Children's Hospital of Orange County
INSTITUTIONAL REVIEW BOARD

INFORMED CONSENT AGREEMENT

Exercise Aspects of Prader-Willi Syndrome and Childhood Obesity

You are being asked to allow your child to participate in a research study. Before you give your consent to allow your child to be a volunteer, it is important that you read the following information and ask as many questions as necessary to be sure that you understand what your child will be asked to do. If you don't understand something in this consent form, please be sure to ask your study doctor to explain.

Investigators and Sponsor

Principal Investigator:	Susan J. Clark MD
Co-Investigator(s):	Daniela Rubin PhD (CSUF), Daniel Judelson PhD (CSUF), Lien Trinh MD, Keirsten Montgomery FNP, Nancy Varni PNP, Joane Less RN BSN MBA, CCRC, Heather Speer MPH CCRC
Sponsor:	US Army Medical Research and Materiel Command (Department of Defense)

Purpose of this Study

Prader-Willi Syndrome (PWS) is the most common genetic cause of obesity in youth. PWS is a genetic disorder characterized by hypotonia (floppy muscles), obesity, and changed hormonal function. There are 2 nutritional stages in PWS: 1) failure to grow as a baby and 2) the inability to stop eating that can lead to being very overweight.

Exercise is a valuable tool for weight control in youth with PWS, as well as youth without PWS, because it results in positive hormonal and metabolic changes. In healthy, normal-weight youth, the hormonal and metabolic response to exercise leads to beneficial changes such as decreased body fat and increased lean mass. Excess body fat appears to alter these hormonal responses. Given the characteristics of PWS, the hormonal and metabolic responses to exercise in these youth are likely to be different.The purpose of this study is to examine how PWS and the amount of body fat affect the hormonal and metabolic responses to exercise.

Why this is a Research Study

This is a research study because it is important to know more about how the body responds to exercise training. The body's response may be different for children with PWS and that could change how these children should exercise. In youth with PWS, this is important in guiding the prescription for exercise. There are very few exercise studies looking at children with PWS. None of these studies have looked at how the body's hormones change during exercise.

This Exercise Study involves a resistance exercise where your child will do a bench stepping exercise while wearing a vest with weights. Your child may have previously participated in the bicycle riding

portion of this study but that part is now closed. Some basic information that may have been collected during the bicycle portion of the study may be used again. This information will be up to the investigator's discretion.

Number of Participants to be Enrolled and How Long You Will be in the Study

Number of Participants: A total of 60 children are being recruited to participate (30 children who have Prader-Willi Syndrome ages 8-18 years at CHOC, and 30 children who do not have this condition and are 8-11 years old at California State University Fullerton (CSUF).
There will be up to 30 children with PWS enrolled in the stepping exercise at CHOC.

Your child may be enrolled in the Exercise Study (stepping exercise) for up to 1 month.

Procedures to be Followed During the Exercise Study (stepping exercise)

This is what will happen if your child participates in this study:

- Your child will visit CHOC twice and will visit the CSUF campus once.

Visit 1 (at CHOC, about 2 hours long) for Exercise Study (stepping exercise):

- You will complete a medical and exercise history form.
- A physician will confirm the PWS status of your child based on your child's medical record
- The research team will conduct a physical screening (blood pressure, waist circumference, and body mass index) of your child.
- The pediatric endocrinologist, a doctor who takes care of children with hormone problems, will do a sexual development evaluation of your child. This will include briefly looking at the private parts (external genital area for both boys and girls and then breast tissue in girls). This will be done only when the parent is in the room at the same time.
- If no risk factors preventing your child to participate in an exercise test are found, then your child will do bench stepping with a weighted vest for about 20 minutes under the supervision of either Dr. Rubin or Dr. Judelson.
- While he or she is exercising, your child will wear a strap around the chest that measures heart rate (how many times the heart beats per minute).

Visit 2 (at CSUF, about 1 hour long) for the Exercise Study (stepping exercise)

- Your child will be evaluated for his/her body composition using a DEXA (dual energy X-ray absorptiometry) scan, a special X-ray that measures body fat, lean body mass and bone density. The DEXA scan will be done by a doctor licensed to perform these tests.
- Before the DEXA scan if your child is a girl and can become pregnant, the research team will do a urine pregnancy test. The pregnancy test is required by law in the State of California and it is done to ensure the safety of your child because the x-rays may be harmful to a fetus.
- If your child is pregnant, she will not have her body composition evaluated using x-rays and she will not be able to be in the study.
- During the DEXA scan, your child will lay still for a few minutes on a flat table while a machine takes a picture of her/his body using a very weak x-ray under the supervision of Dr. Rubin or Dr. Judelson.

Visit 3 (at CHOC, about 3 hours long, to be completed between 8 am-1pm) for the Exercise Study (stepping exercise)

- Your child will do the stepping exercise consisting of stepping on and off a bench a total of six times separated by 1 minute of rest. During each time your child will step up and down the step ten times with each leg. The total time of this exercise including breaks may be up to 30 minutes. The stepping exercise is done under the supervision of Dr. Rubin or Dr. Judelson.
- Before this exercise test, your child will eat only a pre-packaged breakfast that you will be provided during visit 1. Your child will not be allowed eat anything else until after the exercise test and the rest period are completed, for a total of 3.5-4 hours, but can drink plenty of water
- While exercising, your child will wear a strap around the chest that measures heart rate.
- After completing the exercise test, your child will rest, read a book, or watch TV or a movie for one hour.
- Rather than doing repeated blood draws, the nurse will place an intravenous catheter in a large vein to draw the blood. The catheter is a small, hollow, flexible Teflon tube. Once the catheter is in the vein, repeated blood samples can be easily obtained. The nurse will draw small blood samples (10 mL or approximately 2 teaspoons) from your child before exercise, immediately after exercise, and three times during the hour of rest. The total volume of blood drawn from your child during the study will be about 10 teaspoons (less than 2 fluid ounces).

	Medical screening (Bench Stepping)	**Exercise test (Bench Stepping)**	**DEXA**	**Blood test (Bench Stepping)**
Visit 1	✔	✔		
Visit 2 up to 3 weeks			✔	
Visit 3 up to 4 weeks		✔		✔

You will be informed of any significant new information regarding the study or of any changes in the procedures as described.

Would you be willing to be contacted about other future research opportunities for your child for which he/she may qualify?

Yes_____ No_____ Initials_____

Reproductive Risks

Because the x-rays produced by the DEXA scan may affect an unborn baby, a urine pregnancy test will be conducted for those girls who can become pregnant. If your daughter is pregnant, the DEXA scan will NOT be performed and she will not be able to be in the study.

Risks and Discomforts to This Study

There are some risks to participating in the exercise test in this study. During the exercise test or afterwards, your child may experience:

- An increase in how fast his/her heart is beating
- Increased sweating
- Pain or soreness in the legs
- Shortness of breath
- Fainting
- Headache
- Irritability
- Risk of soft tissue injuries (sprains, strains, and in very rare cases, tears)

These risks are not different from those your child may experience while playing outside during a physical education class or playing sports.

There are also risks involved in the blood drawing procedures that your child will undergo. Those risks are:

Catheter placement – This procedure may cause a little pain or a bruise at the site of catheter insertion. There is rarely any infection.

Blood Draw – This procedure may cause a little pain or bruising at the site of the draw. There is rarely any infection.

There are some risks involved with the DEXA scan.

- Your child's participation in this research study involves exposure to radiation from the DEXA scan. We are exposed to radiation every day of our lives from both natural and manmade sources. The effective dose from the DEXA scan is well below the levels that are thought to result in a significant risk of harmful effects.
- Your child may experience some discomfort while lying still on a flat table for a few minutes during the DEXA scan.

There may be some emotional discomfort that is involved with the physical and sexual development exam but this will not be different from when your child is normally examined at the pediatric endocrinologist's office.

These are the risks that we know about. There may be risks to being in this study that we don't know about now. You will be told of any changes in the way the study will be done and any additional identified risks to which your child may be exposed.

Benefits of the Study

We cannot promise that your child will benefit from this study. Others may benefit from the information gathered from this study. Throughout participation in this study, your child may learn about how her/his body reacts to exercise in a controlled environment. Moreover, if your child is not used to being physically active, she/he will be exposed to different exercises in an encouraging and nurturing environment.

Alternative Methods of Treatment

If you don't want your child to be in this research study, your child can receive information for his/her condition:

- A brief brochure including a series of exercises that your child can perform at home.

Removal From This Study

Your child's study doctor can remove your child from the study without your consent: A) based on the study doctor's judgment to improve your child's medical care, B) because you or your child has not followed the study procedures, or C) because the study sponsor decides to stop the study.

You are free to withdraw your consent and discontinue your child's participation in the study at any time. You should inform the physician of this decision immediately and your child will not further be tested.

Emergency, Side Effects, Illness, or Questions About the Study

If your child needs medical treatment, get treatment, and then let your study doctor know. If you or your child have any questions about the study, or need to talk to the study doctor, you may call:

Monday – Friday 8:00am – 4:30pm **Endocrinology 714-532-8634**
You may leave a message with the secretary and the doctor will call you back. Or you can call Dr. Daniela A. Rubin (657) 278-4704 or Dr. Daniel Judelson (657) 278-5423

Evenings, Weekends, & Holidays **CHOC Hospital 714-997-3000 or 800-992-2462 (CA. Only)**
Ask for the on-call physician for **Endocrinology*.*** You may be asked to leave a message with the page operator, and the physician on-call will return your call as soon as possible.

Compensation for Injury

You must notify the study doctor immediately of any injury or illness that you believe to be a result of participation in this study. If it is determined by the study sponsor Army Medical Research and Materiel Command (Department of Defense) that your child has been injured or become ill as a direct result of being involved in this research study, the sponsor agrees to pay all reasonable and necessary medical expenses to treat your child provided that:

A) All study directions provided to you by the study doctor were followed
B) That your insurance or third party payer, such as Medi-CAL, is not willing to cover the expenses.

Your study doctor will provide supporting information to the study sponsor but cannot guarantee reimbursement.

CHOC is not offering to provide financial compensation for lost wages, disability, or discomfort due to research-related injuries or illnesses. Should you require further information regarding research-

related injuries or illnesses you can contact you child's study doctor using the phone numbers provided on page 5 of this document.

If your child gets hurt or sick because of this research study, she or he can receive medical care at an Army hospital or clinic, free of charge. He or she will only be treated for injuries that are directly caused by the research study. The Army will not pay for transportation to and from the hospital or clinic. If you have questions about this medical care, please contact Dr. Daniela Rubin, at (657)278-4704 or Dr. Daniel Judelson at (657) 278- 5423. If you pay out-of pocket for medical care elsewhere for injuries caused to your child by this research study, contact the co-principal investigators Dr. Rubin or Dr. Judelson. If the issue cannot be resolved, contact the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of the Staff Judge Advocate (legal office) at (301)619-7663/2221.

Confidentiality

Information gathered about your child while participating in this study will be kept confidential according to applicable laws and regulations by the study principal investigator and his/her team, except that:

- The Sponsor of the study, **US Army Medical Research and Materiel Command (Department of Defense), California State University Fullerton (authorized CSUF personnel),** and their representatives will receive information concerning the study and will have access to your child's medical records as they relate to this study.
- Certain agencies, either Federal or State may require your child's medical information concerning this study.
- Representatives of the local IRB or the US Army Medical Research and Materiel Command (Department of Defense) are eligible to review records as part of their responsibility to protect human subjects in research.
- Certain legal actions may require disclosure of your child's medical information.
- Your child's medical information may be released to the CHOC Institutional Review Board or its legally authorized representative

By signing the informed consent, you authorize such access to your child's data. If the results of this study are published, your child's identity will be kept confidential.

Cost/Compensation

You and your child will be reimbursed to participate in this research study. Your child will receive a $10 gift for participating in the first exercise study (visit 1) and $25 for participating in the second test (Visit 3). These gifts can be gift certificates, board games, sports equipment, and/or crafts. You will be reimbursed for parking fees and gas mileage to both CHOC and CSUF, The parking reimbursement will be up to $8, and gas mileage at CSUF rates ($ 0.50 per mile) up to $60 for each roundtrip. No other compensation is available for participating in this research study. You will not be charged for any study required tests. No tests will be charged to your insurance and you The Principal Investigator of this study, Dr. Susan Clark and/or her designated CHOC co-investigators, will be reimbursed for their time and expense of doing this research.

The law requires that CHOC submit an IRS 1099 form for individuals to whom it provides compensation exceeding $600 per calendar year. Compensation provided by this research study will count toward the annual total for this purpose.

Participant Rights and Study Withdrawal

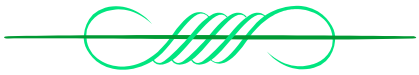
You and your child are agreeing to be in this research study by your own choice. You and your child can decide not to be in the study at all or you can decide to stop being in the study even after the study has started. No matter what you decide your child will still get your doctor's care and won't lose any other benefits you have now. You also won't be giving up any of your child's legal rights by signing this consent form.

It is important that you and your child understand the details about this study. If you or your child have any questions that haven't been answered, please be sure to ask your study doctor or research coordinator.

If you have any questions about your child's rights as a participant in a research study, please contact the CHOC Institutional Review Board for the protection of research participants through:

Office of Research Compliance
(714) 532-8869

This research project has been reviewed by an institutional review board for the protection of the rights of human participants in research projects, in accordance with federal regulations**. This informed consent is not valid without the CHOC Institutional Review Board stamp of approval.**



_____
Parent's Initials
CHOC form version: 12/12/08

Children's Hospital of Orange County
INSTITUTIONAL REVIEW BOARD

PEDIATRIC ASSENT FORM

NOTE: A Pediatric Assent Form is necessary for patients 7-11 years of age.

Study Title: Exercise Aspects of Prader-Willi Syndrome and Childhood Obesity

- I understand that I am being asked to be in this research study because my doctor and his/her helpers want to learn more about how exercise can be used as treatment for my Prader-Willi Syndrome.
- I understand that I will come to CHOC and exercise on two different days, and do a bench stepping exercise while wearing a weighted vest.
- I understand that bench stepping may make me feel tired, or may make my legs tired.
- I understand that at the second visit, the nurse will put a small plastic tube into one of my arm veins so blood can easily be drawn five times without having to poke me.
- I understand that on the second day that I do exercise, I will only have breakfast before exercising.
- I understand that after I exercise on the second day I will rest (sit) for 1 hour while watching a movie or reading a book.
- I understand that I will have x-rays. This is like having a picture taken. This will be at a different place on another day at the California State University Fullerton.
- I understand that I will need to lie still for a few minutes on a flat table while I am having the x-rays.
- I understand that the second study will also have blood draws during the second visit and that I may feel tired after the exercise.
- I understand that I may change my mind about being in this study and that nobody will be angry with me.
- I understand that I can ask questions about what my doctor and his/her helpers are doing and things will be explained to me in a way that I will understand.
- My doctors are Dr. Clark and Dr. Trinh and I can call them at 714-532-8634.
- If I have any exercise questions, I can call Dr. Rubin or Dr. Judelson at 657-278-4704/5423.

_____

Signature of 7 to 11 Year Old Participant Date

_____

Signature of Person Obtaining Consent (Principal or Co- Investigator) Printed Name Date

_____
Parent's Initials

Children's Hospital of Orange County
INSTITUTIONAL REVIEW BOARD

Human Research Participant's Bill of Rights

(For Medical Experiments)

Pursuant to the California Protection of Human Subjects in Medical Experimentation Act, any person who is asked to consent to become a participant in a research study involving a medical experiment or any person who is asked to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedure to be followed in the medical experiment and any drug or devices to be utilized.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the participant reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the participant, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the participant after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the participant may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the participant's decision.

Signature and Consent

My signature below indicates that I am the parent/legal guardian of this child, and that he/she is not a ward of the state or other agency. I have read the above information about the study***, Exercise Aspects of Prader-Willi Syndrome and Childhood Obesity.*** I have had a chance to ask questions to help me understand what will be expected of my child in this study. I agree to allow my child to be in the study and I have been told that I can change my mind later if I want to. I have been told that by signing this consent form I am not giving up any of my child's legal rights. I have been informed that I will be given a signed and dated copy of this agreement which includes the Participant's Bill of Rights for my records.

Name of Participant (printed)	Age	
Signature of Parent/Legal Guardian or Participant if 18 Years of Age or Older		Date
Printed Name of Parent/Legal Guardian if Participant is under 18 Years of Age		Relationship
Signature of Witness	Printed Name	Date
Signature of Person Obtaining Consent (Principal or Co- Investigator)	Printed Name	Date
Signature of Translator (if used)	Printed Name	Date

Assent for Participants Ages 12 Through 17

My signature below means that I have read the above information about the study, ***Exercise Aspects of Prader-Willi Syndrome and Childhood Obesity.*** I have had a chance to ask questions to help me understand what will be expected of me in this study. I agree to be in the study and I have been told that I can change my mind later if I want to. I have been told that by signing this consent form I am not giving up any of my legal rights. I have been informed that I will be given a signed and dated copy of this agreement and of the Subject's Bill of Rights for my records.

Signature of Participant	Date

CHILDREN'S HOSPITAL OF ORANGE COUNTY
INSTITUTIONAL REVIEW BOARD

Authorization To Use, Create and Disclose Health Information for Research

Study Title: Exercise Aspects of Prader-Willi Syndrome and Childhood Obesity

In this form, the word "you" means both the person who takes part in the research and the person who gives permission to be in the research.

Purpose of this Authorization

We are asking you to take part in the research described in the consent form for the study whose title is identified above. To do the research described, the research staff at CHOC needs to use, create and/or disclose your health information during the course of this study. By law, we have to tell you how we do this and get your permission. This form describes what we will do with your information. Please read it carefully. If you agree with it, please sign your name at the bottom. You will get a copy of this form after you have signed it.

Description of Health Information that will be Used/Disclosed

With your permission, the health information that will be used, created and shared includes:

- All information about you that is collected during the research study. This might include the results of exercise, body composition and blood tests that become part of the study records; questionnaires that you might be asked to fill out as part of the study and other records from the study.
- All health information in your medical records that is needed for this research study. These might include the results of physical exams, blood tests, diagnostic and medical procedures and your medical history.

Person/Organization Authorized to Receive Your Health Information

We may share your health information with people at CHOC who help with the research. We may also share your health information with certain people and groups outside of CHOC. These may include:

- The sponsor of the study, **US Army Medical Research and Materiel Command (Department of Defense), California State University-Fullerton (authorized CSUF personnel)**, and its representatives
- Government agencies of the United States and foreign countries, review boards, and others who watch over the safety, effectiveness, and conduct of the research
- Other researchers when a review board approves the sharing of the health information
- Other researchers at California State University Fullerton (Dr. Daniela Rubin, and Dr. Daniel Judelson)
- Others, if the law requires

Duration of Authorization and Future Use of Health Information

This authorization will expire 50 years from the date you signed it unless you revoke (cancel or withdraw) it sooner. If you sign this form, we will use, create, and share your health information

until the end of the research or until the expiration date of your authorization, which ever comes first.

Your information may also be useful for other research studies. We can only use your information again if the CHOC Institutional Review Board gives us permission. This committee may ask us to talk to you again before doing the research. But the committee may also let us do the research without talking to you again if we keep your health information confidential.

Your Privacy Rights in Research
You do not have to sign this authorization form. If you choose not to allow us to use your protected health information, you cannot participate in this research study. You will not be able to receive any research-related treatment described in the study consent form. We will discuss any non-research alternatives available to you. No matter what you decide you will still get your doctor's care and will not lose any of the benefits you have now.

You may revoke this authorization at any time by notifying the principal investigator in writing at the address below. If you do revoke your authorization, any information previously disclosed cannot be withdrawn. Once information about you is disclosed in accordance with this authorization, the recipient may redisclose it and the information may no longer be protected by federal privacy regulations. However, the recipient may be prohibited from disclosing substance abuse information under the Federal Substance Abuse Confidentiality Requirements.

If you do revoke your authorization, you may need to leave the research study if all the necessary information has not been collected. We will tell you if this is the case. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

A copy of CHOC's Notice of Privacy Practices will be given to you upon request.

Access to Protected Health Information Collected, Used, or Disclosed Under this Authorization
You have the right to see and copy your Personal Health Information related to the Study, by contacting the study doctor for as long as this information is held by CHOC. However, to ensure the scientific integrity of the Study, you agree that you may not be able to review some of your records related to the Study until after the Study has been completed.

Questions About this Authorization
If you have any questions, please ask the researcher. You can also call the CHOC Privacy Officer at (714) 532-8466 with questions about the use of your health information.

Signature and Date

My signature below indicates that I am the parent/legal guardian of this child, and that he/she is not a ward of the state or other agency. I have read the above information about the study**, Exercise Aspects of Prader-Willi Syndrome and Childhood Obesity.** I agree to the use, creation, and sharing of my/my child's health information for purposes of the research study described in this form and the study consent form.

Name of Participant (printed)	Age	
Signature of Parent/Legal Guardian or Participant if 18 Years of Age or Older		Date
Printed Name of Parent/Legal Guardian if Participant is under 18 Years of Age		Relationship
Signature of Witness	Printed Name	Date
Signature of Person Obtaining Consent (Principal or Co- Investigator)	Printed Name	Date
Signature of Translator (if used)	Printed Name	Date