EXPERIMENTAL SUBJECT'S BILL OF RIGHTS
Medical Research Studies

The rights below are the rights of every person who is asked to be in a medical research study. As an experimental subject, you have the following rights:

1) To be told what the study is trying to determine.

2) To be told what will happen to you and whether any of the procedures, drugs, or devices is different from what would be used in standard practice.

3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to you for research purposes.

4) To be told if you can expect any benefit from participating and, if so, what the benefit might be.

5) To be told the other choices you have and how they may be better or worse than being in the study.

6) To be allowed to ask any questions concerning the study, both before agreeing to be involved and during the course of the study.

7) To be told what sort of medical treatment is available if any complications arise.

8) To refuse to participate or to change your mind about participating after the study is started. This decision will not affect your right to receive the care you would receive if you were not in the study.

9) To receive a copy of the signed and dated consent form.

10) To be free of pressure when considering whether you wish to agree to be in the study.

If you have other questions, please ask the researcher or research assistant. In addition, you may contact the Institutional Review Board, which is concerned with protecting volunteers in research projects. You may reach the IRB office by calling (916) 703-9151, from 8:00 a.m. to 5:00 p.m., Monday through Friday, or by writing to the Institutional Review Board, CTSC Bldg., Suite 1400, Rm. 1429, 2921 Stockton Blvd., Sacramento, California 95817.

_____ _____

Subject Name Birth Date

_____ _____

Signature of Subject or Guardian Date

Subject's Initials_____

APPROVED by the Institutional Review Board at the University of California, Davis	
Protocol	APPROVED
215635	January 9, 2018

UNIVERSITY OF CALIFORNIA, DAVIS
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Investigator's Name: Simeon A. Boyadjiev Boyd
Department: Pediatrics, Section of Genetics

STUDY TITLE: Genetic Analysis of Craniosynostosis and related Craniofacial Anomalies

INTRODUCTION

This is a research study. Research studies only include subjects who choose to participate. As a study participant you have the right to know about the procedures that will be used in this research study so that you can make the decision whether or not to participate. The information presented here is to make you better informed so that you may give or withhold your consent to participate in this research study. Please take your time to make your decision and discuss it with your family and friends.

You are being asked to take part in this study because you or someone in your family has craniosynostosis (premature closure of the sutures between the skull bones), large fontanels (delayed skull maturation), or facial features that may hint to craniosynostosis. Frequently the manifestation of craniosynostosis is variable, thus we would like to also enroll individuals that have facial features that fall in the spectrum of the craniosynostosis anomalies. These features may include prominent forehead, widely spaced eyes, and unusually-spaced nose and mouth. This research is being done to find out what causes congenital defects of the face and the skull. People with or without abnormalities may join. Studies of family members who do not have these anomalies will aid us in determining which factors may or may not be related to these problems. Only genes for congenital anomalies of the skull and the face will be studied, and testing will be free of charge. No other genetic testing will be done without the specific approval of the study participant. You may be of any age in order to participate. In order to participate in this study, it will be necessary to give your written consent. Approximately 750 participants with be recruited from the clinics of the UC Davis Children's Hospital and the following collaborating sites:

1. University of Iowa – Principal Investigator (PI) Paul Romitti, PhD
2. Children's Hospital Boston – PI Joan Staler, MD
3. Children's Hospital of Los Angeles and University of Southern California - PI Pedro Sanchez, MD
4. Seattle Children's Hospital, University of Washington - PI Michael Cunningham, MD,PhD
5. Stanford University - PI Jonathan Bernstein, MD, PhD
6. University of California Irvine - PI Viriginia Kimonis, MD
7. University of California San Francisco - PI Ophir Klein, MD

The researchers at the institutions listed above will only inform the prospective subjects about the availability of the research, providing information about how to contact the investigator, Dr. Simeon Boyd. They may obtain the prospective subjects' permission to be contacted by the PI (Dr. Boyd) but they cannot obtain consent or act as representatives of the PI. Dr. Boyd will then communicate with the subjects and conduct the consent process.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to find out what causes craniosynostosis. It is a common birth defect that affects approximately 1 out of 2000 newborns and it is believed that certain genes and environmental factors cause this condition. We hope to learn more about the genetic and non-genetic causes of craniosynostosis and to be able to provide better medical care for people with craniosynostosis in the future.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 750 people will take part in this study. It will be conducted in collaborations with the Johns Hopkins University, the Children's Hospital of Boston, Harvard University, and other research collaborators in the study of craniosynostosis that are listed in the International Craniosynostosis Consortium (https://genetics.ucdmc.ucdavis.edu/index.cfm).

BEFORE YOU BEGIN THE STUDY

You will need to sign this Consent Form and the Medical Release form (University of California Permission to Use Personal Health Information for Research). After we verify the craniosynostosis by review of previous medical records we will offer you participation.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

If you decide to participate in this study, you will be asked to do the following:
We will ask you to complete a questionnaire about your family's health. The study will take place at the MIND Institute at UC Davis. You can participate from home, or while in the hospital, or in an outpatient setting. We will ask you/your child to answer questions pertinent to risk factors that may cause birth defects. This will take no more than an hour and can be done in person, through a telephone interview, or online securely at a time convenient for you/your child. The information obtained from the participants in this study will be entered into a corresponding computer database, which will be shared with our research collaborators listed on our study website (https://genetics.ucdmc.ucdavis.edu/index.cfm). In some cases blood will be taken and analyzed by genetic methods to find out if and how these abnormalities are inherited. When blood sample is not available we will collect a cheek (buccal) swab or mouthwash sample. Since only small amount of research material is available we may ask you for additional samples in the future. In order to know whether the experimental design works, it is necessary to compare the information from the affected families with the information provided by control families. You will be assigned to a group based on presence or absence of individuals with craniofacial defects in your family. If you/your child need(s) to have surgery to correct a congenital defect, we ask you to allow us to use skin and/or bone tissues that may be excessive and will be otherwise discarded. If no surgeries are necessary we will not collect these samples. We expect a single research visit that will last approximately 45 to 60 minutes. Telephone interviews and/or follow-up email communications may be needed to obtain the information necessary for this study or to coordinate shipment of medical records and samples. Based on our previous experience with more than 300 recruited families up to 3-5 follow-up contacts may be expected, each one with duration of approximately 10 minutes."

Please check which of the following you/your child agrees to:

_____ Blood Drawing: One to two teaspoons of blood will be drawn.

_____ Cheek (buccal) swabs or mouthwashes: 1. Two cotton swabs will be brushed against the mucosa of the mouth. 2. We will extract a small amount of DNA from these swabs. 3. If you prefer, you can gargle with Scope mouthwash to provide a sample.

____ Skin, muscle and/or bone sample collection: If excess tissue is available during surgical repair procedures, 1-2 grams (pea size) will be collected. These tissue samples will be used to study the genes that may cause birth defects. The study personnel will follow the UCDMC Policy #3078 regarding submission of tissue to Pathology.

_____ Physical Examination and Medical Records release: In some cases, we may perform or ask that you undergo a physical examination pertinent to our studies. We may review medical records pertinent to our studies. Head CT data may be obtained, coded, and shared with our research collaborators who will analyze it.

_____ Digital photography and 3 Dimensional head scan (3dMD). The images will be deposited into an archive and/or shared with other researchers devoid of personal identifiers. An authorization for use of photos outside of research (for teaching or publication purposes) will be obtained using a separate document.

The following procedures are part of regular care and may be done even if you do not join the study:

1. Review of the previous medical history.
2. Physical examination
3. X-ray of CT of the skull
4. Blood draw for clinical genetic tests of genes associated with craniosynostosis

The following procedures are NOT PART OF REGULAR CARE AND WILL ONLY BE DONE IF YOU JOIN THE STUDY:

1. Completion of Epidemiologic Questionnaire
2. Digital photography
3. 3-Dimensional head scanner
4. Blood draw or collection of mouthwash for DNA analysis

Another way to find out what will happen to me during the study is to read the chart/table below.

Read and sign Consent form Registration form and Medical Release Form	→	**Documented Craniosynostosis**	→	**Complete Epidemiologic Questionnaire, Sign Photo Consent and have images taken donate blood or mouthwash ,.**

HOW LONG WILL I BE IN THE STUDY?

You will be asked to participate with a single research visit that will take about 60 minutes. However, the study will continue for undetermined amount of time. After you are finished providing the information and donating blood samples, the Investigator will not ask you to visit the office for follow-up exams. If you prefer to donate mouthwash we may need to contact you in the future for additional samples collection.

CAN I STOP BEING IN THE STUDY?

Yes, you can decide to stop at any time. Tell the Investigator if you decide to stop your participation in this study.

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

1. Blood Drawing: You/your child will feel a little needle stick. It might hurt for a minute and may cause minor bruising and bleeding. Infection rarely occurs.
2. Cheek swabs or Scope mouthwash: minimal risk.
3. Excess Skin and/or Bone Tissue Collection: minimal risk.
4. Physical Examination and Medical Records: minimal risk.
5. Epidemiologic Survey: minimal risk, sensitive information (about illicit drugs, alcohol use, etc.) will not be shared with parties not involved in this research project. Survey data including contact name and information will be shared with our research collaborators to be used strictly only for the purpose of craniosynostosis research.
6. Loss of Confidentiality: There is a risk that people other than the investigators and collaborators on this research will gain access to your records. In order to protect your privacy we will keep all records in a locked file cabinet in a location other than the clinical offices, in a building that has a card-key access, or keyed entry. .
7. There is also the risk we may find that you or a member of your family have a gene that can cause a congenital abnormality. This may cause anxiety. There is also a risk that you or a member of your family may have such a gene and we will not detect it in this study.
8. Digital photography and 3-D head scanner: minimal risks

No medications will be used in this study so you may not have side effects.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You may or may not benefit from taking part in this research. We hope that the information obtained may help us in the diagnosis and counseling of people with congenital abnormalities. Research results will not be available to you or your physician. However, there are situations where we may suspect that your child has a known genetic syndrome, based on our research. In such cases, an earlier diagnosis may prevent or alleviate long-term medical complications. In addition, evaluation of other family members may identify individuals at risk for having a child with a craniosynostosis syndrome. If we suspect a change in your DNA is present based on our research studies, we can contact you if you choose to be notified. Dr. Boyd would provide or arrange a genetic counseling session for your family, and may suggest clinical genetic test in a certified DNA Diagnostic laboratory. You should also be aware that it is possible that we may not suspect craniosynostosis syndromes during our studies, even if they are present. Therefore, you should not assume that you or your child are not at risk for having another child with craniosynostosis, if we do not notify you of any abnormalities.

If we suspect genetic cause of craniosynostosis of potential significance:

Would you like to be notified about our findings? __ Yes __ No

Subject's Initials_____

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Your alternative is not to take part in this study. If you choose not to take part in this study, your future care will not be affected.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. Generally, only people on the research team or our research collaborators will know that you are in the research study and will see your information. However, there are a few exceptions that are listed later in this section of the consent form.

The people working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may collect other information including your name, address, date of birth, and other details.

The research team will need to see your information. Sometimes other people at UC Davis may see or give out your information. These include people who review the research studies, their staff, lawyers, or other UC Davis staff.

People outside of UC Davis may need to see your information for this study. Examples include government groups, safety monitors, other hospitals in the study and companies that sponsor the study.

We cannot do this study without your permission to use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

If you are injured as a direct result of research procedures, you will receive reasonably necessary medical treatment at no cost. The University of California does not provide any other form of compensation for injury. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There is no charge for you to participate in this study. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the sponsor/department.

WILL I BE COMPENSATED FOR BEING IN THIS STUDY?

We can not offer you payment for participation. Samples taken during this study may be used for research and development purposes not related to your treatment or condition. You will not have any property rights or ownership interest in products or data which may be derived from your samples.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or willingness to continue in the study.

DOES THE RESEARCHER HAVE A FINANCIAL INTEREST IN THIS RESEARCH STUDY?

The Investigator does not have any personal or financial interest in this study.

Subject's Initials_____

WILL SPECIMENS (tissue, blood, urine or other body materials) TAKEN FROM ME BE USED FOR FUTURE RESEARCH PURPOSES?

During the course of the research, the investigator will obtain some body materials, such as blood, discarded surgical tissue, or saliva. We would like to keep some of the materials that are left for future research purposes. Your specimen(s) will only be used for research purposes. If you agree, these specimen(s) will be kept and used to learn more about your disease as well as other diseases.

The research that may be done with your specimen(s) will not benefit you directly nor have an effect on your care. It might help people who have your disease and other diseases in the future. Any reports about the research, done with your specimen(s), will not be shared with you or your doctor and the reports will not be put in your health record.

Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results from samples to be linked to you or your family. Also, people outside of research process or research collaboration will not have access to results about any one person which will help to protect your privacy.
The benefits of research using specimens include learning more about what causes diseases, how to prevent them, how to treat them, and how to cure them. There are very few risks to you. The greatest risk is the release of information from your health records which may be necessary for us to obtain along with your specimens. We and our research collaborators in this study will protect your records so that your name, address, and phone number will be kept private. Your information may be placed in the central information place such as the database of genotypes and phenotypes (what the disease looks like) also known as dbGaP or other national repository at United States of America, National Institutes of Health (NIH). Other qualified researchers who obtain proper permission may gain access to your sample and /or data for use in approved research studies that may or may not be related to the present study. Sample and data used through such repositories will be monitored and usage approved by the repositories' administrators.
Samples may be used for reading out all the genetic information (sequencing) and /or studies that show differences in the genetic information across the entire human genome (genome wide studies). The tests we might want to use to study your biological sample may not even exist at this time. Therefore, we are asking for your permission to store your biological sample so that we can study it in the future.

Please read each question below and think about your choice. After reading each question, initial next to "YES" or "NO". If you have any questions, please discuss this with the researcher.

1. My tissue may be kept for use in future research: YES_____ NO_____

2. Someone may contact me in the future to ask me to take part in more research: YES_____ NO_____

For further information on the use of specimens for future research purposes and your rights as a research participant, please visit: http://research.ucdavis.edu/IRBAdmin/Participants .

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

If you have questions, please ask us. You can talk to the Investigator about any questions or concerns you have about this study at:

____Dr. Simeon Boyd _____ at phone number_____(916) 703-0446 _____

For questions about your rights while taking part in this study call the IRB Administration at (916) 703-9151 or write to IRB Administration, CRISP Building, Suite 1400, Room 1429, 2921 Stockton Blvd., Sacramento, CA 95817. The IRB Administration will inform the Institutional Review Board which is a group of people who review the research to protect your rights. The IRB Administration has also developed a web site designed to make you familiar with your rights. The web site discusses your basic rights as a research participant, an explanation of the informed consent process, the basic requirement

that written consent be in a language understandable to you, and suggested sample questions to ask the research investigator regarding your participation in the study. This web site can be accessed at: www.research.ucdavis.edu/IRBAdmin .

This research has received a Certificate of Confidentiality from the Federal government that will help protect the privacy of the research records. The Certificate of Confidentiality allows the Researchers to refuse to disclose identifying information on your participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself and your involvement in this research. If you have given your consent for an insurer or employer to obtain information about you, the Researcher may not use the Certificate of Confidentiality to withhold this information. A Certificate of Confidentiality also does not prevent a Researcher from disclosing information about you to prevent serious harm to yourself or others, such as reporting to the authorities' incidents of child abuse, elder abuse or spousal abuse.

My signature below will indicate that I have decided to participate in this study as a research subject. I have read and understand the information above. I understand that I will be given a signed and dated copy of this consent form and the Bill of Rights.

_____ _____ _____
Signature of Subject or Legal Representative Date Time

_____
Printed Name of Subject or Legal Representative

A Letter of Information was read to my child. _____Please initial

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____
Printed Name of Person Obtaining Consent

Subject's Initials_____