*The Skeletal Dysplasia Registry*
*Genetics and Pathogenesis of Skeletal Disorders*

***Adult Consent Form/Parental Permission Form/Youth (13-17) Assent Form to Participate in Research"***

****(This form will also serve as a Permission Form for your child to participate in this research. In this case, "You" refers to "Your child" and "you")***

## INTRODUCTION

Deborah Krakow, MD, Daniel H. Cohn, PhD and their associates from the Orthopaedic Surgery Department at the University of California, Los Angeles are conducting a research study. Drs. Krakow and Cohn will oversee the collection and storage of specimens and data from their laboratories at UCLA.

The researchers will explain this study to you. **Research studies are voluntary and include only people who choose to take part.** Please take your time about deciding whether to participate in this study. Before deciding:

- You can discuss this study with friends and family.
- You can also discuss it with your health care doctor or request a second opinion.
- If you have any questions, you can ask the researchers for more information before deciding to participate.

The research team is asking you to take part in this Registry (ISDR) because you or your relative has a problem with your skeleton, which results in conditions called skeletal dysplasias or short stature syndromes, as well as fractures, scoliosis, club feet and joint problems. This diagnosis has been established outside of this research study. You have expressed an interest in participating in research that seeks to better understand how such a problem presents and to contribute to knowledge that can be used to build upon the clinical opinion you have received.

## WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to collect information about skeletal disorders that will be used to better understand the clinical characteristics and genetic basis of these conditions and help doctors in their diagnosis and treatment. It is hoped that this study will help identify new types of skeletal disorders, describe their different characteristics, identify their causes and determine how they are inherited. In order to accomplish this, we may ask to review your medical records (ultrasounds, x-rays, MRIs, CT scans, measurements and photographs) and you may be asked to provide a blood/tissue sample when available. Research data will be kept in a Registry and used only for

ongoing research on skeletal disorders, including the study of changes in genes that are associated with skeletal dysplasias.

This Registry (ISDR) is funded by a grant from the National Institutes of Health (NIH/NIAMS) and National Institute for Child Health and Development (NICHD) and Orthopaedic Research Institute for Children.

**HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?**

Several hundred families with skeletal dysplasias are added to this Registry each year.

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

Most of the procedures are part of standard medical care to diagnose and treat your condition. "Standard Procedures" would be conducted even if you did not participate in this Registry. Standard procedures include physical measurements, photographs (to assist in describing features of genetic and skeletal dysplasias), x-rays, physical examinations, detailed family history (including a family tree), and possibly the collection of blood/tissue sample. The Registry also involves the collection, storage and distribution of, fetal tissues for research purposes. In some cases where fetal tissues are collected, we will request blood/tissue sample from the parents and possibly other family members.

"Research Procedures" are performed solely for research purposes; these procedures would not be conducted if you did not participate in this research. Research procedures include:

1. Blood Draw: Up to 12 teaspoons of blood, taking into consideration you or your child's age, will be drawn from a vein with a small sterile needle. This is the standard method used to obtain blood for routine hospital tests.
2. Saliva Collection: Up to 2 teaspoons of saliva are collected.
2. Other Tissue Biopsies: The purpose of these procedures is to establish a diagnosis by examining bone, cartilage and other tissues under the microscope or by studying cells grown in the laboratory. The material collected will be otherwise discarded when you or your child is already undergoing surgery.

Any specimens (e.g., tissue, blood, urine) obtained for the purposes of this study will become the property of the University of California. Once you provide the specimens you will not have access to them. The University may share your specimens in the future with other researchers or outside institutions.

Information that identifies you will not be shared with anyone outside of UCLA. The specimens will be used for research and such use may result in inventions or discoveries that could become the basis for new products or diagnostic or therapeutic agents. In some instances, these inventions and discoveries may be of potential commercial value and may be patented and licensed by the University. You will not receive any money or other benefits derived from any commercial or other products that

may be developed from use of the specimens.

You are being asked for your authorization to allow the research team to review medical records and also to gather or create new health information about you, from any of the following sources:

- laboratory tests to help confirm the diagnosis of your genetic condition
- other laboratory that could rule out the possible causes for your condition
- diagnostic images (Xrays, MRIs, or CT scans) that confirm key findings in your condition
- photographs or videos that demonstrate key features of your clinical evaluation that can be used to compare with published images concerning your condition and its clinical findings
- doctor/clinic records
- hospital/medical records
- pathology reports
- developmental evaluations that document your functional capabilities
- previous genetic, neurological, endocrinological, or craniofacial evaluations
- other types of medical information such as the family history of other similarly affected individuals in your family

You may be asked to sign a release medical records form that will then be sent to the hospital or doctors who have cared for you. In addition, any medical records belonging to University of California and/or the International Skeletal Dysplasia Registry may be reviewed and used as part of this research study. Donation of tissue plus health information together helps researchers to discover relationships between health history and specific characteristics of skeletal disorders and various other genetic diseases and birth defects.

**HOW LONG WILL I BE IN THIS STUDY?**

In many genetic studies, testing of the DNA may go on for very long periods of time. This is true because we are continually finding new genes that may be involved in these disorders. Therefore, while your direct participation in this study will be done once you have completed the procedures/visits described above, the DNA isolated from your blood/tissue sample may continue to be studied for many years. In addition, we may analyze your DNA sample as part of other research activities or share portions of it with other researchers working in other institutions.

Cells, blood, or other specimens removed from you during the course of this study may be valuable for scientific, research or teaching purposes or for the development of a new medical product. By agreeing to participate in this research, you authorize the research team to use your cells, blood or other specimens for these purposes.

Any tissues you have donated which are used in research may result in new tests, discoveries, or products. You no longer own your tissue after it has been donated and therefore you will not share in any revenues from these products, tests, or discoveries should they occur.

UCLA will maintain these routine samples. Samples will be maintained indefinitely or until the samples are exhausted. These samples are unavailable for clinical (diagnostic) purposes. Therefore, any future diagnostic testing as a result of this or other research must be performed using a new sample.

**Will I receive information about my genetic sample(s)?**

Research is a long and complicated process. Obtaining new general information from research may take many years. Even if there is new general information, there may not be information that is specific to you as an individual participant. However, you may request that the results of this research be disclosed to your treating doctor (who will then communicate with you). You and your doctor should understand that the testing and evaluations completed as part of this research have not been validated (confirmed). The findings are for research purposes only, and should not be relied upon for clinical purposes. Incidental findings not relevant to this research will not be disclosed.

At the end of this consent from, you will be given an opportunity to indicate whether you wish to have the results of this research disclosed to your treating doctor. The researchers listed on the first page of this consent document will disseminate the information to your treating doctor. These are research-based results and do not have the same quality control standards found in clinical laboratories. Thus, no clinical decisions should be made based on these findings without confirmation in a properly certified laboratory and without further discussion with a physician or genetics counselor.

## WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT?

**Known risks and discomforts:**
The possible risks and/or discomforts associated with the procedures described in this consent form include:

1. Blood Drawing – There may be discomfort, bruising and swelling at the site. There is a rare risk of infection, but precautions will be taken to avoid this.
2. Saliva collection – The collection of saliva can be associated with some dry mouth after multiple spit collections, but this is very temporary,
3. Other Tissue Collections at time of surgery - All risks will be explained by the appropriate specialist, such as the orthopedic surgeon and anesthesiologist, as part of a standard surgery consent. After appropriate material is collected for pathologic evaluation, remaining material that would be discarded will be collected.

Genetic studies have raised concern as to whether the studies would place research participants at risk for discrimination based on genetics. The federal Genetic Information Nondiscrimination Act (GINA) was passed to address this concern. GINA makes it illegal for medical insurance companies and most employers to discriminate

based on genetic information. The protections of GINA do not apply to life, disability, or long-term-care insurance. Although there are substantial protections against the risk of discrimination, you should be aware of this general concern.

We try to protect all research participants from placing them in a position where sensitive information could be disclosed that could lead to discrimination or the misuse of their information. This consent describes how your identifiable information will be protected under "How Will My Private Information Be Kept Confidential?" In addition, information for this genetic research study is kept separate from the hospital medical records and will not be put in the official record by research staff**.**

Sharing research data with other qualified researchers and the medical community helps to advance many different kinds of medical research, and provides the greatest benefit to public health. If you participate in the registry, we may share some of your de-identified genetic data and medical information. We will only use de-identify data to help protect your privacy. This means that we will not share any personal identifying information, such as name or address. Instead, your genetic data and clinical information will have a special, unrelated number on it, called a code. We may also put some de-identified summary data into publicly available scientific databases. Summary data means that genetic data from you will be combined with many other individuals into a summary or catalog of changes or variants. Researchers looking at the variant data will not be able to tell which variants belong to you or any other individual:

The National Institutes of Health (NIH) have set up a health research database of genotype (genetic data) and phenotype (medical information; for example, information about the disorder in your family) data called the *database of Genotype and Phenotype* (dbGaP). We may want to put de-identified individual genotype (genes) and phenotype data (clinical findings) from this study in dbGaP, or other similar research databases. The purpose of sharing data in research databases is to allow multiple researchers access to data to explore new ideas in discovering how genes interact with human diseases. Access to individual data in dbGaP is restricted to qualified researchers and controlled by the NIH Data Access Committee. In general, research data that are shared (both summary data and individual data) may be used to study diseases, conditions, or traits that are unrelated to the disorder in your family. Qualified researchers that access data can be from the government, academic and commercial institutions. Once submitted, the NIH will control this data. The NIH is committed to protecting the confidentiality of all the information it receives, but will also comply with relevant laws, which might include Freedom of Information Act (FOIA) requests for non-identifiable information.

If you prefer not to have your de-identified individual data shared in this way, there is a place at the end of this consent form for you to opt-out of individual data sharing in dbGaP or other similar research databases.

In the future, you can withdraw your consent to participate in the repository and/or databases such as dbGaP if you don't want your data to be shared. There will be no consequences if you choose to withdraw from the repository study or no longer want

your data shared in these databases. However, data that has already been sent to researchers cannot be retrieved from those researchers.

It is possible that this study will identify information about you that was previously unknown (such as disease status or risk). Such incidental findings, if any, will not be shared with anyone related to you unless the incidental findings regard an inherited risk for a disease known at the time of testing to be likely to cause premature death if untreated. Should such life-threatening results be uncovered through these genetic research studies and, if they are directly applicable to you or to your minor children, you will be notified via certified mail to contact the International Skeletal Dysplasia Registry and principal investigator: Deborah Krakow MD at the University of California, Los Angeles. Notification will be sent to the last address you provided to us. The study staff will not release these specific research findings over the telephone or in the mail. The International Skeletal Dysplasia Registry and principal investigator will arrange for you to meet with him and/or a genetic counselor or other appropriate health care provider either at UCLA or at another institution.

**Unknown risks and discomforts:**
The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

## ARE THERE ANY BENEFITS IF I PARTICIPATE?

**Possible benefits to me:**
There are no possible benefits you may experience from being in this study.

**Possible benefits to others or society:**
The study of your blood/tissue sample may, one day, result in new tests or treatments, or may help to prevent or cure skeletal disorders. Scientific knowledge often advances slowly, but it may greatly benefit future generations.

## WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

You may choose to not participate in this study. Evaluation of morphology (review of skeleton and tissue) can only be done as part of this research program. Genetic testing and additional commentary based on our review of skeleton and tissues have not yet been validated as diagnostic tests. If you do not wish to undergo this testing, our team can provide a clinical evaluation based solely on evaluation of your clinical course.

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Your decision not to participate or to withdraw from the study means that you will not or will no longer undergo any research-related procedures. You will, however, still be able to receive treatment and services at UCLA that are not related to this research. If you leave the study:

- We will no longer be able to allow you to participate in the research study; and

- We will stop collecting any additional identifiable health information about you. However, we are allowed by law to continue to use the health information we already have about you, as necessary to maintain the integrity of the research study and make reports that oversight agencies require of us.
- You also have the right to revoke or withdraw your authorization for us to use your identifiable health information. If you wish to revoke or withdraw your authorization, you must do so in writing, and provide that written revocation to the investigator Deborah Krakow, M.D., whose mailing address is: 615 Charles E. Young Dr. South, Rm 410, Los Angeles, CA 90095.
- In addition, if we have provided your identifiable health information to the National Institutes of Health (NIH) or the Data Coordinating Center, that information cannot be withdrawn.

**CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?**

The researchers may end your participation in this study for a number of reasons, such as if your safety and welfare are at risk, if you do not follow instructions or if you miss scheduled visits. The researchers or the study sponsor might also decide to stop the study at any time.

**HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?**

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security.

It is possible that other investigators conducting other research might request that data collected for this study be shared for further research. For example, investigators associated with the government agency supporting this study might make this request. Even if you agree that your data may be shared with other investigators, your name or other personal identifying information would not be revealed. Though your privacy is very important to us and we will use many safety measures to protect your privacy, it is possible that there may be unforeseen privacy risks. For example, although we would not put any personal identifying information about you in a shared database, someone in the future might find some way to link your medical information or other information collected for this study back to you even in the absence of your name or other personal identifying information. Alternatively, there could be violations to the security of the separate computer systems used to store the codes linking your information to you.

**Use of personal information that can identify you:**
When this information is gathered from your past medical records and/or new medical information about you is created and used for the research study, it may or may not

include information that identifies you, such as your name, medical record number, address, and more. When the medical information includes any of these "identifiers," the medical record information is called "identifiable health information." If all of the identifiers have been removed from the medical information, it is called "de-identified health information." Using or giving other people "de-identified health information" does not affect your privacy. However, this particular research study requires the research team to create, use and disclose "identifiable health information."

Information about you to be recorded for the purposes of this study includes:

- Names;
- Street address (city, county, precinct, zip code, and their equivalent geocodes);
- Birth date;
- Admission date/discharge date;
- Date of death;
- Telephone numbers;
- Fax numbers;
- Electronic mail addresses;
- Medical record numbers;
- Full face photographs and any other comparable image; and
- Any other unique identifying number, characteristic, or code (except one assigned by the research study as long as it is not derived from or related to information about the individual and is not capable of being translated and used to identify the individual, and only specific researchers have access to the unique code).

**How information about you will be stored:**

Each time your identifiable health information is disclosed to any of the individuals listed above, precautions will be taken to minimize the possibility that the information shared could directly identify you. When possible, all identifying information will be coded. This means that the researchers will assign a unique code to represent your identifiable data so that people who see the coded data will not be able to identify you. However, coding is not possible in some cases. In this situation, it would not be possible to withhold this identifying information. You may choose not to participate in this study and, therefore, not authorize disclosure of your private information.

**People and agencies that will have access to your information:**

The research team will share information among themselves as part of the research study process. In addition, various institutional committees and governmental agencies that oversee research may request or require access to your identifiable health information. These include the Institutional Review Boards of ULCA Medical Center, as well as the respective office for human research protection program, the Food and Drug Administration, the Department of Health and Human Services, and other agencies that must receive reports about certain diseases. Additionally, the following parties may receive information about you:

- Other researchers who are participating in this study

- These researchers are on file with the IRB in a separate amendment to our protocol.
- Other researchers for future and related research purposes
- Medical and other health care professional students who are assisting with research study tasks
- The study Sponsor (in other words the organization that is paying for the costs of the study) for matters related to study oversight, data analysis and use of research results in product development
- Data coordinating center for the study
- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, in conjunction with the Sponsor and/or the FDA.

You should be aware that when you authorize the disclosure of your health information by signing at the end of this form, the person or organization might not be required by federal privacy law to keep it confidential. However, California law explicitly prohibits the recipient of your health information from re-disclosing that information without another signed authorization form from you, unless the recipient is required or allowed by law to make a particular disclosure.

**Why would my health information be shared as part of the study?**
Research involves the gathering and analysis of information. With medical research, the research team is gathering and analyzing health information about individuals in the hope that they will be able to answer specific questions about a bodily function, disease, or wellness. Those team members who act in a supportive role to the research study use health information when necessary for various administrative tasks, such as tracking data, making reports that are required by government oversight agencies or the study sponsor, and assisting the researchers with other data-related tasks. The Institutional Review Boards act as watchdog groups for the protection of the rights and interests of research participants.

It is important for you to know that if your health information is used for teaching purposes outside the study, or to prepare a medical journal report about the research study, your identifiable health information will not be made public; your identity will be kept confidential in those circumstances.

**How long information from the study will be kept:**
You are being asked to authorize the research team to use and disclose your identifiable health information until January 1, 2075.

**ARE THERE ANY COSTS FOR TAKING PART IN THIS STUDY?**
You and your insurance company will not be charged for your participation in this research. However all exams, tests and procedures that are part of standard medical care for your condition will be billed to you or your insurance company.

**WILL I BE PAID FOR MY PARTICIPATION?**
You will not be paid for your participation in this research study.

## WHAT OTHER THINGS SHOULD I CONSIDER BEFORE PARTICIPATION?

**Use of My Specimens:**
You may change your mind and refuse to participate in this research at any time. If you withdraw from this research your research records and sample(s) will be removed from the Registry. Withdrawal will not have any effect on the medical care you may be receiving for your condition at UCLA or any other future care or services.

## WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

**The Research Team:**
You may contact Deborah Krakow, M.D., or Daniel H. Cohn at (310) 825-8998 with any questions or concerns about the research or your participation in this study.

**UCLA Office of the Human Research Protection Program (OHRPP):**
If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact the UCLA OHRPP by phone: (310) 825-5344; by email: mirb@research.ucla.edu or U.S. mail: UCLA OHRPP, 11000 Kinross Ave., Suite 211, Box 951694, Los Angeles, CA 90095-1694.

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

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from UCLA. If you decide to take part, you can leave the study at anytime.
- If you decide to stop being in this study you should notify the research team right away. The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still get medical care from UCLA.

## HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE AND MY AUTHORIZATION TO ALLOW FOR THE USE OF MY IDENTIFIABLE HEALTH INFORMATION AS DESCRIBED IN THIS FORM?

If you agree to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You authorize the use and disclosure of your identifiable health information as described in this form.

## SIGNATURE OF THE PARTICIPANT

**Permission to share my sample(s) with other researchers**

By agreeing to participate in this research, your sample(s) may be shared with other researchers performing research on your condition at other institutions.

**Willingness to have results of testing performed as part of research disclosed**

☐ YES ☐ NO I wish to have information about the testing conducted on my sample(s) disclosed to my treating doctor.

☐ YES ☐ NO Should information that may be important to my health become available in the future, I would like to be contacted and given an opportunity to have this information disclosed to my treating doctor. I understand that it is my responsibility to update any changes to my address information.

☐ YES ☐ NO You may share my de-identified individual genetic data and medical information in research databases.

**SIGNATURE BY THE ADULT PARTICIPANT:**
***(NOTE: This form should only be signed after you have had an opportunity to discuss the study with a UCLA investigator)***

| Name of Participant (Print) | Signature of Participant | Date of Signature |
|---|---|---|

**SIGNATURE BY THE ADOLESCENT PARTICIPANT**
**My signature below reflects my agreement to participate in this research.**

| Name of Participant (Print) | Signature of Participant | Date of Signature |
|---|---|---|

**SIGNATURE BY THE PARTICIPANT'S PARENT(S)/GUARDIAN(S)/PARENTAL PERMISSION SIGNATURE**
**By providing my signature below, I consent and give permission for the participation of my child, _____, in the research study**
***Name of child***
**described in this document.**

| Parent/Guardian Name (Print) | Parent/Guardian Signature | Date of Signature |
|---|---|---|

| Parent/Guardian Name (Print) | Parent/Guardian Signature | Date of Signature |
|---|---|---|

**SIGNATURE BY THE UCLA INVESTIGATOR:**
I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge. The participant has been provided with the Experimental Patient's Bill of Rights.

| Signature of the Investigator Who Obtained Consent | Date of Signature |
|---|---|