

TEMPLATE

INFORMED CONSENT FORM FOR RESEARCH WITH HUMAN SUBJECTS

Protocol Title: Genetic Epidemiology of Chronic Obstructive Pulmonary Disease:
The COPDGene® Study: Phase 2

Study Sponsor: US National Heart, Lung, and Blood Institute

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 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 the second phase of the COPDGene® Study. The purpose of this second phase is to learn more about chronic obstructive pulmonary disease (COPD) and how it may progress over time. The additional information obtained during this second phase of the study may help us classify subtypes of COPD and may identify new markers that influence the development of COPD. We will also assess genetic factors that are associated with other smoking-related disorders such as cancer and heart/vascular disease and other diseases not related to cigarette smoking. 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 10,364 people were previously enrolled across all 21 centers in the US participating in this study.

You are being asked to be in the study because you previously participated in the COPDGene study.

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 six 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 information and tests will be collected.

Contact and Personal Information:

You will be asked to provide or update your address, home and cell phone numbers, and email address. We will also collect this contact information on two other people, one of whom is a next of kin, and the other a relative or close friend, one of whom is not living with you. We need this information to regain contact with you in case you move or change your phone number. You will be asked to designate one or more individuals as your next of kin or personal representative for us to contact in the event of your death. 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). We will provide you with a memo to share with these individuals that explains your involvement in the study and their participation. We strongly urge you to give a copy of the memo to your secondary contacts, next of kin and treating physicians.

Your name, address, phone numbers, next of kin and their contact information, and your social security number will be securely transmitted to the Data Coordinating Center at National Jewish Health, where it will be stored separately from the other data collected in the study. This information will be used to check your vital status using the Social Security Death Master File, National Death Index, general internet searches, and obituary postings, in case we can not reach you or one of the other people you gave us. These sources will be used to get your death certificate and medical records to determine why you died, and determine pollution and other environmental exposures that may have affected your lungs. We will also use the social security number to obtain information about your healthcare and costs of care from Medicare data.

If you die, we will conduct an interview with your next of kin, friend, personal representative and your personal physician, to determine the cause of your death. A committee of physicians will review this information and other medical information obtained about your death to determine the cause of your death. The members of this committee will not have any of your personal information.

You will be asked to sign a HIPAA authorization and release of medical records so we may contact doctors and hospitals that have provided medical care to obtain information about your medical condition and other medical problems you may have or develop in the future.

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.

Questionnaires:

You will be given several questionnaires that will ask about symptoms of lung disease including shortness of breath, family history, medical conditions, symptoms of anxiety and depression,

medications you are taking, your current and former address, economic issues that may impact care of your COPD, occupational history, menstrual history if you are a woman, exacerbations of your lung disease, and health-related quality of life. If you have a history of lung cancer, or are later diagnosed with lung cancer, you will be asked to complete a Lung Cancer Data Collection questionnaire to collect additional information about your lung cancer. 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 60 and 120 minutes to complete all the questionnaires in this study.

Blood Sample: About 3 and a third tablespoons (1 tablespoon is the same as 15 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. We may perform a whole genome analysis on your new or previously collected blood sample. Usually researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and used by researchers to study links to diseases.

Breathing Tests (Spirometry and Diffusing Capacity): 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 to get reproducible results. After the test is done, you will be given an inhaled medication (albuterol) to open up your air passages. Twenty minutes after that medication, you will do spirometry again to measure your lung function. Before you are given albuterol, you will be asked some questions to assure your safety when you take this medication. We will also perform a diffusing capacity test that measures how well a test gas (small concentration of carbon monoxide) is transferred through your lungs and into your blood. For this test you will be asked to take a deep breath of the gas mixture, hold it in your lungs for 10 seconds, and then blow it out. You will perform this test at least two times to get reproducible results.

Physical Assessment: Your height, weight, arm span, and waist circumference will be obtained. Your blood pressure will be measured three times. A probe will be placed on your finger to measure the amount of oxygen in your blood 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. You will be asked some questions to assure your safety before performing this test. Immediately following and one minute after the six-minute walk test, your heart rate and oxygen saturation will be measured using a pulse oximeter.

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 your lung disease. 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.

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: The following test results may be obtained from your medical record if records are readily available: high resolution CT scan, pulmonary function tests including lung volumes and diffusing capacity, oxygen level (arterial blood gas), bone density test results, and medical information and pathological specimens for cancers you have had.

Health Care Utilization: Information regarding your health care utilization and costs, if you have Medicare, will be obtained from the Centers for Medicare and Medicaid Services (CMS) databases. Once we receive Medicare information, your identifying information will be removed.

Death Certificate Release: In the event of your death, your clinical center coordinator and/or the central study coordinator from National Jewish Health will obtain your Death Certificate from the State Office of Vital Statistics. Death Certificates will be used to gain information on the cause of death and these records will be held centrally at National Jewish Health.

Release of Medical Records: In the event of your death, medical records from treating physicians, hospitals, clinics and other medical facilities will be obtained and reviewed to determine the cause of death. Medical records from your treating physician(s) and hospital(s) will be stored centrally at National Jewish Health and at your local clinical center.

Informant Interview: In the event of your death, we will contact one of the people that you designated as your next of kin, close friend or personal representative and your treating physician for information about the events surrounding your death, including being contacted for an informant interview. Your treating physician will be contacted to obtain an interview and physician records related to the events and illnesses associated with the cause of death.

Disclosure of Participation in a Research Study: Your participation in the COPDGene research study will be disclosed to your designated next of kin, close friend and personal representative in the event of your death. Your participation in the COPDGene research study will be disclosed in the event that we are unable to contact you and/or in the event of your death. We will provide you with a memo to share with these individuals that explains your involvement in the study and their participation.

Follow-Up Contacts: We will continue to contact you by regular mail, email, or telephone up to four times per year for the next ten years. We will ask about your health and whether you have changed your address or phone numbers. We may also contact you at other times in the next ten years to invite you to participate in other research studies about lung disease and other diseases, and to update you about new findings in this COPDGene study and other COPD studies. 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.

Internet Search: Use of publicly available internet sources will be used in the event that we are unable to contact you and/or in the event of your death. Your study center coordinator and/or a central study coordinator from National Jewish Health will use the personal information you provided us to search for updated contact information (home addresses, phone numbers, and email addresses) only in the event that we are unable to contact you. Publicly available death records will be searched only in the event of your death or if death status is unknown.

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 tests (spirometry and diffusing capacity). 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 feel it is important to send the results of your chest CT scan to your personal physician as well as to you.

Risk of the Depression Questionnaire: This questionnaire may indicate that you may be depressed. If your responses to this questionnaire indicate you may be depressed, we will tell you and we will also send a letter informing your personal physician. You will be asked the name, address and phone number of your doctor so we may contact him/her.

Risks of Research: This study will provide information about your genetic material (DNA). DNA isolated from your blood and other blood samples will be shared with other scientists who work with DNA and other blood samples. These investigators will not be provided with any information that can identify the DNA or blood as yours. The blood and DNA 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.

I understand that by signing this consent I agree that my new and old blood samples will be stored in the COPDGene[®] Study central repositories at Brigham and Women's Hospital and Johns Hopkins University indefinitely for use by study investigators in studies of COPD and other medical problems. In addition, medical and other information collected for this study including questionnaires, breathing tests, six-minute walk test, addresses and chest CT scan will also be stored for future analysis. Your personal identifying information will not be given to other investigators. As required by the terms of this study funded by the National Institutes of Health, my blood samples and medical information will become an important national resource for genetic and other studies of COPD and other medical problems. Your genetic data will be shared with other investigators studying lung and other diseases, but no one will be permitted to publicly release information about your identity. The use of your blood samples, medical information and tests will be monitored and shared only with investigators who agree to maintain confidentiality and respect your privacy. Your identity will not be available to other investigators when sharing your blood samples 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.

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 cannot 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 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. 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 a National Institutes of Health Data Access Committee for dbGaP (the Database of Phenotypes and Genotypes) or the COPDGene[®] Executive Committee. We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and whole genome information with these central repositories. However, we cannot predict how genetic information will be used in the future. Genetic test results will not be stored in your clinical medical records. 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. Research using your samples and whole genome information is important for the study of virtually all diseases and conditions. Therefore, the data repositories will provide study data for researchers working on lung and other diseases.

In this research study, we have obtained a Certificate of Confidentiality from the United States 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 and blood 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 the COPDGene Study and your local clinical center. 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.

Data Storage and Distribution

Your data and identifying information will be stored in the Data Coordinating Center (DCC) at National Jewish Health in Denver. Study questionnaires, forms, test results, and your contact information will be stored both at your local clinical center and in the DCC. The DCC will transfer de-identified subject data to the National Institutes of Health controlled database (dbGaP). dbGaP provides storage, oversight, and a process for distribution of results of studies, including COPDGene, to the scientific community.

The COPDGene Study has twenty-one participating clinical centers that conduct study visits on COPDGene participants. There are ten study cores, which collect, store, analyze and interpret the data collected from COPDGene participants. The cores include:

- Administrative at National Jewish Health, Brigham and Women's Hospital
- Imaging at National Jewish Health, University of Iowa, and Brigham Women's Hospital
- Pulmonary Function Testing (PFT) /Breathing Tests at National Jewish Health, University of Utah
- Biorepository at Brigham and Women's Hospital, Channing Division of Network Medicine
- Genetic Analysis at Harvard School of Public Health, Johns Hopkins University, and University of Colorado, Denver
- Sequencing and Bioinformatics at Brigham and Women's Hospital, Channing Division Network of Medicine, and Johns Hopkins University
- Subtyping at Harvard School of Public Health, Northeastern University and COPDGene Investigators
- Mortality Adjudication at National Jewish Health
- Epidemiology at University of Colorado, Denver

Your blood samples will be stored in the Biorepository at Brigham and Women's Hospital, Channing Division of Network Medicine, and National Jewish Health

Your CT scans will be sent to the Imaging Core at National Jewish Health.

Your breathing test results will be sent to the PFT Core at National Jewish Health and the University of Utah.

Subtyping will be done at Northeastern University and Harvard School of Public Health

Genetic analysis will be done at Johns Hopkins University, Harvard School of Public Health and University of Colorado, Denver

Data from your questionnaires, breathing tests, CT scans, and blood samples may be shared with COPDGene investigators at the twenty-one clinical centers. This information will also be shared with other researchers for COPD approved ancillary studies. All investigators will have Institutional Review Board approval and will protect your identity. Your identity will not be disclosed in any scientific publication.

Study Data, Personal Identifiers and Other Medical Information To Be Used By the Study

My study data, personal identifiers and other medical information that may be used to conduct this research includes:

- Tests: pulmonary function tests, six-minute walk test, breathing tests, and physical assessments
- Blood samples
- CT scans
- Study Questionnaires
- Personal Identifiers: Name, social security number, current and previous addresses, phone number, date of birth, date of study tests
- Name and address of primary doctor
- Doctor/clinical records, Hospital medical records, laboratory tests, pathology results and specimens, and/ or radiology tests and results

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
- COPDGene Administrative Core
- COPDGene Data Coordinating Center

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