Please take your time making a decision and feel free to discuss it with your friends and family. Before agreeing to take part in this research study, it is important that you read this consent form because it describes the study and any risks that it may involve. It is important that you understand that no guarantees or promises can be made regarding the results of the study. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand.

Why is this study being done?

You are being invited to take part in a research study of chronic obstructive pulmonary disease (COPD). Millions of Americans have this condition. Smoking is the number one risk factor for the development of COPD, yet only a minority of smokers gets COPD. The factors that distinguish the smokers who get COPD from those who do not are not known. Some people may develop COPD because their genetic make-up makes them either more or less susceptible to the effects of cigarette smoke. **The purpose of this study is to discover genetic factors that might predict who will develop COPD.** We will also assess genetic factors that are associated with other smoking-related disorders such as cancer and heart/vascular disease. The findings in this study are considered research and are not the same as "genetic testing."

Up to_____ people will be enrolling in this study at _____ _____Center. A total of 12,000 people will be enrolled across all 21 centers in the US participating in this study.

You are being asked to be in the study because you are between 45 and 80 years of age. You may or may not be a smoker or have COPD.

What is involved in the study?

If you agree to take part in this study the research team will review this consent with you and ask you to sign it. You will have one to two visits for this study which will take a total of about four hours. However, if any of the tests need to be repeated because they were not completed or not done well enough, we may call you back for another visit. The following tests will be performed.

Questionnaires: You will be asked to complete a screening questionnaire to determine if you qualify for the study. This questionnaire asks about your lung and selected other medical conditions, lung surgery, smoking history, previous studies, recent surgery and hospitalizations, heart conditions, and your age, race and ethnicity. Only non-Hispanic Caucasian (White) and non-Hispanic African-American subjects can participate in this study. If you do not qualify for the study, you will not have any additional procedures.

If you meet the inclusion criteria for the study you will be given several questionnaires that will ask about symptoms of lung disease, shortness of breath, family history, medical conditions, medications you are taking, and health-related quality of life. Some of these questions are taken from standardized commonly used questionnaires. You will be asked to complete the questionnaires by yourself or the study coordinator will ask you the questions either on the computer or using a paper questionnaire. It will take between 45 and 90 minutes to complete all the questionnaires in this study.

You will be asked to provide your address, home and cell phone numbers, and email address. We will also collect this contact information on two other people you know well including one close relative not living with you; we need this information in case you move or change your phone number. We will not give this information to anyone else. We will ask you the name and address of your primary physician and pulmonary (lung) doctor so we can send them some of the results of this study that may be of medical importance to you. We will also collect your social security number (but not the social security numbers of your friends/relatives); this will be used to check your vital status in case we can not reach you or one of the other people you gave us.

You will be asked whether you have any relatives participating in this study. You may not participate if you have a relative in this study.

You will be asked if you are currently participating, expect to participate or have in the past participated in other research studies about lung disease. If you participated in other trials, we would like to obtain information about your results in the other studies to see if there is an association with those results and your genetic and other test results in the COPDGene® study.

If I have been or expect to be in other research studies, I **DO** give my permission to link the information from other studies to the genetic and other test results in this COPDGene® study:

☐ Initials _____

Blood Sample: About 8 teaspoons (1 teaspoon is the same as 5 ml) of blood will be removed by putting a needle into a vein in your arm or the back of your hand. This is the standard method used to obtain blood for testing.

Breathing Test (Spirometry): Spirometry is a breathing test that measures how much air you can blow out of your lungs and how fast you can blow out that air. You will be asked to forcefully blow into a lung testing machine. This test will be performed at least three times. After the test is done, you will be given an inhaled medication (albuterol) to open up your air passages. Twenty to thirty minutes after that medication, you will do spirometry again to measure your lung function. You will also be asked to breathe in and out normally and then take a slow deep breath in several times. Before you are given albuterol, you will be asked some questions to assure your safety when you take this medication and have the six-minute walk test.

Physical Assessment: Your blood pressure, height and weight will be obtained. A probe will be placed on your finger to measure your oxygen saturation and heart rate while you are resting and breathing room air. If you use oxygen, your oxygen will be removed for 10 minutes to check your oxygen level while you are breathing room air sitting and resting in a chair. If your oxygen level falls to 82% or less or if you become short of breath your oxygen will be replaced.

Six-Minute Walk Test: You will be asked to walk for 6 minutes on a level surface to see how far you can go. If you use oxygen when you walk, you will use it for this test.

High Resolution Chest CT Scan: You will have a chest CT scan. Before the CT scan, we will ask you about recent bronchodilator medication that you have taken. For the CT scan, you will lie on a table and the table will move through the middle of an x-ray machine that looks like a large round donut. You will be asked to lie quietly and take a deep breath in and hold it for the scan. Then you will be asked at the end of a normal breath to hold your breath for a second scan. The amount of radiation for the second scan is a quarter (25%) of the amount of radiation for the first scan. If you had a chest CT scan in the previous year and if that chest CT scan is of sufficient quality to measure the amount of emphysema you may have and measure the size of the air passages in your lungs, we may be able to use that chest CT scan; if so you will not have to have a new chest CT scan.

Pregnancy Test: Women who are pregnant are not eligible for this study. If you are capable of being pregnant, you will have a urine pregnancy test before the chest CT scan to be sure you are not pregnant.

Medical Record Review (performed only if you have COPD): The following test results will be obtained from your medical record if records are readily available: high resolution CT scan if done within the last year, pulmonary function tests including lung volumes and diffusing capacity, and oxygen level (arterial blood gas).

Follow-Up Contacts: We will contact you by regular mail, email, newsletter or telephone up to four times a year for the next ten years. We will ask about your health and whether you have changed your address or phone numbers, and we will mail you a newsletter about lung disease and progress in the COPDGene® Study. We may also contact you to invite you to participate in other research studies about lung disease in the next ten years. We plan to apply for additional funding in the future to follow you for a longer period of time. We will ask you if you want to be a part of future extensions of the COPDGene® study.

You will be encouraged to tell your friends and spouse who have a history of cigarette smoking about this study. You will be asked to give a brochure to your friends and ask them to contact us to enroll in the study.

What are the risks and discomforts of the study?

Risks of Blood Draws: Risks associated with drawing blood from your arm include some pain when the needle is inserted. There is a small risk of bruising and/or infection at the place where the needle entered your arm. Some people may experience lightheadedness, nausea or fainting. Treatment will be available if this occurs.

Risks of Breathing Tests: You may become short of breath or experience chest tightness while doing the pulmonary function test (spirometry). Occasionally after using the albuterol inhaler a temporary sensation of "heart racing" and shakiness may develop. Treatment will be available if this occurs.

Risks of Stopping Your Oxygen: You may become short of breath when your oxygen is temporarily stopped. We will monitor the oxygen level in your finger and if it gets too low or you get short of breath, your oxygen will be restarted.

Risks of Six-Minute Walk Test: You may become short of breath or experience chest tightness while doing the walking test. Treatment will be available if this occurs. There is a small risk of abnormal blood pressure (up or down), fainting, disorders of the heartbeat (too fast, too slow, or irregular), and heart attack. To reduce the risk of these complications, you will be asked questions about your medications, medical condition, and potential heart problems before the walk test.

Risks of Chest CT Scan: You will be exposed to radiation. The maximum amount of radiation exposure during the chest CT scan is approximately 10 mSv. The average amount of background doses of radiation that the general population is exposed to in the United States is 3 mSv per year. Thus, the maximum amount of radiation you will receive is equivalent to about three years of normal background radiation. The more radiation received over the course of a life, the greater risk of having cancerous tumors or of inducing changes in genes. The changes in genes possibly could cause abnormalities or disease in your future offspring. The radiation in this study is not expected to greatly increase these risks, but the exact increase in such risks is not known. You will be asked questions to determine if you might be pregnant. If you might be pregnant, we will check your urine to make sure you are not pregnant. Women who are pregnant may not participate in the study.

The chest CT scan can provide important clinical information such as the presence of lung nodules, which may require additional medical testing. The investigators in this study would like to send the results of your chest CT scan to your personal physician as well as to you. Please indicate if you do NOT want us to send the results to your doctor.

I **DO NOT** give permission for the investigators in this study to send results of my chest CT scan to my personal physician. I understand that I will assume responsibility for any

medical follow-up which may be required as a result of my chest CT scan, including pulmonary nodules that could represent a lung cancer.

☐ Initials _____

Risks of Research: This study will provide genetic information about your genetic material (DNA). DNA isolated from your blood will be shared with other scientists who work with DNA. These investigators will not be provided with any information that can identify the DNA as yours. The test results from this study are not known to have any clinical significance at this time, and we will not tell you or any other individual about your specific genetic results.

In this study we will analyze your blood samples for a gene called alpha 1-antitrypsin. People that inherit a gene associated with a low level of alpha 1-antitrypsin are more likely to develop COPD. We will perform analysis of all blood samples for alpha 1-antitrypsin, but it will be done in a research laboratory rather than an approved clinical laboratory. Therefore, any abnormal results would need to be confirmed in a clinical laboratory. However, if you would like to know if it is abnormal in our research laboratory, please check the box on the consent form below. This test may not be available until several years after your blood is drawn.

Would you like to be informed about any abnormal alpha 1-antitrypsin results?

☐ Yes ☐ No Initials _____

I understand that by signing this consent I agree that my blood sample will be stored in the COPDGene® Study central repository indefinitely for use by study investigators in studies of COPD and other smoking-related disorders. In addition, other medical information collected for this study including questionnaires, breathing tests, six-minute walk test and chest CT scan will also be stored for future analysis. As required by the terms this study, my blood samples and medical information will become an important national resource for genetic and other studies of COPD and other smoking-related disorders. My genetic data will be shared with other investigators for similar studies, but no one will be permitted to release specific information about me. The use of my blood sample and medical information and tests will be monitored and shared only with investigators who agree to maintain confidentiality and respect my privacy. My personal information will not be available to other investigators when sharing my blood sample and medical information and tests. However, a possible risk of study participation is the loss of confidentiality about your medical information.

The blood samples and other study information and tests taken from you may be used for the development of one or more research, diagnostic, or therapeutic products. Blood provided by you during the course of the study may be valuable for scientific research, or testing purposes for development of a new product that may be distributed commercially. You are not entitled to any financial compensation should this occur. By signing this consent form, you authorize

_____ Center, members of its Professional Staff and other study investigators to use your blood for these purposes.

Although the primary focus of this research project is COPD and other smoking-related disorders, the samples and other study information and tests collected during this study could also be useful for research into a variety of other health problems. We will only use your blood samples, other study information and tests for research into these other health problems if you give your permission below.

I give permission for my blood to be used for research about other health problems (for example, causes of diabetes, Alzheimer's disease, etc).

☐ Yes ☐ No Initials _____

What will happen if I am injured in this study?

In the event of an injury or illness resulting from your participation in this research study, your study doctor will assist you in receiving appropriate health care, including first aid, emergency treatment and follow-up care either at _____ Center or another appropriate health care facility. If medical costs are incurred, your insurance company may be billed. In accordance with general policy, _____ Center makes no commitment to provide free medical care or other compensation for injury or illness resulting from your participation in this study. By signing this form you have not given up your legal rights. For further information, please contact Dr. _____ (____-____-_____), the Principal Investigator of this study.

If you believe you have experienced any study related illness, adverse event, or injury, you must notify the study doctor as soon as possible.

☐ This has been explained to me and all my questions have been answered.
Initials _____

Are there benefits to taking part in this study?

There will be no direct medical benefit to you for taking part in this study. This study is not designed to treat any illness or to improve your health.

What other options are there?

You have the option not to take part in this study. The study physician may be both your health care provider and the investigator for this study. This doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study, or at any time during the

research, you may ask for a second opinion about your care from another doctor who is not associated in any way with this study.

Who is paying for this study?

_____ Center and Dr. _____ are receiving funding from the National Institutes of Health to carry out this study.

What are my costs?

There are no costs to you or your insurance company for participating in this study. You will be responsible for the costs of your lodging, meals, and travel to the Medical Center.

Will I be paid to participate in this study?

You will be compensated for your time and expense for participating in this study. You will be reimbursed $75 for your time and expenses associated with the study visits for taking part in this research study if you complete the breathing test, questionnaires, physical examination, six-minute walk test, chest CT scan, medical record review, and donate blood.

What if I want to withdraw, or am asked to withdraw from this study?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in the study, your doctor will still take care of you. You will not lose any benefits or medical care to which you are entitled.

If you choose to take part, you have the right to stop at any time. However, we encourage you to talk to a member of the research staff so that they know why you are leaving the study. If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

The study doctor may decide to stop your participation without your permission if he or she thinks that being in the study may cause you harm, if you are unable to follow the study schedule, or if funding for this project ends. The sponsor may also stop the study at any time.

Who do I call if I have questions or problems?

You may ask any questions you have now. If you have questions later, you may contact _____ at (____) ____-_____ or Dr. _____ at (____) ____-_____.

If you have questions or concerns during your participation as a research subject, please call the Institutional Review Board (IRB) at _____ at (____) ____-_____.

What about confidentiality?

Sample and Medical Information and Test Storage
Information obtained as a result of participation in this study that can be identified with you will remain strictly confidential. Your medical information, tests and blood sample will be assigned a unique letter and number code that can not be used to identify you. Research often involves the use of stored human samples or data. Your samples and medical information will be stored indefinitely without any personal identifiers in the central laboratory. The intended long-term use will be to look for new markers in genes and proteins based on future research. Your study test results may be shared with other investigators that agree to preserve the confidentiality of these test results. No identifying information will be shared with other investigators. Your coded medical information and information from more detailed analysis of your coded samples will be put in a controlled-access database. The information in this database will be available only to researchers who have received approval from an NIH Data Access Committee or the COPDGene® Executive Committee. Genetic test results will not be stored in your medical charts. Your samples and medical information and tests will not be labeled with any information that would readily identify you, and this will minimize the risk that your genetic and medical information might be used inappropriately.

In this research study, we have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). By granting this Certificate, DHHS is not approving the research itself, but is helping us strengthen the privacy protections for your health information and other identifying information from the research. With the Certificate, we cannot be forced (for example by court order or subpoena) to disclose your health information or other identifying information from the research in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings. (Note that information that is not from this research, such as existing hospital or office health records, is protected by general privacy law but does not receive the Certificate's stronger protection. The Certificate also does not prevent you or a member of your family from voluntarily releasing any information about yourself or your involvement in this research study.)

As part of the responsibility to ensure that clinical studies are carried out in accordance with internationally agreed standards, representatives of government agencies such as the Food and Drug Administration, or the Institutional Review Board may require access to the records. Your medical information will be kept as confidential as possible in accordance with local, state and federal law.

If you agree to donate a sample of your blood, the DNA sample will be identified by a code that will link it to information about your other study-related measurements. If you donate blood and then change your mind, this code will be used to track and destroy the samples. Otherwise, the samples will be stored indefinitely for future studies on COPD, or for future studies of other diseases. The samples and other medical information and tests may be shared with other investigators inside or outside _____ Center; however, all identifying information that may link the samples and other study information and tests to you will be removed. If you choose to withdraw from the study in the future, it may not be possible to

remove your previously generated study information from the controlled-access data repository. Study information and DNA may move with the principal investigator if relocated in order to continue research in this area.

Personal and Medical Information
Efforts will be made to keep your information confidential. Your personal and medical information may be disclosed if required by law. Organizations that may inspect and/or copy your research and medical records for quality assurance and data analysis include, but are not necessarily limited to:

- The National Institutes of Health or other government agencies
- The Food and Drug Administration
- Department of Health and Human Services
- The Medical Center Institutional Review Board

Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. The results of this research study may be presented at meetings or in publications; however, your identity will not be disclosed in those presentations.

Authorization

I have read and initialed each page of this paper about the study (or it was read to me). I understand the possible risk and benefits of this study. I know that being in this study is voluntary. I choose to be in this study. I know I can stop being in this study and I will still get the usual medical care. I will get a copy of this consent form.

Signature of Participant	Date	Printed Name of Participant
Signature of Person Obtaining Consent	Date	Printed Name of Person Obtaining Consent