

Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT
Alpha-1 Clinical Resource Center Research Registry

If participants include those under 18 years of age: 1) The subject's parent or legal guardian will be present when the informed consent form is provided. 2) The subject will be able to participate only if the parent or legal guardian provides permission and the adolescent provides his/her assent. 3) In statements below, the word "you" refers to your child or adolescent who is being asked to participate in the study.

A. PURPOSE AND BACKGROUND

You are invited to participate in a research study called the Alpha-1 Foundation Clinical Resource Center (CRC) Research Registry because you have been diagnosed with severe deficiency or are a carrier of an abnormal alpha-1 antitrypsin (Alpha-1) gene. A Registry is a place where medical information, family history, blood and tissue samples and other related information from individuals is collected and stored for medical research.

The purpose of the Alpha-1 Foundation CRC Research Registry is to collect and store medical information from individuals with alpha-1 antitrypsin deficiency (AATD or Alpha-1) or who are a carrier of Alpha-1 (carrying one normal gene and one abnormal gene). There are many types of abnormal alpha-1 antitrypsin genes. The most common abnormal genes are called S and Z. Normal genes are called M. Alpha-1 deficient individuals produce a low level of a protein called alpha-1 antitrypsin (AAT). Normal AAT protects the lungs from damage. AAT deficiency may result in serious lung disease and/or liver disease.

If you join the Registry, you will be asked to provide medical information on your disease and diagnosis. The goal of the Registry is to share detailed medical and other information with researchers.

The investigator in charge of this study at the Medical University of South Carolina (MUSC) is Dr. Charlie Strange. Dr. Strange will receive grant money from the Alpha-1 Foundation to support the Registry. The study will use up to 20 centers at different sites with a goal of enrolling 5,000 participants. The information that you provide will be stored in the Registry and made available to researchers who are part of the Alpha-1 CRC Registry and to individuals including patients who have interest in Alpha-1. There will be 500 participants enrolled at MUSC.

B. PROCEDURES

If you join the Alpha-1 CRC Registry, the following procedures will occur:

Consent

You must sign this consent form to participate in this study.

Minors may be enrolled in the Registry with the consent of their parents or legal guardian. Parents or legal guardians must sign the questionnaire on behalf of their children. Upon reaching the age of 18 years, each minor will be given the opportunity to re-enroll in the Alpha-1 CRC Registry.

Once the consent form is signed and dated, it is scanned and submitted to the electronic database established for the study. This consent will reside on the computer servers at MUSC.

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Baseline Visit

As part of your enrollment, the study coordinator will collect medical information, family history and other related information for use in medical research. The study coordinator will also collect your social security number (SSN) in order to query death records. You will be asked about exposure to cigarette smoke and other dusts and fumes throughout your life. You will fill in questionnaires about your symptoms and quality of life. It is estimated that you will spend 30 minutes completing these questionnaires. Your answers will be reviewed by your study coordinators and physicians to assure the questions are answered as completely as possible. You should also bring information about your medical history including results of laboratory tests that show your Alpha-1 genes and/or level.

Blood Draw and Biorepository

The word that is used for samples of blood and other biologic materials collected with the goal of sharing them with other researchers is a biorepository. You will be asked to give a blood sample of 30 ml (2 tablespoons) of blood for research. At the biorepository your sample will be given an identifying code which links it to your data in the Registry. None of your identifying information will be kept with the sample although linkage will be preserved by your sample number. You will have the option to consent for the donated blood to be used for genetic studies. Although the blood sample will be stored at the Clinical Resource Center, research success often depends on sharing your blood sample with other researchers at other sites. You will be given the option later in this consent to allow moving your biorepository samples if another Alpha-1 biorepository is established. Individuals not donating blood or other biologic samples may still participate in the Registry.

Your study coordinator will discuss if past blood samples or other biologic samples collected from another research protocol may be linked with your Registry number. The presence of this sample will be communicated to other researchers to increase the chance that this sample will be used for research. You may choose to not link previous samples to the Registry.

One important goal of the Registry is to preserve linkage between your biologic samples and the clinical events that happen with your Alpha-1. In this way, the blood samples collected in the past can be useful for researchers asking important questions about your Alpha-1 today. Therefore, you are being asked to allow use of these samples until the samples are used up, even if this occurs after your death. Samples will be sent to researchers coded with the identifying number, but not with your name. If you change your mind, you may choose to have your biorepository specimens removed from the Registry at any time prior to the sample being analyzed or sent to another researcher.

Samples stored in the Alpha-1 MUSC biorepository will have security measures in place. Only the site investigator, study coordinator, and approved researchers will have access to your samples. Your samples may be used for future alpha-1 antitrypsin, COPD, or liver disease research without additional consent forms required. There are no plans to destroy samples at this time. Samples may be used after your death. Individuals will be informed of research results from their samples by general articles in the *Registry Update*, the Research Registry newsletter, although you will not be personally notified. If there is any research finding that generates commercial value, this consent waives control over sample data and you will not receive a portion of profits. You may choose to participate in the registry without biological materials being given.

Images

After you consent to be in the Alpha-1 CRC Registry you may be asked for previous CT scans or other images collected in studies or for clinical care. Any identifying information will be removed from these images and



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they will be linked to your unique study number and uploaded to the Alpha-1 CRC Research Registry. These images may be shared electronically with other researchers.

Information Updates

You will be asked to update your registry information intermittently. The registry will send you a reminder to do this. The registry may also ask you to fax medical results to a secure fax machine. Your registry account can be updated whenever there is a change in your health, change in Alpha-1 medications, or important new medical event such as hospitalization, transplantation, or death.

After you have enrolled in the Registry and your data has been collected at MUSC, the following may occur:

- You will be invited to visit MUSC for visits as long as you are willing to continue. You give permission to the CRC Registry Coordinating Center to inform a CRC if you choose to visit a CRC other than MUSC.
- Your CRC physician may suggest that you receive a yearly spirometry, other breathing tests, liver function tests, and/or imaging as a standard test. With your permission, data from these standard tests will be collected and stored in the Alpha-1 CRC Registry.
- You may be invited to participate in research studies from the Alpha-1 CRC Research Registry Coordinating Center. If this occurs, the Alpha-1 CRC Coordinating Center will inform MUSC of your enrollment. The invitation to participate in research will be shared with both MUSC and the Alpha-1 CRC Research Registry Coordinating Center. You will be contacted for these study opportunities by invitation letters, telephone calls, or emails sent by the Alpha-1 CRC Coordinating Center.. If you receive an invitation, you will have the opportunity to assess the study and contact the researcher if you are willing to participate. If you choose not to participate, you can simply disregard the invitation. No researcher except Dr. Strange or the Alpha-1 CRC Coordinating Center staff at MUSC will ever contact you directly, unless you have a previous patient/physician relationship with that individual.

Study invitations may be done specifically to your personal Alpha-1 characteristics. This is done by hiding the name, address and other “identifying” information from the researchers. We call this information “de-identified” because it has been removed of all personal identifiers. Your personal information will be labeled with a code number and stored in a secure place and protected with a password. Only authorized people who work in the registry will know the code and be able to identify you if needed. Your identifiable information will not be shared with anyone outside the registry (unless you give your permission to share it). Scientists, researchers, and clinicians, will be allowed to see only the de-identified information and may search the de-identified data for patients for their studies. If a patient looks like a good match for a study and a researcher wants to contact you, he can do it only through the Alpha-1 CRC Registry. The Alpha-1 CRC Registry staff will then contact you and invite you to contact the researcher.

- You will be invited to allow sharing of data collected during other research studies with the Alpha-1 CRC Registry. To share data collected in another research study, you will need to obtain your study identifying number from the other research study coordinator and provide it to the Alpha-1 CRC Registry staff.
- Your de-identified information (information that has been removed of all identifiers) may be shared with other databases such as the Global Rare Disease Patient Registry and Data Repository (GRDR) at the National Institute of Health (NIH). This database seeks to understand common aspects of many rare diseases.
- You will be invited to join the Chronic Obstructive Pulmonary Disease (COPD) Foundation Patient Powered Research Network (PPRN) Registry if you are an adult with COPD. The COPD PPRN Registry is funded by the National Patient-Centered Clinical Research Network or PCORnet. The COPD PPRN wants people with COPD to share their medical information for research purposes. The goal of the COPD PPRN registry is to compare COPD outcomes between patients. You will be asked later to share some identifying



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information with the COPD PPRN in order to link these registries. You may still enroll in the Alpha-1 CRC Registry without enrolling in the COPD PPRN Registry.

- You will get newsletters from the Registry.

You will be asked to sign a separate consent form to participate in the COPD PPRN Registry based on your selection below. Please initial one of the following options:

_____ I agree to share my protected health information and information collected by the CRC Registry with the Chronic Obstructive Pulmonary Disease (COPD) Foundation Patient Powered Research Network (PPRN) Registry.

_____ I do not agree to share my protected health information and information collected by the CRC Registry with the Chronic Obstructive Pulmonary Disease (COPD) Foundation Patient Powered Research Network (PPRN) Registry.

_____ I do not qualify to be a participant of the Chronic Obstructive Pulmonary Disease (COPD) Foundation Patient Powered Research Network (PPRN) Registry at this time since I do not have COPD.

C. DURATION

Participation in the Alpha-1 CRC Registry is for life. Should later versions of this consent form be modified, data and biorepository samples collected prior to new consent versions will remain in the Registry. The data collected during your life can be used after your death. You may choose to end enrollment in the Registry at any time by contacting the Registry staff.

D. RISKS/DISCOMFORTS

Risks fall into two major categories with this Registry.

The first category is the risk associated with the procedures done during your Registry visit. The second are the risks to confidentiality associated with collection and use of data and genetic samples.

Questionnaires

Answering questionnaires can cause fatigue. The registry includes questions that can be sensitive and you may feel uncomfortable answering. You may refuse to answer any questions.

Blood drawing

If you consent to have blood samples in the biorepository there are risks to collecting samples. The risks of drawing blood include temporary discomfort from the needle stick, bruising and infection. Fainting could occur.

Genetic Studies

There are risks to donating blood for genetic studies because your identity can be discovered. The genetic studies planned in this biorepository will include whole genome sequencing which can discover risks for other diseases. This risk is further described in the section called GENETIC SAMPLES below.

Confidentiality

There is a risk of loss of confidentiality in this study particularly if you agree to share your information with other groups. Although we have taken steps to protect confidentiality we cannot guarantee that your identity will not be known to others. If you have concerns about this, you should not agree to have your data shared. We will collect data that is linked to your identifying information. We will assign you with a study number and report study findings online in a way that will not identify you.



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Potential breaches in the computer system will be reported to all participants. Although every reasonable effort will be made to keep your identifying information confidential, there can be no guarantees that errors in protecting this information will not be made. If it became known that you have alpha-1 antitrypsin deficiency, there may be risks to you related to your employment, health, or life insurance.

Please select one of the following options:

I agree to have study data and biological materials from all past, current, and future research studies in which I have participated shared with the Alpha-1 CRC Registry to the extent to which this is possible. I agree to allow the study identifiers from each of these studies to be shared with the Alpha-1 CRC Registry.

I do not wish to share any study data or biological samples with the Alpha-1 CRC Registry.

E. BENEFITS

Participation is not expected to benefit you personally, medically or financially. However, it is hoped that the information gained from your clinical data (medical history, family history, questionnaires), imaging and biological samples will help in the treatment of future patients with conditions like yours and will help the researchers learn more about Alpha-1. Collected data may help speed up research. Researchers may learn whether/how treatments work. Medical professionals may be able to improve how they treat Alpha-1. Participants may receive information in a newsletter or in person about opportunities to participate in research and hear about medical advances.

F. COSTS

There is no cost to you to be a member of the Alpha-1 CRC Registry and have your blood drawn for the biorepository.

G. PAYMENT TO PARTICIPANTS

There is no compensation for joining the Alpha-1 CRC Registry. The Alpha-1 Foundation offers a program to help with the cost of visiting a CRC. If you have not previously used this program to visit a CRC, you may be eligible for a travel stipend up to \$500 to visit a CRC at your baseline visit. This is determined by the Alpha-1 Foundation.

H. RIGHT OF WITHDRAWAL:

You have the option of withdrawing from the Registry at any time for any reason. Should you change your mind and wish to withdraw your data from the Registry, you will be free to do so without having to provide any explanation.

At the time of withdrawal you may 1) decline to provide any more data or samples to the study but allow use of previously collected data and/or samples, 2) request withdrawal of all your data from study databases and request that any stored samples be destroyed, or 3) withdraw some portion of the data collected (i.e., you may withdraw samples but not exam or questionnaire data or vice versa).

If you choose to withdraw from the study, the research coordinator at the clinical site will conduct an exit interview to determine what you choose to have done with your data and samples. The coordinator will also provide you with any clinically relevant study results. They will also determine or establish how you would like to be contacted if relevant results become available in the future. If you decline an exit interview, the consent form in place at the time of study withdrawal is used to determine the future status of your data. Data assigned



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to a specific study prior to your request for removal cannot be retrieved from researchers that have already accessed it.

You may withdraw by written request mailed to the Alpha-1 CRC Research Registry at 96 Jonathan Lucas St. CSB 812 MSC 630 Charleston, SC 296425.

I. GENETIC SAMPLES

Many medical problems may arise due to the environment or from genetic factors. Your diseases may come from one or both of these causes. Genetic factors are those that people are born with and that can affect other family members. There may be genetic testing done in the future that would provide information about traits that were passed on to you from your parents or from you to your children.

Linkage of biological samples

Research to identify genes that cause or contribute to a disease or trait is an increasingly important way to try to understand the role of genes in human disease. You have been given this consent form because the Medical University of South Carolina investigators want to include your tissue, cell or blood sample in a research project, or because they want to save such biological samples for future research. There are several things you should know before allowing your tissues, cells or blood to be studied or to be stored.

1. Your tissue, cell or blood sample will be stored under your name or some other type of identifier which could be linked to you. Sometimes these samples are shared for research purposes with other investigators at other research sites. If this is done, the other investigators would not know your name.
2. In addition to your name, other information about you might be connected to your blood or tissue sample. For instance, information about race, ethnicity, sex, your medical history, and so forth might be available to investigators studying your tissue or blood. Such information is important for scientific reasons and sometimes for public health. It is possible that genetic information might come to be associated with your racial or ethnic group.
3. Genetic information about you will often apply (in one degree or another) to family members. It is not generally the University's policy to provide genetic information about you to your family members. However, certain studies, called "pedigree studies", share such information among family members. For this and related research you will be asked if you are willing to share your genetic information with your family members.
4. You have the right to refuse to allow your tissue or blood to be studied or saved for future research studies. You may withdraw from this study at any time and remove any samples that contain identifiers from research use after the date of your withdrawal. This means that while the University might retain the identified samples- the law often requires this-they would not be used for research.
5. South Carolina law mandates that your genetic information obtained from any tests or from this research be kept confidential. Our state law prohibits any insurer using this information in a discriminatory manner against you or any of your family in issuing or renewing insurance coverage for you or your family. Our state law further prohibits our sharing your genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board and then we must take all steps to protect your identity. You will still be responsible for paying for healthcare, however. The Medical University of South Carolina will not be responsible for such costs, even if care is needed for a condition revealed during research or clinical testing.



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6. Genetic research raises difficult questions about informing you and other subjects of any results, or of future results. Some people feel anxious about the possibility of having a defective gene that would place them or their children at risk. Some people want to know what is found out about them; others do not. The risks of knowing include anxiety and other psychological distress. The risks of not knowing what is found include not being aware if there is treatment for the problem being studied. But these risks can change depending on whether there is a treatment or cure for a particular disease, and on how clear the results are. If there is a medical reason to seek specific information from you, your doctor will tell you this. A process called "genetic counseling" is often appropriate in such cases; you should ask your doctor or nurse about this if you have any questions. In this study, investigators will not tell you what they find out about you, nor will they contact you if a test becomes available to diagnose a condition you might have or later develop.

7. If you are concerned about a potential genetic disorder, you and your doctor might choose to test specifically for it. This would require additional blood or tissue samples and would not be part of this research project. You should discuss this option with your doctor or genetic counselor.

8. The presence of a genetic marker does not necessarily mean that an individual will develop a disease. Informing people of all such markers independently of medical need can cause unnecessary anxiety. On the other hand, the absence of a marker does not mean that someone will not get the disease. Genetic diseases appear as a result of a complex mixture of hereditary, environmental, behavioral and other factors.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

These are the best-known risks and challenges of genetic research. There might be other risks we do not know about yet. It is important that you talk to your doctor, nurse or genetic counselor if you have questions or concerns about the research study. The MUSC Alpha-1 Foundation Genetic Counseling Program has a toll free number (800-785-3177) that can be accessed from 8 AM - 4:30 PM Monday through Friday Eastern Time to discuss any aspect of the Alpha-1 MUSC CRC Alpha-1 Biorepository.

Please initial one of the following statements:

____ I agree to collection of blood, DNA, and RNA that will be linked to my clinical information for life. I also agree that my samples CAN be moved to a different biorepository, if one is established by the Alpha-1 Foundation.

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_____ I agree to have my blood, DNA and RNA stored indefinitely in a biorepository. I request that the samples NOT be moved to a different biorepository if one is established by the Alpha-1 Foundation.

_____ I do not agree to collection of DNA and RNA but you may collect my blood for other tests. You may still participate in the Registry with this option selected.

_____ I do not agree to the collection of blood but wish to be in the Alpha-1 CRC Registry.

J. RELEASE OF MEDICAL RECORDS TO ANYONE OTHER THAN THE INVESTIGATORS

You will be asked to sign a separate release for the release of your medical records.

K. MUSC STATEMENTS

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Strange at (843) 792-3174. I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of



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Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

If you wish to participate, you should sign below.

Signature of Person Obtaining Consent Date

Signature of Participant Date

Signature of Legal Guardian (if applicable) Date

CHILD/ADULT COMBO

I agree to participate in this study. I have been given a copy of this form for my own records.

If you wish to participate, you should sign below.

Signature of Person Obtaining Consent Date *Printed Name of Participant

Signature of Adult Participant Date

Signature of Parent/Legal Representative (if applicable) Date

*For Minors 12-17 years of age: "My participation has been explained to me, and all of my questions have been answered. I am willing to participate."

Signature: _____

Age: _____ Date of Birth: _____