OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: 6509

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

Clinical Research Consent Summary

TITLE: Magnetic Resonance Imaging and Biomarkers for Muscular Dystrophy

PRINCIPAL INVESTIGATOR: William Rooney, PhD (503) 494-1840

You are being asked to join a research study. You do not have to join the study. Even if you decide to join now, you can change your mind later.

Some parts of this study are optional, and are not part of the original study. You may participate in the main study without participating in the optional parts. The optional portion is the collection of saliva, blood and/or urine. There is a separate consent form for the optional portion of this study, where the risks and procedures are discussed in detail. By consenting in this form, you are not agreeing to be a part of the optional study.

1. The purpose of this study is to learn more about Duchenne muscular dystrophy.
2. National Institutes of Health is paying for the research study.
3. The length of this study is 5-10 years. The length of the time in this study depends on your individual schedule and date of enrollment. You will be asked to come annually for a study visit. Some individuals will be asked to come for 3 month or 6 month visits in between annual visits.
4. There are risks involved in participating in the study, which will be discussed in the Risks and Discomforts section of this form.
5. If you agree, samples and information collected during the study may be saved for future research.
6. Samples collected during the study may be used for genetic research.

CO1450

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
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BIRTHDATE _____

IRB#: 6509

Clinical Research Consent and Authorization Form

TITLE: Magnetic Resonance Imaging and Biomarkers for Muscular Dystrophy

PRINCIPAL INVESTIGATOR:

William Rooney, PhD (503) 494-1840

CO-INVESTIGATORS:

Erika Finanger, MD (503) 494-2598
Barry Russman, M.D. (503) 221-3424
Eric Baetscher, B.S. (503) 418-1529
Laura McMahon, B.S. (503) 418-1540
Catherine Strauss, B.S. (503) 494-1592

FUNDED BY: National Institutes of Health

PURPOSE:

"You" means your child in this consent form.

You have been invited to be in this research study because you have Duchenne muscular dystrophy (DMD), a genetic muscle condition seen only in boys. DMD causes weakness of large hip and shoulder muscles which later spreads to the small muscles of the body. This weakness is responsible for a decreased ability to walk and to perform other daily tasks. The purpose of this research study is to learn more about the functional and strength changes that occur in muscles of the lower leg and/or arms in boys with DMD. In addition, the goal of this study is to develop an improved MRI (imaging) procedure to monitor the progression of disease in children with DMD. The study aims to establish and confirm an improved imaging procedure to study muscle damage in patients with DMD. We will compare the muscles of boys with DMD with muscles of children of the same age who do not have DMD and determine whether this new technique can be used to monitor disease progression. The amount of muscle damage that we measure will be related to your performance in daily activities such as walking and use of the arms.

CO1450

This study requires annual visits to OHSU, and may include 3 month and 6 month visits in between annual visits. The length of your participation in this study is 5 to 10 years, depending on your enrollment date. If you began the study in the first 5 years (before 2010), you will be asked to participate for 5 more years. If you began the study after 2015, you will participate for up to 5 years.

There will be approximately 200 DMD and 100 control subjects involved in this study at three separate sites (here, at Shriners Hospital for Children and OHSU in Portland, the Children's Hospital of Philadelphia, and the University of Florida at Gainesville). At Shriners Hospitals for

Children – Portland/Oregon Health & Science University we expect that about 100 subjects will participate.

PROCEDURES:
If you agree to participate, Magnetic Resonance Imaging (MRI), and Magnetic Resonance Spectroscopy (MRS) measurements will be performed on your leg and/or arm muscles. The MRI technique allows us to get pictures of your leg and/or arm muscles and MRS gives us biochemical information of your leg muscles. With this information we can tell damaged muscle from your healthy muscle. It will also give us more information about the fat inside of your muscles. To see how strong your leg and/or arm muscles are, we may ask you to walk around the lab, climb a few steps, and perform functional arm movements. We will also look at your medical records to get information about what medicines you take. We will also take a small blood sample for genetic testing of the dystrophin gene if it has not already been done.

You must have the gene abnormality (mutation) associated with DMD in order to participate in this study. All boys with DMD who are between 3 and 18 years of age are eligible for this project, with the exception of those with any metal in their bodies that makes it unsafe to have an MRI/MRS. In addition, we cannot include patients who have had an injury to their legs and/or arms that make their muscles weaker.

If you choose to participate in this study, you will be asked to attend at least one session each year consisting of MRI/MRS, strength, functional testing and quality of life measures at regular intervals (6 or 12 months) over a period of 5-10 years. Depending on your performance of daily activities, we expect that you will participate in about eight to twelve sessions. At the beginning of the study, you will need to participate in two MRI/MRS sessions distributed over 1-2 days.

In a small group of subjects that enter into the study steroid naïve, if and when you decide to start steroids, we may request two additional sessions in between your annual visits which would be at 3 month and 6 month intervals.

If you are unable to complete the 10m walk/run at your annual visit, you may be asked to come back in 6 months for a follow-up visit, and then continue with your annual visit schedule.

The nature of the study, risks, inconveniences, discomfort, and other additional information is outlined below. You are urged to discuss any questions you have concerning the study with the staff members.

For subjects entering study on corticosteroids:

	Baseline	Annual Visits	*6month follow-up
Consent Discussion, Screening tests and medical history	X	X	X
Arm MRI	X	X	X
Leg MRI	X	X	X
Functional Testing	X	X	X
Total time	4-6 hours	4-6 hours	4-6 hours

For some subjects not entering on corticosteroids:

	Baseline	3month visit	6month visit	Annual Visits	*6month follow-up
Consent Discussion, Screening tests and medical history	X	X	X	X	X
Arm MRI	X	X	X	X	X
Leg MRI	X	X	X	X	X
Functional Testing	X	X	X	X	X
Total time	4-6 hours	4-6 hours	4-6 hours	4-6 hours	4-6 hours

Your child will be given a $20 Toys R Us gift card for your participation in this study.

You may be asked to give us health information about your relatives. Any information you give us will be kept confidential as described in this consent. We will not contact your relatives without their permission. We may discuss with you the possibility of including your relatives in the study in the future.

The ways we will collect data about you for this study are outlined below.

Magnetic Resonance Imaging (MRI)
This part of the study will be done at the Advanced Imaging Research Center (AIRC) at OHSU.

MRI is a procedure that allows doctors to look inside the body by using a scanner that sends out a strong magnetic field and radio waves. You will lie on a platform inside the magnet. A series of images will be taken from your thigh and lower leg and/or arms. There may be two separate scanning periods for your arm and leg. Each scanning period will take approximately 90-120 minutes, during which you are required to lie still. During the entire procedure, one of the investigators will be present with you and will advise you of the progress of the study, making sure that you are comfortable. Although the measurement is painless, it will be somewhat noisy inside the magnet due to a hammering sound made when a large electrical current is pulsed through the magnet. Disposable earplugs will be provided to reduce the noise.

Magnetic Resonance Spectroscopy (MRS)
This procedure will give us biochemical information about your muscles and will help us discriminate between damaged muscle, healthy muscle and fat inside of your muscles. These measurements will be performed at the same time as the MRI procedure.

Muscle and Functional Performance tests
This part of the study will be done at Rehabilitation Services at OHSU.

Range of motion (ROM) measurements may be taken for the joints in your legs and/or arms. Your thigh and knee muscles, calf muscles and your ankle dorsiflexors (muscles on the front of your leg that allow you to pull up your toes) and/or selected arm muscles will then be tested using one of the strength testing methods. We may ask you to push or pull your foot or kick out your leg as hard as you can in order to determine your muscle strength and/or pull or push your arm to determine your muscle strength in your arms. Your knee and ankle or shoulder and elbow will not move during the testing itself. We may also test your muscle strength manually by demonstrating a movement and then asking you to perform the movement with your arms or legs. If you are able to complete the ROM against gravity we may apply graded resistance with our hand or a hand held device called a dynamometry to see if you can hold that position. In addition to testing your muscles, you may be required to perform simple tasks such as getting

up from the floor, climbing steps, and walking at different speeds and distances for up to 6 minutes. You may also be asked to perform simple tasks with your arms to determine your arm function. If at any time you become tired you will be allowed to rest.

You may be asked to participate in motion analysis which would look at your walking pattern. If you are asked to do this you will have several small reflective balls which are self-adhesive placed on bony landmarks on your arms, legs, trunk, and head that will allow for several high speed cameras to capture your walking pattern. You will then be asked to walk at different speeds with the markers on your body. If at any time you become tired you will be allowed to rest.

Blood Sample
We may also ask you to donate a blood sample to perform genetic testing of the dystrophin gene. For this purpose a single blood sample will be taken from your arm by a member of the research team at Oregon Health and Sciences University (OHSU). A small, sterile needle will be inserted into a vein in your arm and less than 1 teaspoon of blood will be taken. A small bandage will be placed over the puncture site to reduce the risk of bleeding. This sample will only be asked to be taken if genotyping of the dystrophin gene has not already been done.

Previously Collected Skin Samples
We are no longer collecting skin samples for this study.

You may have had a skin sample collected in previous years of the study. As originally described in the consent form, the skin sample was collected and is stored in a tissue bank for future research and is only labeled with a code that will not identify you.

In the future, the collected skin sample may continue to be given to researchers for other research studies. These studies may include genetic research. The samples will be labeled as described in the Confidentiality section of this form.

The Optional Study
There is an optional portion to this study that has a separate consent form that we may ask you to participate in. You are not consenting to be a part of the optional study by signing this consent form. The optional study includes collecting saliva, blood, and urine samples. The optional study blood sample is different from the blood sample described above under Blood Sample.

Medical information
We will also get information about the medicine you take, your medical history, and the stage of puberty you are in. Your parent will be asked to login to the ImagingDMD secure website (http://imagingdmd.org) with a username and password to complete an online medical history, medication log, and questions to determine your stage of puberty. Depending on your parent's availability, we may collect this medical information over the phone or during your visit to OHSU. Your parent will be asked to update any changes to this information at every visit. This will take about 10 minutes or less to complete.

If your parent is not comfortable performing the puberty assessment, Dr. Barry Russman, Dr. Finanger, or an OHSU registered nurse will briefly look at your pubic area to assess what stage of puberty you have reached. This will be done in the presence of one of your parents or guardian.

The medical history will ask questions about your physical strength, use of assistive devices, recent surgeries or injuries, and other information. This medical information is collected for research correlations as well as your safety and eligibility in the study.

Consent for future contact
We would also like to know whether you would like to be contacted and asked about possible participation in future research studies related to muscular dystrophy. If you check the box below you may be sent an informational letter about your possible participation in other research studies involving muscular dystrophy from other agencies including but not limited to Parent Project Muscular Dystrophy. Please indicate your preference by checking yes or no below:

Yes: _____ No: _____ Your initials: _____

ACCESS TO YOUR TEST RESULTS
If genotyping of the dystrophin gene has not already been done, and a blood draw and genetic testing is performed as outlined in the Procedures section under the title Blood Sample, we will give you the results. This is not a full genetic report, but only analysis of the dystrophin gene. Dr. Erika Finanger will share the results with you. The results will not be put into your medical record.

Because genetic information is complex and sensitive, the results should be discussed with a genetic counselor or your primary care provider who can answer your questions or discuss your concerns. You would be responsible for all costs associated with having the test repeated and visiting a doctor or genetic counselor to discuss the results.

The MRI/MRS scan is being done to answer research questions, not to examine your leg or arm for medical reasons. This MRI scan is not a substitute for a clinical scan (the type a doctor would order). The research scan may not show problems that may be picked up by a clinical MRI scan. If we find an abnormality that requires urgent follow-up, we will contact you and your doctor (with your permission) to help answer questions and get the right follow-up care for you. It is possible that you could be unnecessarily worried if a problem were suspected, but not actually found.

You may request copies of your MRI/MRS scan to be burned to a disc. A radiologist report will not be provided to you. The disc will be marked for research use only, and specified that it is not to be used for clinical use. The results of the research MRI/MRS scan will not be made available to you because the research is in an early phase and the reliability of the results is unknown.

RISKS AND DISCOMFORTS:
The magnetic resonance imaging (MRI) machine is a powerful magnet. There are no known risks from the magnet itself. However, if you have metal in your body, the magnet may cause the metal to move. If you know of any metal in your body, tell the investigator because you may not be able to have an MRI. Review any dental treatments you have had with the investigator, since these may involve metal. The most common discomfort of an MRI is the length of time you must lie still or flat while the scan is being performed. Some people with claustrophobia (fear of closed spaces) may find the MRI machine too confining. Finally, the MRI scanner makes loud beeping or thumping noises, so you may be offered protective earplugs to wear during the scan.

If you have not had genotyping of the dystrophin gene, we will draw blood from your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

Some of the questions we ask regarding your puberty stage, medical history, and disease progression may seem very personal or embarrassing. They may upset you. You may refuse

to answer any of the questions that you do not wish to answer. If the questions make you very upset, we will help you to find a counselor.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.

Although we have made efforts to protect your identity, there is a small risk of loss of confidentiality. If the results of these studies of your genetic makeup were to be accidentally released, it might be possible that the information we will gather about you as part of this study could become available to an insurer or an employer, or a relative, or someone else outside the study. Even though there are certain genetic discrimination and confidentiality protections in both Oregon law and federal law, there is still a small chance that you could be harmed if a release occurred.

BENEFITS:
You may or may not personally benefit from being in this study. However, by serving as a subject, you may help us learn how to benefit patients in the future.

ALTERNATIVES:
You may choose not to be in this study.

CONFIDENTIALITY
We will take steps to keep your personal information confidential, but we cannot guarantee total privacy.

We will create and collect health information about you as described in the Purpose and Procedures sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The funder of this study, National Institutes of Health, and the funder's representatives
- University of Florida
- The Office for Human Research Protections, a federal agency that oversees research involving humans
- The Department of Health and Human Services

Those listed above may also be permitted to review and copy your records.

We may also share your information with other researchers, who may use it for future research studies.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

Under Oregon law, suspected child or elder abuse must be reported to appropriate authorities. OHSU complies with Oregon state requirements for reporting certain diseases and conditions to local health departments.

When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

Data from this study may be shared with other investigators for future research studies. All identifying information about you will be removed from the samples before they are released to any other investigators.

We may continue to use and disclose your information as described above indefinitely.

COMMERCIAL DEVELOPMENT:
Information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

COSTS:
There will be no cost to you or your insurance company to participate in this study.

We may request your social security number in order to process any payments for participation.

LIABILITY:
If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Erika Finanger [503-494-2598 (work) or 503-308-0702 (cell)].

If you are injured or harmed by the study procedures, you will be treated. OHSU and National Institutes of Health do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.
If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

This federally funded study also does not have the ability to provide compensation for research-related injury. If you are injured or become ill from taking part in this study, it is important to tell your study doctor. Emergency treatment may be available but you or your insurance company will be charged for this treatment.

PARTICIPATION:
If you have any questions, concerns, or complaints regarding this study now or in the future, contact Erika Finanger [503-494-2598 (work) or 503-308-0702 (cell)], or Bill Rooney [503-494-1840 (work) or 503-944-9065 (cell)].

This research is being overseen by an Institutional Review Board ("IRB"). You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study. Some parts of the study are optional. You can choose not to participate in some or all of the optional parts but still participate in the rest of the study.

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. You can choose to withdraw from some or all of the optional parts of this study without withdrawing from the whole study. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study or change which parts of the study you are participating in.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Laura McMahon
Oregon Health & Science University
Advanced Imaging Research Center
3181 SW Sam Jackson Park Road
Mailstop Code L452
Portland, OR 97239-3098
mcmahola@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If in the future you decide you no longer want to participate in this research, no one will be upset, and you will not be asked to come to any further visits. However, the MRI/MRS data and information acquired about you in the study will not be destroyed and we will continue to use it for research.

You may be removed from the study if you fail to meet eligibility criteria or if you do not follow study instructions.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

The participation of OHSU students or employees in OHSU research is completely voluntary and you are free to choose not to serve as a research subject in this protocol for any reason. If you do elect to participate in this study, you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator's department, or your grade in any course.

Children between 7 and 17 will be provided with their own assent form.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

OREGON HEALTH & SCIENCE UNIVERSITY
INSTITUTIONAL REVIEW BOARD
PHONE NUMBER (503) 494-7887
CONSENT/AUTHORIZATION FORM APPROVAL DATE

APR 26, 2016

Do not sign this form aft8r the expiration date of: APR 25 2017

Subject Printed Name		
Parent, Guardian, or legally authorized representative Printed Name	Parent, Guardian, or legally authorized representative Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only. If the interpreter is affiliated with the study team, the signature of an impartial witness is also required.

Print name of interpreter: _____

Signature of interpreter: _____ Date: _____

An oral translation of this document was administered to the subject in _____ (state language) by an individual proficient in English and _____ (state language).

If applicable:

Print name of impartial witness: _____

Signature of impartial witness: _____Date: _____

See the attached short form for documentation.