Emory University
Consent to be a Research Subject

Title: Clinical Research in Genetics (CRIG)

Principal Investigator: Stephen Warren, PhD; Department of Human Genetics

If you are the legal guardian of a child who is being asked to participate, the term "you" used in this consent refers to your child.

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:
- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

Study Overview
The purpose of this study is to help researchers understand if particular physical and/or health characteristics (called "phenotypes") are caused by particular changes in a person's genes. Genes are the instructions that tell the body how to grow and develop properly. Genes are found inside each cell of the body and are made of DNA. Genes are found on structures called chromosomes. Chromosomes help keep the genes organized. People get half of their chromosomes from their biological mother and half from their biological father.

If we learn that your (or your family member's) health concerns are caused by a genetic reason, it may also be helpful to study other family members. This would help researchers learn more about how gene changes are passed on in families and how these gene changes affect different family members.

Procedures
You will be asked to provide at least one of the following types of samples:
- A small sample of blood (up to 20ccs = 4 teaspoons), usually collected from a vein in your arm by a healthcare professional.
- A saliva sample (collected by spitting in a cup), or a sample of the cells on the inside of your cheek (a "buccal" sample, collected by rubbing a cotton swab on the inside of your cheek for 30 seconds).
- A urine sample (collected in a plastic specimen cup).

The entire procedure should take less than one hour. You will typically only need to provide samples one time. Rarely, you may be asked for another sample if the testing of the first sample fails (for example, if the cells do not grow, the sample has bacteria in it, technical problems with the testing of your sample, etc).

In some cases, we may ask you to provide samples of other types of tissue, such as skin or amniotic fluid. Collecting these types of tissue may be more invasive than a simple blood draw (for example, a skin biopsy). Because of this, we will only ask you for this type of sample if you are already undergoing a procedure to collect this type of tissue as part of your routine medical care. For example, a skin biopsy may be needed to diagnose certain genetic conditions. If you were having this done as part of your regular clinical genetics care, we might ask if we could include any remaining skin sample not needed for the clinical test as part of this research project.

Your urine, blood, saliva, and/or buccal sample may be processed in several ways, one of which may include making an unlimited source of material for future study. By making an unlimited source, we will be able to continue this study for a long time without asking you for a fresh sample. Your blood sample will not be used for cloning. Different types of tests will be performed on your sample(s) in order to study the genetic causes of the health concerns in you or your family. These tests may include those that look at the structure, sequence, and function of genetic material (such as gene sequencing tests, microarray tests, etc), biochemical tests, and new types of tests as they are developed.

In order to fully understand your health or developmental concerns, you may be asked to complete an initial evaluation which includes tests designed to evaluate your developmental skills, vocabulary, and ability to solve simple problems. You may be asked to complete a short neurological and/or psychological exam. The complete initial evaluation will take between 20 minutes and about 2 hours. You may be asked to return yearly to complete a similar evaluation. All of your information will be entered into a secure, password-protected computer database.

Any biological products that are made from your sample will become the property of Emory University or the researcher studying your sample. In order to protect your privacy, all samples and products made from your sample will be assigned an identification code that does not include any of your personal information. Your sample will be stored for as long as it is useful, unless you ask us to destroy it sooner. You may request that your sample be destroyed at any time, simply by contacting the repository administrator, Audrey Bibb at 404-778-8597. The Principal Investigator of this study may also share stored samples with other scientists for research purposes, but your name or other identifying information will not be given to them.

Risks and Discomforts

Possible risks include:

1) Blood draw: carries a risk of pain and bruising (very likely), and infection (less likely). Care will be taken to minimize these risks.

2) Emotional distress or a disruption in family relationships: If a genetic reason for the health/developmental issues in the family is found, most families find this information helpful. This is because it may explain why the person has a developmental disability, birth defect, health problem, etc. It also provides the information needed for thorough genetic counseling. However, learning that a person has a genetic abnormality can cause emotional problems or a disruption in family relationships. In order to lessen these risks, results are sent to you through doctors and genetic counselors that have experience in helping people and families understand the results and implications of genetic testing. The doctors and genetic counselors can provide support, information and referrals to other medical or counseling specialists in order to help people and families adjust to results of genetic testing in a healthy manner.

3) Unexpected results: Taking part in this study could turn up unexpected results, such as finding a genetic abnormality unrelated to your current health problems, or the discovery that the man said to be the father of a pregnancy or child is not the true biological father. This information will not be given to you unless it will impact your healthcare or if it alters your genetic risk (for example, risk of miscarriage, risk of having a child with birth

defects, risk of developing a genetic condition). This information would be given to your doctor or genetic counselor.

4) Loss of privacy: Some people believe that the using DNA in research brings up special concerns about your privacy. For example, it is possible that an employer could try to deny employment, or an insurance company could try to deny insurance if information about a person's DNA were known. For this reason, the research team works hard to keep DNA information private. We will not reveal your genetic information to any third party without your permission, unless required by law. Dr. Warren has spent many years conducting DNA-based research involving thousands of samples. He does not know of any research participant who has been harmed by donating DNA to research. We therefore believe that risks associated with donating DNA are very low.

New Information

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

You will be asked at the end of this form if you would like to be informed of clinically significant results of this study. If a clinically significant result is learned from this research and you tell us you want to learn the results, you will be contacted by a study administrator to discuss the process. If you still wish to learn the results, you will be asked to sign a release form and make an appointment with one of the genetics professionals in the Department of Human Genetics to discuss the results. During this appointment we will discuss how this finding may or may not affect your medical care. Under federal law, results from research laboratories cannot be used in clinical care of an individual. Therefore, before results can be released to you, the research results are confirmed by a clinical laboratory. The cost of a genetics clinical evaluation and confirmation in the clinical laboratory are not covered by this research study. Therefore, you or your insurance company will be billed for these services. Once research results are confirmed in a clinical laboratory, your medical care will be according to standard of care at the time.

Benefits

There is no treatment as part of this study. Although your participation in this study may not directly help you or your relatives, the results of this research project could help us understand more about the genetic causes of human diseases. In addition, this research may help you or your family understand more about the cause of the health or developmental concerns in your family. Please see the "New Information" section above to learn more about how results will be reported.

Compensation

You and/or your relatives will not be offered payment for being in this study. You should also understand that samples removed from you for this study may be valuable for scientific, research, or teaching purposes, or for the development of new medical products. By agreeing to participate in this research, you authorize Emory University and members of its staff to use your blood for these purposes. If this future research leads to the development of new diagnostic tests, new medicines, or other uses that may be commercially valuable, you will receive no financial benefits.

Confidentiality

Certain offices and people other than the researchers may look at your medical charts and study records. Government agencies and Emory employees overseeing proper study conduct may look at your study records. These offices include the Emory Institutional Review Board, the Emory Office of Research Compliance, and the Office for Clinical Research. Emory will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present this study or publish its results. Study records can be opened by court order. They may also be produced in response to a subpoena or a request for production of documents.

Research Information Will Go Into the Medical Record:
If you are or have been an Emory Healthcare patient, you have an Emory Healthcare medical record. If you are not and have never been an Emory Healthcare patient, you do not have one. Please note that an Emory Healthcare medical record **will** be created if you have any services or procedures done by an Emory provider or facility for this study.

If you agree to be in this study, a copy of the consent form and HIPAA patient form that you sign **will** be placed in your Emory Healthcare medical record. Emory Healthcare may create study information about you that can help Emory Healthcare take care of you (for example, the results of study tests or procedures). These useful study results will be placed in your Emory Healthcare medical record. Anyone who has access to your medical record will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA Privacy Rule. On the other hand, some state and federal laws and rules may not protect the research information from disclosure.

Emory does not control results from tests and procedures done at other places, so these results would not be placed in your Emory Healthcare medical record. They will not likely be available to Emory Healthcare to help take care of you. Emory also does not have control over any other medical records that you may have with other healthcare providers. Emory will not send any test or procedure results from the study to these providers. If you decide to be in this study, it is up to you to let them know.

The researchers will review the results of certain study tests and procedures **only for the research**. The researchers **will not** be looking at the results of these tests and procedures to make decisions about your personal health or treatment. For this study, those things include: results of genetic, biochemical, developmental, neurological, and/or psychological assessments.

Costs
There will be no extra costs to you or your insurance company for providing a sample in this study. However, as stated above in the "New Information" section, if you wish to learn about potentially significant results from this study, additional clinical visits and tests may be required. The cost of the genetics clinic evaluation and confirmation of results is not covered by this study, and would need to be covered by yourself or your insurance company.

Withdrawal from the Study
You have the right to leave a study at any time without penalty. Your decision will not affect in any way your current or future medical care or any other benefits to which you are otherwise entitled.

Contact Information
Contact Audrey Bibb at 404-778-8597:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

For Phone Consent
I have read this authorization form and have been given the chance to ask questions about it.

I spoke with a study investigator, _____, on

_____/_____/_____ at _____ to discuss the study and ask questions.

Consent

Please, print your name and sign below if you agree to be in this study. By signing this consent form, you will not give up any of your legal rights. We will give you a copy of the signed consent, to keep.

_____
Name of Subject

_____ _____
Signature of Subject Date Time

_____ _____
Signature of Person Conducting Informed Consent Discussion Date Time

_____
Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Legally Authorized Representative Date Time

_____
Authority of Legally Authorized Representative or Relationship to Subject

_____ _____
Signature of Assent for 17 year old Subject Date Time

Other options

If you would like to be informed of research findings that may be clinically relevant, please initial in the space provided.

_____ _____/_____/_____

Initials Date

If we may contact you as needed to gather updated health information, please initial in the space provided.

_____ _____/_____/_____

Initials Date

If you would like your sample to be *stripped of identifying information* and considered for use in further research unrelated to the current study, please initial in the space provided.

_____ _____/_____/_____

Initials Date

If you would like your *identified* sample to be considered for use in research unrelated to the current study, please initial in the space provided. You will be contacted to give or refuse consent prior to your sample being used.

_____ _____/_____/_____

Initials Date

Documentation of Assent from Pediatric Subjects

Title: Clinical Research in Genetics (CRIG)

Principal Investigator: Stephen Warren, PhD; Department of Human Genetics

Subject age: _____ years

For subjects in this study who are minors, one of the following Pediatric Assent sections must be satisfied. Place a checkmark beside the method used.

1._____ (<6 years) NO ASSENT REQUIRED

2._____ (ages 6-10) VERBAL ASSENT
The study has been explained to this child in an age-appropriate manner. The child has asked questions, verbalizes understanding of the information, and provides verbal assent.

_____ _____
Person Soliciting Assent ---------- Date Time

3._____ (ages 11-16) WRITTEN ASSENT See attached Written Assent document.

4._____ (age 17) READ/SIGN MAIN CONSENT DOCUMENT WITH GUARDIAN

5._____ (any age) UNABLE TO PROVIDE ASSENT

In my opinion, this child cannot give informed assent.

Reason(s):_____

_____

_____
Person Soliciting Assent ---------- Date Time

_____
Principal Investigator ---------- Date Time

Written Assent Document

We are asking you to volunteer to be in a medical research study. The study is to help us explain why some children have medical or learning problems. We hope this study will help us to find ways to help other children with medical or learning problems in the future. To be in the study, we will need to draw a tube of blood from your arm, collect a urine sample in a plastic cup, collect a sample of your saliva in a small cup, and/or rub a small cotton swab on the inside of your cheek to collect some skin cells. Most people say that taking blood from their arm hurts, sort of like a bee sting. Collecting the urine sample, the saliva sample, or the sample from the inside of your cheek does not hurt.

However, it is important to us that you are only in the study if you want to be in it. You can refuse (say no) to be in this study. Your doctors or your parents cannot make you be in the study if you don't want to be in it. If you agree to be in the study but change your mind about it later, you can stop being in the study.

Your doctor will talk to you about what it means to be in a research study. He or she will also talk to you about what it means to have medical or learning problems. You should ask your doctor all of the questions you have. You should also talk to your parents about the study and tell them if you want to be in it.

Before you sign this form, you will be asked to speak with someone at the doctor's office. You can ask this person any questions you have about the study.

If you agree to be in the study, sign here:

_____

Participant ---------- Date Time

Emory University Research Subject HIPAA Authorization to Use or Disclose Health Information that Identifies You for a Research Study

Title: Clinical Research in Genetics (CRIG)

Principal Investigator: Stephen Warren, PhD; Department of Human Genetics

Introduction

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act (HIPAA). We refer to all of these laws in this form as the Privacy Rules. This form explains how we will use your PHI for this study.

Please read this form carefully and if you agree with it, sign it at the end.

Description of Research Study

The purpose of this research is to get a better understanding of the genetic causes of human diseases.

PHI That Will Be Used/Disclosed

The PHI that we may use or disclose (share) for this research study includes: A copy of your entire genetics clinic medical record, and the results of research tests and evaluations.

Purposes for Which Your PHI Will Be Used

If you sign this form, you give us your permission to use your PHI for the conduct and oversight of this research study.

People That Will Use or Disclose Your PHI and Purpose of Use/Disclosure

Different people and groups will use and disclose your PHI. They will do this only in connection with the research study. The following persons or groups may use and/or disclose your PHI:

- The Principal Investigator and the research staff.
- The Principal Investigator may use other people and groups to help conduct the study. These people and groups will use your PHI to do this work.
- The following groups may also use and disclose your PHI. They will do this to make sure the research is done correctly and safely. The groups are:
    - the Emory University Institutional Review Board
    - the Emory University Office of Research Compliance
    - research monitors and reviewers
    - data and safety monitoring boards
    - public health agencies

We will use or disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or elder abuse. We also will comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Revoking Your Authorization

You do not have to sign this form. Even if you do, at any time later on you may revoke (take back) your permission. If you want to do this, you must write to:
Drs. Stephen Warren
2165 N. Decatur Road
Decatur, GA 30033

We have provided you with a pre-written letter for this purpose.

After that point, the researchers would not collect any more of your PHI. But they may use or pass along the information you already gave them so they can follow the law, protect your safety, or make sure the research was done properly. If you have any questions about this, please ask.

Other Items You Should Know

If we disclose information to people who do not have to follow the Privacy Rules, your information will no longer be protected by the Privacy Rules. People who do not have to follow the Privacy Rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. Let us know if you have questions about this.

You do not have to sign this form. If you do not sign, you may not participate in the research study.

We will put a copy of your signed informed consent form for the research study and your signed HIPAA Authorization form into your Emory Genetics medical chart.

During the study you will generally not have access to records related to the research study. This is to preserve the integrity of the research. You may have access to these records when the study is complete. These records may include research related PHI your health care providers use to make decisions about your care. If necessary for your care, this information may be available to your doctor before the end of the study.

If identifiers are removed from your PHI, then the remaining information will not be subject to the Privacy Rules. It may be used or disclosed with other people or organizations, and/or for other purposes.

Expiration Date

Your permission to use and disclose your PHI will expire. The expiration will be at the end of the research study and any required record-keeping period.

Contacts

If you have any questions regarding the study, you may call Audrey Bibb at 404-778-8597.

If you have any questions about the study, or your rights as a study subject, you may contact the Emory University Institutional Review Board at 404-712-0720 or 1-877-503-9797, by email at irb@emory.edu.

Authorization

A copy of this form will be given to you.

_____

Signature of Study Subject OR Subject's Legal Authorized Representative

_____ _____

Date Time

_____

Printed Name of Study Subject OR Subject's Legally Authorized Representative

If Representative, Relationship to Study Subject: _____

_____

Signature of Person Obtaining Authorization

_____ _____

Date Time

_____

Printed Name of Person Obtaining Authorization

_____ _____

Date Time