UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT
Form 2

Prader-Willi Syndrome and Early-onset Morbid Obesity Natural History Clinical

If you are a parent, as you read the information in this Consent Form, you should put yourself in your child's place to decide whether or not to allow your child to take part in this study. Therefore, for the rest of the form, the word "you" refers to your child.

Participation in this study is completely voluntary. Please read the information below and ask questions about anything that you do not understand before deciding if you want to participate. A researcher listed below will be available to answer your questions.

RESEARCH TEAM AND SPONSORS

Lead Researcher:
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Study Locations:
Institute for Clinical & Translational Science (ICTS), UC Medical Center, Orange, CA
Institute for Clinical & Translational Science (ICTS) UC, Irvine, CA
Children's Hospital of Orange County (CHOC)

Study Sponsor: NIH

PURPOSE OF STUDY

The purpose of this study is to collect natural history information on Prader-Willi syndrome and early-onset morbid (severe) obesity to learn more about how these conditions can affect a person throughout his or her life, from birth to adulthood. This is a group effort involving other hospitals. The information will be stored here at the University of California, Irvine, and at the Data and Technology Coordinating Center at the University of South Florida in Tampa, Florida.

WHY IS THIS RESEARCH?

This is a research study because the researchers are interested in learning more about your condition/disorder. Prader-Willi syndrome and early-onset morbid (severe) obesity are rare disorders and it is hoped that research will help in understanding and improving the treatment of these disorders. Only by studying a large number of patients with a rare disorder can meaningful data be obtained that will help patients.

Study Design

Subjects who agree to participate will participate in a natural history study. A natural history study refers to a study in which the medical aspects of the disorder is monitored long-term without active treatment. The main purpose of the study is:

- To learn more about how Prader-Willi syndrome affects someone over his or her lifetime
- To learn more about how obesity affects someone over his or her lifetime
- To learn more about what gene(s) are involved in Prader-Willi syndrome and early onset obesity

SUBJECTS

Inclusion Requirements

You are eligible to participate in this study if:

1. You have Prader-Willi syndrome (PWS) or Early-onset childhood Morbid Obesity (EMO).

Exclusion Requirements:

1. Pregnant women will be excluded from the DEXA scan procedure.
2. If you do not have Prader Willi or morbid obesity syndrome.

Number of Participants and Time Commitment

This study will include approximately 70 subjects (50 PWS and 20 EMO) and will involve approximately four hours of your time at each annual visit over the next five years or longer if funding for this study continues, in which case we will follow you annually till the age of 3 years. After the age of 3 years, follow-up will be every two years. It is hoped that the study will continue indefinitely and we are optimistic that funding will continue for several years through the National Institute of Health.

PROCEDURES

The study will be conducted in two Phases:

Part 1 – Review of medical records. Consent for medical record review will be via telephone. Medical record review is necessary to determine eligibility in to the study. Review of notes will not occur prior to receiving the signed consent form 1 and assent form 1.

Part 2 – Main procedural study. Consent form 2 and Assent form 2 for children between the ages of 7-17 years, will be signed at the initial visit. No data will be collected or procedures undertaken prior to the understanding and signature on this consent form 2. For children who participate, both parents or guardians will need to sign both consent forms unless a parent is deceased, unknown, incompetent, or not reasonably available, or when one parent has legal responsibility for the care and custody of the child.

An interview will take place between you and the study coordinator or the doctor. During this interview, you will be asked many detailed questions about your medical, developmental, weight, education, behavior and family history. The questionnaire can be mailed ahead of time so that you can review the questions before the visit. You have the right to keep private any information that you want to.

The doctor will perform a complete physical examination of you. This will include taking certain measurements such as your weight, height, body measurements and skin fold measurements. The doctor will perform an examination of the face, the rest of your body, including your genitalia.

Pictures will be taken of you so we can see how you change from year to year and to compare how you look with other patients in the study. These pictures will be of the face and the body from the front and the side. We will do our very best to ensure that your identity is kept strictly confidential. When these photographs are shown, however, others may be able to recognize you if they know you. We will keep the print photographs in a locked cabinet and the digital photographs in a password-protected, secure database. Please write your initials next to one of the following statements (indicating your permission) regarding this photograph:

_____ You may take my pictures to use only for this research project. The pictures will include the front and side of your face and body.
_____ You may take my pictures to use for this research project and for presentations at scientific meetings.
_____ You may take my pictures to use for this research project and for presentations at scientific meetings AND scientific publications.
_____ You may not take my pictures.

May we share the pictures with the main Data and Technology Coordinating Center in Tampa? (circle one & initial) YES_____ NO _____

List any exceptions to using the picture(s): _____

A complete review of your medical records will be done to document past lab results, x-rays, hospitalizations, etc.

We will ask you to bring in a diet history that lists what foods you ate over a period of several days.

A DEXA scan will be done to look at your body composition (i.e. how much fat and muscle you have). A DEXA scan is a painless low dose X-ray procedure. For the test, a patient lies down on an examining table, and the scanner rapidly directs x-ray energy from two different sources towards the bone being examined. This may take 15-20 minutes. Women of child bearing potential will have a pregnancy test prior to the procedure. Women who are pregnant will not have the DEXA scan but can participate in the other procedures. DEXA scan can be done at the next visit if the pregnancy test is then negative.

Standard psychological testing will be done to measure your intelligence including knowledge and reasoning abilities. This testing will take up to 15-30 minutes of your time.

You, your parent (s) and teacher will be asked to fill out a standard behavioral assessment of you. This will take about 10-15 minutes of their time.

Blood test for DNA and RNA studies. (DNA is what makes up our genes. RNA is made from DNA, and it in turn makes proteins. Chromosomes are what "carry" our genes.) We will draw 5-20 ml (1-4 teaspoons). Less than 1 teaspoon of blood will be drawn from small children (0-1 years) and 4 teaspoons from adults. In rare cases a buccal swab (from the mouth) may be done for DNA collection if the collection of blood for DNA was difficult. This may be the case if the veins are very tiny or difficult to find or if you have strong feelings about having a blood test.

The DNA and RNA samples will be anonymously stored ("banked") in our laboratory and Dr. Arthur Beaudet's laboratory at Baylor University with a special code number. At some future date, any unused samples may be destroyed because of the cost of the banking. Some samples may be kept for a very long time or indefinitely. Blood will be sent to the Coriell repository, Camden, NJ to establish cell lines that can be kept growing indefinitely with your consent. All identifiable information that will be collected about you will be removed from the sample and replaced with a code. The Coriell repository may sell your de-identified sample to scientists in research and teaching.

In addition, small amounts of DNA and RNA samples may be shared with other researchers around the world. This sharing occurs to learn more about PWS and early-onset morbid obesity. The samples may be used in related research we hope to be of possible benefit to individuals with PWS and early-onset morbid obesity. The samples may be used for completely unrelated research. The study doctors and the researchers they share samples with get no financial benefit from your sample. Your name is removed from any sample that is shared with other investigators.

- All of the above procedures listed above may be repeated in approximately one year and periodically thereafter, but no more often than once a year.
- Furthermore, someone from this study may call or write you with additional questions.

_____ You may share my blood for storage of DNA and RNA.

_____ You may share my blood for the Coriell Repository to establish cell lines.

_____ You may share my de-identified sample with other researchers, who are interested in my study.

You are free to choose to not participate in any part of this study. If you participate in this study, all of your information will be stored in a locked, password-protected computer, which will be accessible to the principal investigator and her staff. Your name and identifiers will be removed from any data shared with the Data Technology Coordinating Center (DTCC) and the NIH Rare Disease Clinical Research Network (RDCRN). You will be assigned a study number from which people will not be able to identify your family or name. In addition, your records will be kept in a locked chart room. The information may be kept forever.

The genetic and other tests are performed solely for the purpose of research and no results will be released to the subject from any tests performed as part of this research project.

RISKS AND DISCOMFORTS

The possible risks and/or discomforts associated with the procedures described in this study include:

There are no anticipated discomforts or risks from the family history, psychological tests or the physical exam. This study may include risks that are unknown at this time.

The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness or dizziness from the puncture.

The DEXA scan emits a very low level radiation similar to an X-ray that causes no harm. X-rays have the potential of causing harm to the unborn child therefore this test will not be performed in pregnant women.

If you wish to discuss the information above or any discomforts you may experience, you may ask questions now or call the Principal Investigator listed on the front page of this form.
There is a risk of breach of confidentiality however we will ensure that all efforts to minimize this risk will be made.

Answering questions regarding your diet, questionnaires, and the physical exam might cause embarrassment or you may be uncomfortable in answering some of the questions.

There is potential risk of loss of privacy associated with photographs of your face and body. However we will make every effort to remove all identifying information. Some individuals may feel uncomfortable about the photographs being taken.

UNKNOWN RISKS
There may be risks to being in this study that we don't know about now. You will be informed of any changes in the way the study will be done and any additional identified risks to which you may be exposed.

BENEFITS
Subject Benefits
You will not directly benefit from participation in this study.

Benefits to Others or Society
In the long term, we will gain a better understanding of PWS and obesity, which may lead to better diagnostic tests, treatments and therapies for future patients.

ALTERNATIVES TO PARTICIPATION
There are no alternative treatments or procedures available. The only alternative is not to participate in this study.

COMPENSATION, COSTS AND REIMBURSEMENT
Compensation for Participation
You will be compensated $50/visit for travel expenses.

Costs
The only cost involved with this study is the cost of travel to UCI.
There is no cost to you or your insured/third party payer for participation in this study as the procedures are research related.

Reimbursement
You will not be reimbursed for any out of pocket expenses, such as parking or transportation fees.

Compensation for Injury
If you are injured as a direct result of your participation in this study, the University of California will provide reasonable and necessary medical care to treat the injury at no cost to you or to your insurer/third party payer. The University of California does not routinely provide any other form of compensation for injury. It is important that you report any suspected study-related injury to the research team listed at the top of this form immediately.

WITHDRAWAL OR TERMINATION FROM THE STUDY AND CONSEQUENCES
You are free to withdraw from this study at any time. If you decide to withdraw from this study you should notify the research team immediately. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, your safety and welfare are at risk, or the study sponsor decides to stop the study.

If you experience any of the side effects listed in the Risks and Discomforts section or if you become ill during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make the decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

If you withdraw or are removed from the study, the researcher may ask you to complete an exit telephone interview.

CONFIDENTIALITY
Identifiable information will be removed and replaced with a code which will not be shared with anyone outside of the study team to minimize any potential risks of loss of privacy.

All identifiable information will be removed and replaced with a code before the information is loaded on the DTCC database in Tampa for access by other researchers.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Even with the Certificate of Confidentiality, the investigators continue to have ethical and legal obligations to report child abuse or neglect and to prevent you from carrying out any threats to do serious harm to yourself or others. If keeping information private would immediately put you or someone else in danger, the investigators would release information to protect you or another person.

Department of Health and Human Services (DHHS) personnel may request identifying information for purposes of performing audits, carrying out investigations of DHHS grant recipients, or evaluating DHHS funded research projects.

Data Storage
All identifiable research data will be maintained in a secure location at UCI. Only authorized individuals will have access to it. Research data will also be stored electronically on a secure network with password protection. The photographs will also be stored electronically on a secure network with password protection.

The coded data will also be stored at the RDCRN Data Technology Coordinating Center (DTCC) indefinitely.

Data Access
The research team, authorized UCI personnel, the study sponsor National Institute of Health (NIH), and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare. Any information derived from this research project that personally identifies you will not be voluntarily released or disclosed by these entities without your separate consent, except as specifically required by law. Research records provided to authorized, non-UCI entities will not contain identifiable information about you. Publications and/or presentations that result from this study will not include identifiable information about you.

Data Retention
The researchers intend to keep the research data at the RDCRN Data Technology Coordinating Center (DTCC) indefinitely. Other researchers will have access to the data for future research.

NEW FINDINGS

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

OTHER CONSIDERATIONS

Use of Specimens

Any specimen(s) (e.g., blood, urine) obtained for the purposes of this study will become the property of the University of California, Irvine (UCI). The specimen(s) will be discarded or destroyed once they have been used for the purposes described in the protocol. With your consent, blood will be sent to the Coriell repository, Camden, NJ to establish cell lines that can be kept growing indefinitely. All identifiable information that will be collected about you will be removed from the sample and replaced with a code. Coriell is a non-profit organization. The Coriell repository may sell your de-identified sample to scientists in research and teaching. These charges are a processing fee charged to cover costs. These items are not being marketed to make a profit. Researchers who purchase them must all sign an Assurance Form that states they will use them for research only and not commercialize them in any way. Once you provide the specimens to University of California, Irvine (UCI) and Coriell repository you will not have access to them.

Investigator Financial Conflict of Interest

No one on the study team has a disclosable financial interest related to this research project.

IF YOU HAVE QUESTIONS

If you have any comments, concerns, or questions regarding the conduct of this research please contact the research team listed at the top of this form.

If you are unable to reach a member of the research team listed at the top of the form and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact UCI's Office of Research by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@rgs.uci.edu or in person at 5171 California Avenue, Suite 150, Irvine, CA 92697-7600.

VOLUNTARY PARTICIPATION STATEMENT

You should not sign this form unless you have read the attached "Experimental Subject's Bill of Rights" and have been given a copy of it and this consent form to keep. Participation in this study is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center. Your signature below indicates that you have read the information in this consent form and have had a chance to ask any questions that you have about the study.

I agree to participate in the study.

_____ _____

Subject Signature Date

_____

Printed Name of Subject

_____ _____

Legally Authorized Representative/Guardian Signature Date

_____

Printed Name of Legally Authorized Representative/Guardian

_____ _____

Legally Authorized Representative/Guardian Signature Date

_____

Printed Name of Legally Authorized Representative/Guardian

_____ _____

Researcher Signature Date

_____

Printed Name of Researcher

_____ _____

Witness Signature Date

_____

Printed Name of Witness

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

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

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@rgs.uci.edu; or by writing us at 5171 California Avenue, Suite 150, Irvine, CA 92697-7600.