University of North Carolina-Chapel Hill
Parental Permission for a Minor Child to Participate in a Research Study
Social Behavioral Form

IRB Study #08-1725
Consent Form Version Date: 12/08/2010
Title of Study: NENA - Neuroblastoma Epidemiology in North America
Principal Investigator: Andrew F. Olshan, PhD
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This form has been approved by the IRB for use until 04/17/2013

What are some general things you should know about research studies?

You are being asked to allow your child to take part in a research study. To join the study is voluntary. You may refuse to give permission, or you may withdraw your permission for your child to be in the study, for any reason.

Research studies are designed to obtain new knowledge. This new information may help people in the future. Your child may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about your child being in this research study.
You will be given a copy of this permission form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

Who is sponsoring this research?

This research is funded by the National Cancer Institute at the U.S. National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What is the purpose of this study?

The purpose of this research study is to understand how genes might affect young children's chances of developing neuroblastoma. To do this, we will compare the genes of children with neuroblastoma to the genes of their parents. We ask parents to use a saliva collection kit designed specifically for use with young children to collect a DNA sample from their participating child. Our study lab can then extract genes of interest from those DNA samples. By including samples from children with the disease, as well as from their biological parents, our study has the unique opportunity to analyze genetic pathways in the development of neuroblastoma.

We are inviting your child to participate in this study because he/she is registered with the Children's Oncology Group (COG) and the Childhood Cancer Research Network (CCRN). During that registration process, **you or another guardian indicated willingness to be contacted for non-therapeutic studies.** The NENA study is a non-therapeutic study that is approved by the

Children's Oncology Group. COG provided us with your contact information because your child was diagnosed with neuroblastoma, making him/her eligible for participation. This study is voluntary and separate from your child's treatment. You and/or your child do not have to be involved with research in order for you or your child to receive medical treatment.

This consent form explains what participation means for **your child** if you agree to provide parental consent for your child to participate in the NENA study.

Are there any reasons your child should not be in this study?
Your child should not be in this study if he/she has a medical or dental condition or a current injury that would make it uncomfortable for them to have a series of very small sponges swabbed along the inside of their cheek.

How many people will take part in this study?
If your child is in this study, s/he will be one of approximately 600 children in this research study.

How long will your child's part in this study last?
Study participation for your child will last approximately 30 minutes. During this time your child will have saliva DNA collected from the inside of his/her cheek using a 5 sponge ORAgene-250 collection kit. You will determine when your child has completed participation, either because all of the sponges in the kit have been used for collection or because you decide that your child has done as many sponges as are comfortable for him or her. Once the saliva sample is obtained, we ask the parent doing the collection to mail it to our study lab in the included prepaid mailer. Once your child has completed their saliva DNA collection and it has been sent to our lab, your child has concluded their participation in the study. If the lab discovers that there is insufficient DNA in your child's saliva sample, we may seek a replacement sample from your child by asking you to repeat the collection process with a second kit that we send to you. For the vast majority of children, they will only need to do the collection process once.

DNA use and storage
Your child's DNA sample will be used for research by Andrew F. Olshan, Ph.D. and his associates for the purposes of learning more about neuroblastoma. We are now aware of some of the genes that we will study, but there may be other genes that we plan to study in the future. Therefore, we would like to keep your child's DNA sample for a period of time after this study ends. In some cases, your child's DNA sample could be sent to other research groups for analysis. You would not be notified if this occurs, but any samples we send to another researcher would be identified only with a number that could not be traced back to your child. Your child will not be identified in any publications or reports from this study.

What is the purpose of this specimen repository or "biobank?"
Research with blood, tissue or body fluids (specimens) such as saliva can help researchers understand how the human body works as well as answer other questions by using specimens. Researchers may develop new tests to find diseases or new ways to treat diseases. In the future, research may help to develop new products, such as drugs. Specimens are commonly used for genetic research. Sometimes researchers collect and store many specimens together and use them for different kinds of research, or share them with other scientists; this is called a specimen repository or "biobank".

The purpose of this study's biobank is to collect and store saliva samples from children with neuroblastoma along with samples from their biological parents as well. By analyzing genes from these saliva samples, our research team and others in the future can investigate genetic pathways

related to neuroblastoma.

Will researchers seek approval from you to do future studies involving the specimen from your child?

By signing this consent form, you are giving your permission for researchers to use your child's specimens as described above. Current and future research is overseen by a committee called the Institutional Review Board (IRB). The role of the IRB is to protect the rights and welfare of research participants. In some cases, the IRB may require that you be re-contacted and asked for parental consent to use your child's specimens in a different, specific research study. If you are contacted for that reason, you have the right not to have your child participate in any research study for which your consent is sought. Refusal to have your child participate will not affect your or your child's medical care or result in loss of benefits to which you or your child are entitled.

You can request that your child's DNA sample for this study be destroyed at any time up until 2014 by contacting Dr. Olshan. After 2014, we will remove your child's name from our files, and we will not be able to tell which DNA sample is your child's.

What will happen if your child takes part in the study?

If your child takes part in this study, you will be provided with the following materials in order to assist you in collecting his/her saliva DNA sample:

Parental Consent Form

This parental consent form is included in your child's folder for you to sign and return to the study office in the prepaid mailer that comes with it. Study team members are available by phone to answer any questions that you have about the form and about having your child participate in NENA. An extra copy of this parental consent form is included in your child's folder for you to keep for your child's records.

The ORAgene-250 DNA Collection Kit and Instructions

An ORAgene-250 collection kit is provided for use with your child. This kit contains one packet of 5 sponges and a blue and white collection container as well as complete instructions for using this kit to collect your child's DNA sample.

You will be asked to read through the instructions and set aside a time to do the collection at your child's home. The procedure will necessitate that your child not eat food or be breastfed for at least 20 minutes before the collection, nor at any time during the collection. We will ask you to use the long-handled sponges to swab along the cheek inside your child's mouth, place the sponge into the well of the collection container and use the enclosed scissors to cut the sponge tip off of the handle. This process is repeated for all 5 sponges or as many as you and your child can tolerate. Once collection is completed, you will close the collection container and shake it slightly to distribute the preservative liquid inside. You will then put the completed sample in the prepaid envelope included with the kit and place the envelope in the mail. Your child's sample will arrive at our study lab at the University of North Carolina-Chapel Hill (UNC-CH) where it will be processed and analyzed.

Frequently Asked Questions (FAQ)

A list of frequently asked questions, along with answers, is included with your child's saliva DNA collection kit. The study team has supplied answers for some of the most common questions other parents have asked about using this kit with their own young children. If you have questions about the collection process and/or your child's participation in NENA that are not on the list, or need further explanation for questions already in our FAQ, we encourage you to contact our study team.

What are Genome Wide Association Studies (GWAS)?
The National Institutes of Health (NIH) has established a national database that will hold information from many individuals across the country, including medical information and genetic information. Your child's saliva contains genes which are made of DNA that is unique to him/her. If coded information about your child is sent to this national database, access will be controlled and limited to other researchers.

DNA is the genetic material in a person's cells that makes each person unique. There are thousands of genes made up of DNA in each cell. By studying the DNA, scientists can discover the genes that might be involved in the development of neuroblastoma.

We know little about the factors we are studying, so the results will not provide information that is useful to your child or your family. This information is for research purposes only, and you will not be informed of your child's individual DNA results. However, you have the option to receive or not to receive information about the overall findings from the study once the study has been completed.

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. Your child may not benefit personally from being in this research study.

Will you receive results from research involving your child's specimen?
Research with your child's specimen is not expected to yield new information that would be meaningful to share with you personally. There are no plans to re-contact you or other subjects with individualized results.

What are the possible risks or discomforts involved from being in this study?
The risks for your child from participating in the saliva DNA collection using the ORAgene-250 kit are that discomfort may occur from having the swabs in their mouth or feeling very slight irritation from the swab inside their cheek. Because this kit was created for use with very young children, we expect the risk of discomfort to be quite minimal. There is a risk that your child may become emotionally irritated by the procedure, specifically, by having the series of sponges swabbed inside the mouth. Should this occur, the collection procedure allows for numerous breaks between sponges. We strongly encourage parents to follow the included instructions and to read through the FAQ for suggestions on how to make the collection process easiest for you and your child. You are also advised to simply stop the collection method if you feel your child is upset.

There may be uncommon or previously unknown risks. You should report any problems to the researcher and/or study's Project Director.

What are the possible risks or discomforts involved with the use of your child's specimen?
There is a risk of breach of confidentiality. Because this research involves genetics, there is also a potential risk for some of your child's relatives and other members of your child's ethnic group, since they share some of your child's genetic makeup.

What will happen if your child is injured by this research?
All research involves a chance that something bad might happen. This may include the risk of personal injury. In spite of all safety measures, your child might develop a reaction or injury from having his/her specimen collected. If such problems occur, the researchers will help you get medical care for your child, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries your child may experience, or for the related medical care for

your child. However, by signing this form, you do not give up any of your legal rights for your child.

Who owns the specimens?

The saliva sample that your child provides becomes the exclusive property of the University of North Carolina at Chapel Hill. This organization may retain, preserve or dispose of your child's specimen and may use this specimen for research that may result in commercial applications. There are no plans to compensate your child for any future commercial use of his/her specimen.

How will your child's privacy be protected?

The ORAgene-250 DNA collection kits are labeled with study-specific identification numbers only, and only the Project Director and a small core staff are able to link participants with saliva DNA specimens. Once DNA are analyzed at the lab, results will only appear in deidentified format.

All linking information will be kept in locked and/or password protected files accessible only to the core study team. All members of the core research team have completed human subjects training through the IRB and signed a study-specific confidentiality pledge.

Participants *will not* be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your child's information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies for purposes such as quality control or safety.

Certificate of Confidentiality

The Children's Oncology Group has received a Certificate of Confidentiality. Information about the certificate is described below.

The Children's Oncology Group has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

Efforts will be made to keep your and your child's personal information confidential. We cannot guarantee absolute confidentiality. Your child's personal information may be disclosed if required by law.

Organizations that may inspect and/or copy your child's research records for quality assurance and data analysis include groups such as:

- Children's Oncology Group
  - Representatives of the National Cancer Institute (NCI), Food and Drug Administration (FDA), and other U.S. and international governmental regulatory agencies involved in keeping research safe for people
- The Institutional Review Board of this hospital
- Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute

Your child's specimen may be shared with researchers at this or other institutions. Research studies may be done at many places at the same time. Your child's personal identifying information will not be sent to other researchers.

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 your child based on his/her genetic information. GINA does not protect your child against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect your child against discrimination based on an already-diagnosed genetic condition or disease.

The saliva sample your child provides for this study will be stored long-term, unless you request that it be destroyed before then. Your child's privacy will be protected through 2014 by the protections explained above in this consent form, and furthermore by coverage from the COG Certificate of Confidentiality. After 2014, all identifying linkages will be destroyed, and our study will not know which sample is from your child.

Privacy protections for Spanish speaking participants

Interpreters are available for this study for Spanish-speaking parents. The interpreters have completed human subjects training at UNC and signed an additional study confidentiality form to help protect your and your child's privacy. The same steps this study takes to protect privacy for English-speaking participants are put into place for Spanish speaking participants, including the way IDs are used and the limited number of staff available to link participants to their data.

What if you want to stop your child's participation before your child's part in the study is complete?

You can withdraw your child from this study at any time, without penalty. The investigators also have the right to stop your child's participation at any time. This could be because your child no longer meets eligibility criteria or because the entire study has been stopped. If this occurs and your child has already provided a saliva sample, you can either allow it to remain with the study for analysis or ask that it be destroyed or removed from all lab processes.

Can you withdraw the specimens from the research repository?

If you decide that you no longer wish for your child's specimens to be stored, you should contact the researchers on the front page of this form. It is best to make your request in writing.

Any analysis in progress at the time of your request for your child or already performed prior to your request for your child being received by the researcher will continue to be used as part of the research study. Once the researchers have been notified, your child's remaining specimens will be destroyed. If you do not make such a request, your child's specimens may be stored forever. The researchers may choose to destroy the specimens at any time.

Will your child receive anything for being in this study?
The study will send an incentive check in the amount of $10 to you, the parent completing this parental consent form, upon receipt of your child's saliva DNA sample.

If you are asked to repeat the saliva collection process for your child due to insufficient DNA amounts the first time, you will not receive an additional incentive check.

Will it cost you anything for your child to be in this study?
There are no costs for your child to be in the study.

Will it cost you anything for storage of your child's specimen?
There will be no cost to you for the storage and use of your child's specimen.

What if you are a UNC student?
You may choose not to give permission for your child to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if your child takes part in this research.

What if you are a UNC employee?
Your child's taking part in this research is not a part of your University duties, and refusing to give permission will not affect your job. You will not be offered or receive any special job-related consideration if your child takes part in this research.

What if you or your child has questions about this study?
You and your child have the right to ask, and have answered, any questions you may have about this research. If you have questions, or concerns, you should contact the researchers listed on the first page of this form.

What if you or your child has questions about your child's rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your child's rights and welfare. If you or your child has questions or concerns about your child's rights as a research subject you may contact, anonymously if you wish, the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

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Title of Study: NENA - Neuroblastoma Epidemiology in North America
Principal Investigator: Andrew F. Olshan, PhD

Parent's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily give permission to allow my child to participate in this research study.

____
Printed Name of Research Participant (Child)

____ _________________
Signature of Parent/Guardian Date

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Printed Name of Parent/Guardian