Boston Children's Hospital

RESEARCH CONSENT FORM

This section only to be edited by IRB office.

DO NOT PLACE IN MEDICAL RECORD

Use Plate or Print:

MRN#:

DOB:

Subject's Name:

Gender:

Protocol Title: Genetic studies of Strabismus, Congenital Cranial Dysinnervation Disorders (CCDDs) and their associated anomalies

Principal Investigator: Elizabeth Engle, MD

Please check one of the following:

_____ You are an adult participant in this study (your name is listed above as 'subject name').
_____ You are the parent or guardian granting permission for a minor or dependent individual to participate in this study. If the participant is a child/dependent, "you" throughout this form references that individual.

Introduction

This consent form gives you important information about our research study. A research study helps scientists and doctors learn new information to improve medical practice and patient care. Participation in this research is voluntary. You are free to say yes or no and your decision will not impact the care you receive at Boston Children's Hospital. You can withdraw from the study at any time. A description of the study and its risks, potential benefits and other important information are in this consent form. Please read this consent form carefully and take your time making decisions about participation. The form may contain words that you do not understand. Please ask questions about anything you do not understand. We encourage you to talk to others (for example, your family, friends or other doctors or health care providers) before you decide to participate.

How are individuals selected for this research study?

You have been asked to be a part of this study because you or a member of your family have been identified or suspected of having strabismus, eye or facial movement disorders, sometimes referred to as congenital cranial dysinnervation disorders (CCDDs), another disorder of cranial nerve, muscle and/or brain development or related conditions. Individuals and their family members from Boston Children's Hospital, across the United States and around the world are being enrolled in this study. No preference will be given to an individual's gender, racial or ethnic origin, though some disorders are more prevalent in particular ethnic groups.

Why is this research study being done?

We are a group of scientists and doctors at Boston Children's Hospital trying to learn more about genes related to strabismus, CCDDs and their associated anomalies. We work to (1) identify new genes related to the development and function of cranial nerve, muscle and brain development and related disorders, (2) characterize the normal and abnormal function of these genes, and (3) better understand how variants in these genes are inherited in and related to medical conditions affecting the human population.

Genes are found in the cells of our body and are the instructions that tell our body how to grow and develop. They are passed on to individuals (inherited) from their parents. The DNA sequence that makes up genes is

remarkably similar from one person to the next, but tiny variations do occur, rendering each person a unique individual. Most of these gene changes are harmless and are responsible for variations in eye color and height and other features. There can also be changes in genes that cause them not to work properly and lead to developmental disorders, health problems or disease. We wish to determine and understand which genes are important for cranial nerve, muscle and brain development by studying the changes in genes of individuals who have disorders affecting their eye movement, cranial nerve abnormalities and associated anomalies. We hope that the knowledge we gain from this research will lead to improved diagnosis, management and treatment of these conditions

Who is conducting this research study, and where is it being conducted? The lead investigator for this study is Elizabeth C. Engle, MD and the research is based in the Engle Laboratory at the Center for Life Sciences Building at Boston Children's Hospital in Boston, MA. Though this work takes place in Boston, Dr. Engle has established collaborative relationships with researchers and clinicians around the U.S. and the world which greatly helps these research efforts. Approved research using your samples and data will be conducted by faculty at Boston Children's Hospital and potentially other approved collaborating researchers. This research is federally funded by the National Institute of Health (NIH).

How many people will participate in this research study? We have enrolled over 4000 affected individuals and their families in this research in order to identify the many genes important for cranial nerve, muscle and brain development. We plan to continue enrolling patients in this research on an ongoing basis.

What do I have to do if I am in this research study?

Interview and Screening to Obtain Medical and Family History: We are asking you to participate because you are an individual, either affected or unaffected, in a family affected by one of the disorders we study. If you choose to participate, you may be asked to complete screening forms and may be interviewed by telephone or in person about the medical history for you and other family members. Questions will focus on the pattern and development of the disorder in your family. Other questions may include age, ethnic background, and biological relationships between individuals. With your permission, we will review your hospital records available to us at Boston Children's Hospital, ask you to send us records from other institutions, or contact your health care provider to obtain relevant clinical information, including clinical exams, results of imaging and laboratory tests you have undergone. In addition, we may ask you to complete a detailed medical history form. This step of the study should not take more than an hour total. As this is an ongoing study, we would like to be able to review your records throughout the study.

Photographing and Videotaping Eye Movements: We may ask to photograph and/or video-record eye movements as well as facial and physical features using 2D and/or 3D photography. We may also ask you to send us photos or videos. These images will be used to review your eye movements and facial features. You may opt in or out of this step. With your permission, we may use these recordings for medical teaching and publications. These recordings will not be used except as described, and will not be released to anyone else.

Recontacting for additional information or participation in future studies: Over time we may wish to obtain updated information from participants. In addition, other studies may arise, some as a direct result of this

study, for which you and your family may be appropriate. You will be given an opportunity to provide consent to allow us to contact you for these purposes in the future.

Sample collection: You will be asked to provide a biological sample, usually by giving a sample of saliva or blood, from which we extract and study genetic material (including DNA RNA). Providing a blood sample will involve our taking approximately 1 to 6 teaspoons of blood from a vein in your arm. If there are costs for your blood draw or transportation to the appointment to have your blood drawn for participation in this research, we will refund these costs to you if you give us the receipt(s) showing the exact cost and date of service. For some individuals we may ask for a different sample to be able to obtain your genetic material. Other samples could be cheek cells from a small brush used on the inside of your cheek, a hair sample from pulling a few hairs from your head or extracted DNA stored in another location. If you had a surgical procedure and a tissue sample is saved that is not needed for other purposes, we may request some of this tissue. For instance, if someone is scheduled to undergo medically indicated surgery, we may ask your surgeon if any tissue normally removed during the surgery is available to provide to us for examination and study. Additionally, participants or family members may provide permission for us to obtain post-mortem or autopsy samples. The sample donation typically is requested only once. However, if the sample is used up or the laboratory procedures fail, we may request a second sample to ensure you can remain included.

Research Use of Samples

You, your information, and your samples collected during this study will be given unique codes and will not be put in your medical record. Your sample(s) and research data will be associated with your unique code only and stored without your name, medical record number or other identifying information. Personal identifiers will be stored within the research laboratory in a secure and locked location and/or on a password-protected databases.

DNA obtained from your sample may be used to search, identify and study genes and genetic mutations. We may use techniques that study all of your genes, only some of your genes and/or parts of your genetic material that do not have a currently known purpose or function. We may undertake linkage analysis on your DNA and others to determine the genetic location where a gene associated with your disorder may lie. Once a region has been localized to a chromosomal location, it is possible to identify the causative gene by screening sequences within that region. If a genetic change is identified, then we may sequence a subset of the population to help determine whether the change in the normal gene sequence is a polymorphism (non-disease causing) or pathogenic (disease causing). We may also use your blood to examine your chromosomes for large genetic abnormalities that may cause your medical condition.

Cell Lines: In some cases we may use blood or tissue that has been collected to create a "cell line" that can be grown in the laboratory. A cell line grown in this manner can survive indefinitely, providing a greater source of genetic material allowing researchers to have an unlimited supply of your cells in the future without asking for more samples from you. The researchers will use these cells to try to learn more about strabismus, CCDDs and their associated anomalies.

Induced Pluripotent Stem Cells: We may use the cells taken from your blood to create a type of cell known as a pluripotent stem cell. Stem cells can be used to create other types of cells and tissue, including nerve, muscle

and brain cells. Your cells might be used to study genetic disorders or variants. The researchers will use your cells to try to learn more about strabismus, CCDDs and their associated anomalies.

Storage & Future Use: At the completion of this research, we would like to store any remaining sample(s) for possible future use. Because our study is funded by NIH and is subject to the Genomic Data Sharing policy and submitted to dbGaP, the NIH asks investigators to obtain consent from participants for their genomic and phenotypic data to be used for future research purposes and to be shared broadly for future unspecified uses. Therefore, the remaining samples may be stored indefinitely and may be used for future unspecified research. Your sample will not be stored with identifiers, such as your name or medical record number. The Boston Children's Hospital research staff will have a list to know which sample is linked to which participant and this list will be kept confidential in a secure location. If the research investigator distributes your samples to other researchers or institutions, they will be labeled with a research code without identifiers so that you cannot be identified.

If you have questions about storing samples or would like to request that samples be removed from storage, please let us know. It is not always possible to remove samples from storage or to retrieve samples that have already been sent to other investigators.

Data Sharing:
As this study is funded by the National Institutes of Health (NIH), it is subject to the federal Genomic Data Sharing (GDS) Policy (effective January 25, 2015). It requires investigators to obtain participants' consent for their sample and genomic (genetic) and phenotypic (clinical) data to be used for future research purposes, submitted to the respository, dbGaP, and to be shared broadly for future unspecified uses. In order to allow researchers to share results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) "banks" that collect the results and analyze data from genetic studies. These central banks may also analyze and store samples and health information form research conducted by Boston Children's Hospital. These central banks will store your genetic and health information and/or samples and give them to other qualified and approved researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your health information, samples and/or genetic information with these banks. However, we cannot predict how genetic information will be used in the future. The samples and data will be sent with only your research code number attached. Your name or other directly identifiable information will not be given to these central banks. There are many safeguards in place to protect your privacy.

RISKS & BENEFITS

What are the risks of this research study? What could go wrong? Risks associated with a blood draw may include minor discomfort, bruising, fainting, and infection. When possible, we will draw blood at the time of a clinically-indicated procedure to reduce the number of needle sticks. There is no risk associated with providing a saliva sample.

There is a chance that participation in this study could cause psychological distress. Some people involved in genetic studies have felt anxious about the possibility of carrying an altered gene that places them at risk or that

may be passed on to children and affect other relatives. You may be asked questions that make you feel uncomfortable. If these feelings arise at any time during the study, you may contact us and we will arrange for you to speak with a genetic counselor.

There might be social and economic disadvantages associated with the gathering of genetic information. For example, genetic information provided to the wrong source could affect you and your family. A U.S. law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for most health insurance companies, group health plans, and employers to discriminate against you based on your genetic information. Under this law, health insurance companies, group health plans, and most employers may not request your genetic information that we get from this research. For more information about GINA, please see: http://www.eeoc.gov/laws/types/genetic.cfm. This law does not protect information for being used when applying for life or long term care insurance. We will do our best to keep all information confidential and only with your permission would we share this information with others.

You should be aware that because we are testing family members, we may find out that someone else might have fathered a child (non-paternity), or that a child had been adopted. These details can affect our analyses. If you wish, you may let us know in confidence if this is a possibility. In all cases, this information will be kept in the strictest confidence and will not be shared with you or anyone outside of the research staff.

Potential Benefits: Being in this research may not help you right now. Through the research however, we hope that we will know more about genetic causes of strabismus, CCDDs and associated anomalies. This may help other children/adults with these conditions in the future.

What are costs and time commitment? Will I receive payments? Your participation in the study should take no more than an hour. There is no fee for you to participate, as the costs associated with this study are covered by research funds. You will not be paid or otherwise compensated for your participation.

Research, Results, Options and Reporting:

This research study was established to find and characterize genes important for cranial nerve, muscle and brain development and cannot study all possible diseases and genes. During the course of this research, we might identify the genetic cause of the disorder being studied in you/your family. In addition, though we are not seeking, expected or required to identify other findings, due to advances in genetic technologies, we might also find a genetic cause of another disorder or uncover a risk of developing a disorder or disease in the future that is completely unrelated to the reason for your participation in this study.

We are a research laboratory and we are not a laboratory with certified procedures for reporting clinical results and therefore we cannot directly give you the full results from this research. However, if information is learned that we determine might be important for your family (e.g., discovering a gene that may cause a disease or condition) we may be able to facilitate having these results confirmed by a CLIA-certified clinical laboratory that is allowed to generate and provide diagnostic results. There may be costs for the diagnostic lab to perform the tests. These tests may not be covered by your insurance and in that case if you choose for you and your doctors to know the details of the results and undergo testing, you will be responsible for the costs of the tests. Most CLIA laboratories will ask for new blood or tissue in order to ensure the

research results are correct. If your results are confirmed, they will be given to the doctor you choose, who will arrange for these results to be discussed with you.

Please read the statements below. Please mark and initial next to the option (1, 2 or 3) that states your current wishes regarding notification of results from this research study.

1. _____☐ I **do not** want to learn about results found out about me. Please **do not** contact me.

   -OR-

2. _____☐ I **do want** to learn **only** about results found about me that could explain the condition that was the reason for original research participation (e.g. strabismus, CCDD or associated anomaly).

   -OR-

3. _____☐ I **do want** to learn about results found about me, including results that could (a) explain the condition (strabismus, CCDD or associate anomaly) **and/or** (b) be the cause of another disorder or disease that could significantly affect my health or medical care but is unrelated to the reason for my child's research participation.

You can change your mind about whether or not to receive results from this research at any time by contacting the Study Contacts at the end of the form. The Study Contacts are also available to discuss your options further at your request. If you choose to be contacted, please indicate the name of the health care provider(s) that we should contact to discuss making arrangements with a CLIA lab. We will make every reasonable effort to get in touch with the clinician(s) you specify.

The health care provider(s) who can assist with confirmation of research results:

Name: _____

Institution: _____

Phone: _____

Address: _____

Other Study Related Options: (please check and initial one to indicate your choice)

Permission for Obtaining Photographs, Videos:

_____☐ Yes, I do agree to photographs or videos being recorded and collected for research purposes.

_____☐ No, I do NOT agree to photographs or videos being recorded and collected.

Permission for Use of Photographs, Videos:

_____☐ Yes, I do agree to the use of above for medical teaching, presentations or publications.
_____☐ No, I do NOT agree to the use of above for medical teaching, presentations or publications.

Permission to Contact for More Clinical Information and Future Studies:

_____☐ Yes, my records at Boston Children's Hospital may be searched and/or I may be contacted by the Engle Lab to provide more medical and clinical information over time.
_____☐ No, do not contact me to provide more medical and clinical information.

Permission to Contact for Future Studies: Your participation in any research is completely voluntary. You should feel no pressure to participate if you are contacted about another research study. **Please check one** of the options below regarding being contacted about other research opportunities.

_____☐ Yes, I may be contacted by the Engle Lab about participating in other research projects.
_____☐ Yes, I may be contacted about participating in other research projects by **other researchers** working with the study investigator at Boston Children's Hospital.
_____☐ No, I do not want to be contacted about other research projects. **Do not** give my contact information to the staff of any other research studies.

Permission to Store and Use Samples and Data for Future, UnspecifiedBroad Use: This study is partially funded by NIH and is subject to the Genomic Data Sharing policy. NIH expects investigators to obtain participant consent for their genomic and phenotypic data to be used for future research purposes and to be shared broadly for future unspecified uses**.**

_____☐ Yes, I allow my samples & information to be stored and used for future research as described. The samples and data will be coded with a unique code number and the link to that code will not be shared.
_____☐ No, I do NOT allow my samples & information to be stored and used broadly for future unspecified research.. I understand my samples and information WILL still be used for research on strabismus, congenital cranial dysinnervation disorders (CCDDs) and their associated anomalies as previously described and conducted by Dr. Engle and approved collaborating researchers.

Other information that may help you:
Boston Children's Hospital has developed a web-based, interactive educational program for parents called "A Parent's Guide to Medical Research." To find out more about research at Children's, please visit the program at www.researchchildren.org.

Boston Children's Hospital is interested in hearing your comments, answering your questions, and responding to any concerns regarding clinical research. If you have questions or concerns, you may email IRB@childrens.harvard.edu or call (617) 355-7052 between the hours of 8:30 and 5:00, Monday through Friday.

Who may see, use or share your health information?

A copy of this consent form will not be placed in your medical record. The results of the tests performed for research purposes will not be placed in your medical record. Because of this, it is unlikely that others within the hospital, an insurance company, or employer would ever learn of such results.

The National Institutes of Health has issued a Certificate of Confidentiality for this research. This adds special protection for the research information and specimens that may identify you. The researchers may not disclose information that may identify you, even under a court order or subpoena unless you give permission. However, a Certificate of Confidentiality does not prevent researchers from disclosing information about you if required by law (such as to report child abuse, communicable diseases or harm to self or others); if you have consented to the disclosure (such as for your medical treatment); or if it is used for other research as allowed by law. In addition the Certificate cannot be used to refuse a request if a governmental agency sponsoring the project wants to audit the research. Any research information that is placed in your medical record would not be covered under this Certificate. The Certificate will not be used to prevent disclosure for any purpose you have consented to in this informed consent document. The Certificate does not stop you from voluntarily releasing information about yourself or your involvement in this research. If others obtain your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What should you know about HIPAA and confidentiality?

Your health information is protected by a law called the Health Information Portability and Accountability act (HIPAA). In general, anyone who is involved in this research, including those funding and regulating the study, may see the data, including information about you. For example, the following people might see information about you:

- Research staff at Boston Children's Hospital involved in this study;
- Medical staff at Boston Children's Hospital directly involved in your care that is related to the research or arises from it;
- Other researchers and centers that are a part of this study, including people who oversee research at that hospital;
- People at Boston Children's Hospital who oversee, advise, and evaluate research and care. This includes the ethics board and quality improvement program;
- People from agencies and organizations that provide accreditation and oversight of research;
- People that oversee the study information, such as data safety monitoring boards, clinical research organizations, data coordinating centers, and others;
- Sponsors or others who fund the research, including the government or private sponsors.
- Companies that manufacture drugs or devices used in this research;

- Federal and state agencies that oversee or review research information, such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and public health and safety authorities;
- People or groups that are hired to provide services related to this research or research at Boston Children's Hospital, including services providers, such as laboratories and others;
- And/or your health insurer, for portions of the research and related care that are considered billable.

If some law or court requires us to share the information, we would have to follow that law or final ruling.

Some people or groups who get your health information might not have to follow the same privacy rules. Once your information is shared outside of Boston Children's Hospital, we cannot promise that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect privacy may no longer apply to this information. Other laws may or may not protect sharing of private health information. If you have a question about this, you may contact the Boston Children's Hospital Privacy Officer at (857) 218-4680, which is set up to help you understand privacy and confidentiality.
Because research is ongoing, we cannot give you an exact time when we will destroy this information. Researchers continue to use data for many years, so it is not possible to know when they will be done.

We will also create a code for the research information we collect about you so identifying information will not remain with the data and will be kept separately. The results of this research may be published in a medical book or journal or be used for teaching purposes. However, your name or identifying information will not be used without your specific permission.

Your privacy rights

If you want to participate in this research study, you must sign this form. If you do not sign this form, it will not affect your care at Boston Children's Hospital now or in the future and there will be no penalty or loss of benefits. You can withdraw from the study and end your permission for Boston Children's Hospital to use or share the protected information that was collected as part of the research; however you cannot get back information that was already shared with others. Once you remove your permission, no more private health information will be collected. If you wish to withdraw your health information, please contact the research team.
You may have the right to find out if information collected for this study was shared with others for research, treatment or payment. You may not be allowed to review the information, including information recorded in your medical record, until after the study is completed. When the study is over, you will have the right to access the information again. To request the information, please contact the Hospital's Privacy Officer at (857) 218-4680.

Contact Information

I understand that I may use the following contact information to reach the appropriate person/office to address any questions or concerns I may have about this study. I know:

I can call…	At	If I have questions or concerns about

Investigator: **Dr. Engle**	Phone: **617-919-4030**	▪ General questions about the research ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints
Research Contact **Brenda Barry**	Phone: **617-919-2168**	▪ General questions about the study ▪ Research-related injuries or emergencies ▪ Any research-related concerns or complaints
Institutional Review Board	Phone: **617-355-7052**	▪ Rights of a research participant ▪ Use of protected health information. ▪ Compensation in event of research-related injury ▪ Any research-related concerns or complaints. ▪ If investigator/research contact cannot be reached. ▪ If I want to speak with someone other than the Investigator, Research Contact or research staff.

Documentation of Informed Consent and Authorization

- I have read this consent form and was given enough time to consider the decision to participate in this research.
- This research has been satisfactorily explained to me, including possible risks and benefits.
- All my questions were satisfactorily answered.
- I understand that participation in this research is voluntary and that I can withdraw at any time.
- I am signing this consent form prior to participation in any research activities.
- I give permission for participation in this research and for the use of associated protected health information as described above (HIPAA).

Parent/Legal Guardian Permission (if applicable)

If the child to be involved in this research is a foster child or a ward of the state please notify the researcher or their staff who is obtaining your consent.

■ If child/adolescent's assent is **not** documented above, please indicate reason below (check one):

☐ Assent is documented on a separate IRB-approved assent form
☐ Child is too young
☐ Other reason (e.g. sedated), please specify: _____

Research Investigator /or Associate's Statement & Signature

- I have fully explained the research described above, including the possible risks and benefits, to all involved parties (participant /parents/legal guardian as applicable).
- I have answered and will answer all questions to the best of my ability.
- I will inform all involved parties of any changes (if applicable) to the research procedures or the risks and benefits during or after the course of the research.
- I have provided a copy of the consent form signed by the participant / parent / guardian and a copy of the hospital's privacy notification (if requested).

■ _____ _____

Date (MM/DD/YEAR) Signature of **Research Investigator or Associate**

Witness Statement & Signature

A witness must be present for the entire consent process in the following situations (please check the appropriate box)

☐ The individual cannot read and this consent document was read to the participant or legal representative, **or**

☐ The individual has certain communication impairments that limit the participant's ability to clearly express consent **or**

☐ Situations where the IRB requests a witness be present: please specify _____

I confirm that the information in this consent form was accurately explained to the participant, parent or legally authorized representative, the individual appeared to understand the information and had the opportunity to ask questions, and that informed consent was given freely.

_____ _____

Date (MM/DD/YEAR) Signature of Witness

Or

☐ The individual is not English speaking and, through an interpreter, a short form consent document was presented orally to the participant or legal representative and this consent document serves as the summary for such consent.

I confirm that the information in this consent form was presented orally to the participant, parent or legally authorized representative, in a language they could understand and the individual had the opportunity to ask questions.

_____ _____

Date (MM/DD/YEAR) Signature of Witness