CHILDREN'S NATIONAL MEDICAL CENTER

Department of Research Center for Genetic Medicine
111 Michigan Avenue, NW
Washington, DC 20010
(202) 476-6011

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY AND AUTHORIZATION TO USE PROTECTED HEALTH INFORMATION

TITLE OF STUDY: An Exercise Intervention in Insulin-Resistant Minority Adolescents

PRINCIPAL INVESTIGATOR: Eric P. Hoffman, PhD; Director, Center for Genetic Medicine

"You" refers to "You" or "Your Child" throughout this document

INTRODUCTION: We would like to invite you to be part of a research study at Children's National Medical Center. Before you decide if you would like to participate, we want you to know why we are doing the study. We also want you to know about any risks (anything unexpected that might happen) and what you will be expected to do in the study.

This form gives you information about the study. Your doctor will talk to you about the study and answer any questions you have. We encourage you to discuss this study with your family and anyone else you trust before making your decision. We will ask you to sign this form to show that you understand the study. If your child is seven years old or older, we may talk to your child about the study and ask your child to sign a form like this one but shorter. We will give you a copy of this form to keep. It is important that you know:

- You do not have to join the study;
- You may change your mind and stop being in the study any time you want.
- If we make any important change to the study we will tell you about it and make sure you still want to be in the study.

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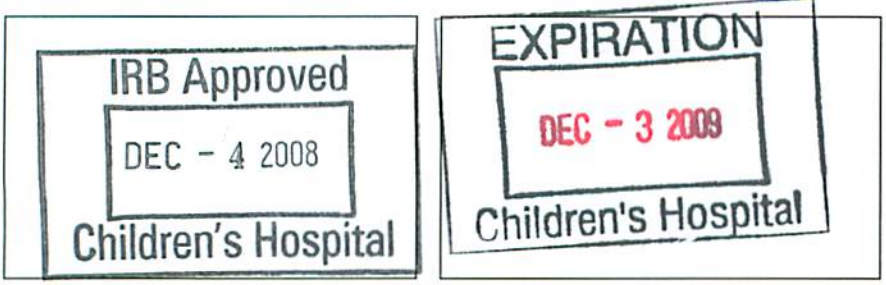

A. PURPOSE OF STUDY

1. The purpose of this study is to determine the effects of 3 months of supervised exercise on children aged 14 to 18 with insulin resistance.
2. You are being asked to participate in this study because you are 14 to 18 years old; African American or Hispanic; sedentary (exercising less than twice a week for less than 20 minutes); a non-smoker; at high risk for developing insulin resistance; has a BMI-for-age greater than or equal to the 95th percentile; no history of chronic illnesses related to metabolism; no thyroid dysfunction; not taking any medications know to affect metabolism; and not pregnant nor lactating.

B. PROCEDURE

1. Screening Visits

a. *Screening Visit #1*: The first screening visit will include filling out medical and physical activity questionnaires. Height and weight measurements will be taken. Interested participants that meet the study inclusion criteria (outlined above) will be invited to a second screening to further assess study eligibility.

b. *Screening Visit #2:* The second screening visit includes a physical examination, urine pregnancy test (for female subjects only) and Oral Glucose Tolerance Test (OGTT). During the OGTT a blood draw of about 2 teaspoons (8mL) for fasting plasma glucose and insulin and about 1 teaspoon (4mL) for 2-hour plasma glucose will be drawn.

After this visit, results will be reviewed and reported to you. *You will only be allowed to participate in the study if you meet the OGTT inclusion criteria* (fasting plasma glucose greater than or equal to 100 mg/dl and less than 126 mg/dl or/and 2-hour OGTT plasma glucose greater than or equal to 140 mg/d and less than 200 mg/dl and fasting insulin greater than 17 µU/ml) *and all* of the previously stated inclusion criteria.

If you have had an oral glucose tolerance test within the last 3 months and meet the OGTT inclusion criteria, you will be asked to complete a physical examination and pregnancy test (female subjects only) to further determine eligibility.

If you do not meet the OGTT and/or the other previously defined inclusion criteria, you will be notified and will not be eligible to continue study

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participation. If a female subject becomes pregnant anytime during the study, she will have to notify a study team member immediately and discontinue participation. With her permission, the parent(s) or legal guardian(s) will then be notified.

2. **Study Participation:**
   Participants with insulin resistance including impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) will be invited to continue with the study.
   a. You will meet with a registered dietitian to discuss dietary intake. You will be encouraged not to make any drastic changes to your current food intake throughout the study and be taught how to complete a 3-day food record. A nutrition session will be provided to address any dietary concerns after the exercise period.
   b. Following dietary assessment, participants will have percent body fat and lean muscle mass determined by dual-energy x-ray absorptimetry (DEXA) and skinfold caliper. A waist circumference will be measured. A treadmill exercise test will be done to measure cardiovascular fitness. All tests listed above will be conducted at the Children's National Medical Center, General Clinical Research Center (GCRC), except for insulin testing which will be performed by Quest Diagnostics in Chantilly, V.A.
   c. To determine insulin sensitivity (this will require a 12-hour overnight fast), an intravenous glucose tolerance test (IVGTT) will be performed at the Georgetown University Medical Center, GCRC. One intravenous catheter will be inserted into the participant's arm where insulin and glucose will be injected. Another catheter will be inserted at the hand where about total 9 tablespoons (~135mL) of blood samples will be collected during this 3-hour procedure. The blood drawn in this test will also be used for measuring plasma lipids. With your permission, some of your drawn blood here will be banked for future analysis of other biochemical markers related to metabolism.
   d. After the completion of all preliminary testing, you will be enrolled into a 3-month supervised exercise program. You will be asked to come into Children's National Medical Center, 2 to 4 times a week, depending on the amount of exercise per session, to complete about 170 minutes of supervised moderate-intensity exercise per week. The equipment used will be a stationary bike, an elliptical trainer, and/or a treadmill. A heart rate monitor and blood pressure monitor will be used during all exercise sessions to record data. The exercise sessions will be experimental in nature; they are being conducted to determine

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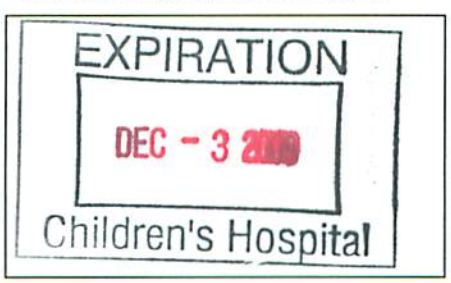

if your impaired glucose levels and other blood markers change after participation.

e. Following the exercise period, you will be asked to provide 3-day food records from each week of the 3-month period. These will be analyzed and discussed in a nutrition session. You will undergo a second IVGTT, DEXA, treadmill exercise testing, and anthropometric measurements (ie. height, weight, abdominal skinfold, waist circumference), to determine if any physical changes occurred after the exercise intervention. Urine pregnancy testing will be done again on all female subjects.

C. POTENTIAL RISKS/DISCOMFORT

1. Screening Visit #2, Blood draw: The needle puncture of your vein to obtain the blood sample (ie. OGTT) may result in bleeding, pain, soreness or bruising. To minimize these risks, the procedure will be performed by individuals trained and experienced in obtaining blood samples.

2. Study Participation:

a. Exercise Test: Minimal risk of cardiovascular events such as abnormal heart rate (arrhythmias) or heart attack exists with any exercise training as well as the maximal exercise test. These risks will be minimized by conducting a physical exam during the screening phase as well as by the use of a heart rate monitor while exercising.

b. Exercise Sessions: Minimal risk of cardiovascular events also occur with supervised exercise; the risk of an event is further reduced by pre-screening (physical and Exercise Test). Additional symptoms that may occur with the exercise sessions include fainting, dizziness and muscle soreness.

c. DEXA Scan: The risk associated with body composition testing (DEXA) consists of exposure to low levels of radiation. It must be noted, however, that this radiation is not necessary for your medical care and is for research purposes only. The total amount of radiation you will receive from this study is from 2 tests (Study Visits 1 & 4). The NIH Radiation Safety Committee has reviewed the use of radiation in this research study and has approved this use as involving minimal risk and necessary to obtain the research information desired. From 2 DEXA scans, you will receive an effective dose of less than one thousandth of one rem (unit of measure for scan). An average person in the United States receives this much radiation every day from natural background sources such as the sun, outer space and from radioactive materials that are found naturally in the air and

soil. In this scan, the skin is the only part of the body that is exposed, which is less vulnerable to radiation than most other parts of the body. The chance anyone has of eventually dying of cancer is 1 in 4. After receiving these tests, that chance remains the same at 1 in 4, which means these tests do not increase your chance of developing cancer. If you are pregnant, you cannot participate in this study. The human embryo is more sensitive to radiation than adults or children.

c. IVGTT: Risks associated with IVGTT include low blood sugar at the completion of the test, bruising or infection at the site of the catheter. In order to minimize risk of bruising and infection, a trained nurse will perform this test using aseptic techniques. When the study team attempts to locate your veins for venipuncture, multiple needle-sticks may occur, with a maximum of 3 needle sticks per arm. If the study team is still unable to locate your veins for venipuncture, you will not be able to complete the IVGTT and will no longer be eligible to be in the study. In order to reduce the risk of hypoglycemia at the completion of the test, a meal high in carbohydrates will be provided for you at the completion of the test.

D. VOLUNTARY PARTICIPATION

There will be no penalty or loss of benefits to which you are otherwise entitled if you decide to withdraw from the study.

E. POTENTIAL BENEFITS

1. Screening Visit #2:

You will receive a free screening test for diabetes by measuring fasting plasma glucose and insulin levels and 2-hour plasma glucose levels.

2. Study Participation:

a. Individual evaluation of body composition and cardiorespiratory function.
b. Individual exercise prescription for the exercise period.
c. Individual dietary evaluation and nutrition counseling.
d. Increased knowledge of exercise to reduce the risk of diabetes and other complications.
e. Increased knowledge of exercise equipment.
f. Improved strength and endurance.
g. Improvement of laboratory markers (eg. blood glucose and insulin levels).
h. Information obtained from your participation in this research study may eventually lead to better methods of preventing type 2 diabetes.

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F. ALTERNATIVES TO PARTICIPATION

No treatment other than exercise is offered or recommended for participants in this study. If you decline to participate in this research study, your medical care here at CNMC will not be affected in any way.

G. QUESTIONS – WHO TO CALL

We want you to ask questions about any part of this study or consent form either now or at any time in the future. If you have any questions about this study, call the Principal Investigator, Dr. Eric Hoffman, at 202-476-6011 or Maria-Eugenia Hurtado (Study Coordinator) and Gina Many (Research Assistant) at 202-476-4943. If you believe you have been injured as a result of being in this study, you should call, Dr. Christopher Spurney, Cardiologist, at 202-476-5654. If you have any questions or concerns about your rights in this research study at any time, please call Children's National Medical Center's Manager of Patient Relations, the Chief Academic Officer, or the Chair of the Institutional Review Board of the Children's National Medical Center. All parties may be reached at (202) 476-5000.

H. CONFIDENTIALITY

We will keep the records of this study confidential. Only the people working on the study will know your name. They will keep this information in case we have to find you later to let you know of any new information that may affect your health. The federal government can review the study records and medical records to make sure we are following the law and protecting the children in the study. Your medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY

In 1996 the government passed a law known as The Health Insurance Portability and Accountability Act (HIPAA). This privacy law protects your individually identifiable health information (Protected Health Information or **PHI**). The privacy law requires you to sign an agreement so researchers can use or share your PHI for research purposes. This describes to you how information about you may be used or shared if you are in a research study. It is important that you read this carefully and ask a member of the research team to explain anything you do not understand.

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I authorize Dr. Eric P. Hoffman and his research staff to create, access, use, and disclose my PHI for the purposes described below.

Protected Health Information that may be used and shared includes:

☒ Information that identifies you such as name, address, telephone number, date of birth, Social Security number, demographic information, and other details about you
☒ Information that relates to your health or medical condition from your medical records
☒ Information obtained from the study procedures outlined in this consent form, for example: things done to see if you can join the study such as physical exams, blood and urine tests, and any other medical information we learn from you about your health history and family history; laboratory data, as well as physiological data from a heart rate monitor and exercise treadmill testing and diet histories
☒ Laboratory results obtained on specimens collected from you (blood and urine)
☒ Questionnaires or surveys you complete (eg. Physical activity questionnaires)
☒ Interviews conducted with you by members of the research team
☐ Audio/ video recordings
☒ Other*: Research Triangle Institute (Bethesda, MD), a data coordinating center and collaborative partner in the DC-Initiative project.

*Example: *list any additional information that may be obtained from participants that is listed above such as information about financial and social circumstances, or educational level.*

The Researchers may use and share my Protected Health Information with:

- Dr. Eric Hoffman (PI),), Dr. Jung-Jun Park (Exercise Physiologist), Dr. Chris Spurney (Cardiologist), Maria-Eugenia Hurtado (Study Coordinator), Gina Many (Research Assistant), and the GCRC Nursing Staff.
- Government agencies that have the right to see or review your PHI, including but not limited to the Office of Human Research Protections and the Food and Drug Administration;
- Children's National Medical Center Institutional Review Board;
- Audit Committee of the Children's National Medical Center Institutional Review Board;
- Quality Improvement Program Coordinator and other staff in the Office for the

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DEC - 4 2008
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EXPIRATION
DEC - 3 2009
Children's Hospital

Protection of Human Subjects at Children's National Medical Center.

In addition to the above people and organizations, the Researchers may also use and share my Protected Health Information with:

☒ Doctors and staff at other places that are participating in the study. The names of the other staff that are participating in this study are Georgetown University Medical Center GCRC staff, Dr. Yanicic, Co-investigator from the Georgetown University Hospital and the National Institute of Health, National Institute for Child Health and Human Development Institutional Review Board.

☒ Laboratories and other people or organizations that look at your health information in connection with this study. The laboratories are from Children's National Medical Center and Quest Diagnostics in Chantilly, V.A.

☒ The Sponsor of the study and people that the Sponsor may contract with for the study. The Sponsor of the study is the National Institute of Health, National Institute for Child Health and Human Development.

☐ The Contract Research Organization (an organization that helps the Sponsor run the study).

☐ The Data Safety Monitoring Board (a group of people who examine the medical information during the study).

☒ The Medical Monitor for the Study (a person who reviews medical information during the study). The Medical Monitor is Dr. James Hagberg from the Department of Kinesiology, University of Maryland.

☒ The Patient Advocate or Research Ombudsman (person who watches out for your best interest)

☐ Any other outside entity who will receive health information
Please list:

Also, your primary physician will be contacted if during the course of the study the researcher learns of a medical condition that needs immediate attention.

Should your health information be disclosed to anyone outside of the study, your information may no longer be protected by HIPAA and this Authorization. However, the use of your health information will still be regulated by applicable federal and state laws.

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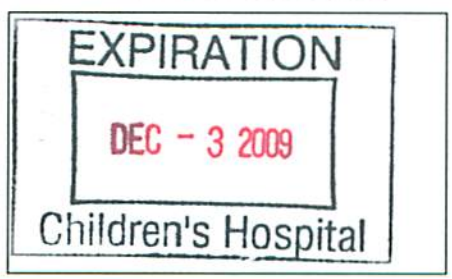

Banking of Blood Sample:

We would like to store blood samples collected from you in this study in a blood bank for future research as identified below. The blood bank is maintained by Dr. Eric Hoffman's Laboratory within the Center for Genetic Medicine at Children's National Medical Center.

Please indicate your approval of any or all of the following by initialing next to the statement:

My blood may be stored in the above named bank for future analysis related to this study. ☐ Yes ☐ No _____ initials

My blood may be stored in the above named bank for future analysis related to metabolic syndrome. ☐ Yes ☐ No _____ initials

My blood may be stored in the above named bank. Researchers may contact me to request my authorization for future studies that are not related to this study or the disease named above. ☐ Yes ☐ No _____ initials

My blood may be stored without any of my identifying information for use in other studies of other disease. ☐ Yes ☐ No _____ initials

I may change my mind at a later time and request that my blood sample be destroyed. If I change my mind and want to request that my blood sample be destroyed, I must do so in writing to Dr. Eric Hoffman.

Storage of PHI in a Database:

We would like to store personal health information collected from you in this study in a database for future research. The database is maintained by Children's Hospital, Department of Research Center for Genetic Medicine and Research Triangle Institute (Bethesda, MD), a data coordinating center and collaborative partner in the DC-Initiative project.

Please indicate your approval of any or all of the following by initialing next to the statement:

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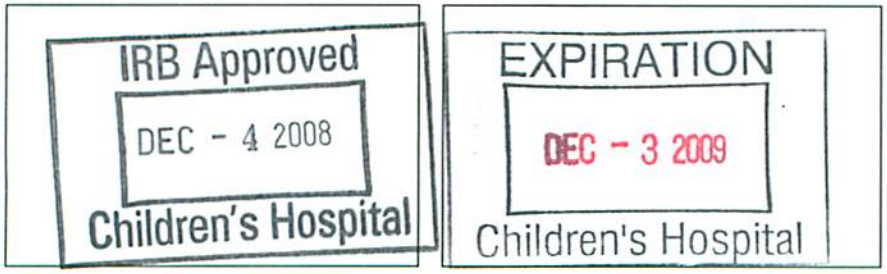

My personal health information may be stored in the above named database for future analysis related to this study. ☐ Yes ☐ No _____ initials

My personal health information may be stored in the above named database for future analysis related to An Exercise Intervention Study in Insulin-Resistant Minority Adolescents. ☐ Yes ☐ No _____initials

My personal health information may be stored in the above named database. Researchers may contact me to request my authorization for future studies that are not related to this study or the disease named above.
☐ Yes ☐ No _____ initials

My personal health information may be stored without any of my identifying information for use in other studies of other diseases. ☐ Yes ☐ No _____ initials

If you agree to participate in this research study, the research team, the research sponsor (when applicable) and the sponsor's representatives, may use Personally Unidentified Study Data. The Personally Unidentified Study Data does not include your name, address, telephone, or social security number. Instead, the researcher assigns a code to the Personally Unidentified Study Data. Personally Unidentified Study Data may include your date of birth, initials, and dates you received medical care. Personally Unidentified Study Data may also include the health information used, created, or collected in the research study. The research team or the research sponsor may share the Personally Unidentified Study Data with others to perform additional research, place it into research databases, share it with researchers in the U.S. or other countries, or use it to improve the design of future studies. They may also publish it in scientific journals, or share it with business partners of the sponsor and to file applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

You do not have to sign this Consent/Authorization. If you decide not to sign the Authorization, you will not be allowed to participate in the research study.

After signing the Consent/Authorization, you can change your mind and:

- Revoke this Authorization. If you revoke the Authorization, you will send a written letter to Dr. Eric Hoffman, at:
  Center of Genetics Medicine Research

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DEC - 3 2009
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111 Michigan Avenue, N.W.
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to inform him of your decision.

- If you revoke this Authorization, researchers may only use and disclose the PHI that was collected for this research study before you revoked the Authorization.
- If you revoke this Authorization your PHI may still be used and disclosed if you should have an adverse event (unexpected side effect).
- If you change your mind and withdraw the Authorization, you will not be allowed to participate in the study.

You will not be allowed to review the information collected for this research study until after the study is completed. If you are not allowed to review your information during participation in the study, when the study is over you will have the right to access the information.
This Authorization does not have an expiration date.

If you have not already received a Notice of Privacy Practices from Children's National Medical Center, you may request a copy and will be given one. If you have any questions or concerns about your privacy rights, you may contact the Children's Hospital Privacy Officer at 202-476-4550.

I. COMPENSATION

We will compensate you/your child for the time your child takes to participate. You will be given a parking voucher for each screening visit. By the end of the study, you will be given up to $300. This compensation will be divided according to each completed stage of the study ($25 Dietary Monitoring Period, $25 Study Visit#1, $25 Study Visit#2, $25 Exercise Intervention, $25 Study Visit #3, $25 Study Visit #4, $150 Study completion). The $25 may be in the form of a voucher or gift card. Also, at the successful completion of the study, an iPOD nano (2GB) will be given as an incentive. This will be effective until 12/31/09.

If your child is asked to participate in this study after the first two screening visits, Children's Hospital cannot promise that the risks we have told you about or other unknown problems will not happen. If you think that something bad happened because your child was in the study, please call the Chief Academic Officer of the Children's

National Medical Center at (202) 476-5000. We will give your child any emergency treatment needed.

J. ADDITIONAL ELEMENTS

You, or your representative, will be promptly notified if any other information, either good or bad, about this research study develops during the course of this study which may cause you to change your mind about continuing to participate.

You/your child will not be charged for additional tests and procedures that are performed only because you are participating in this research. Your responsibility to pay for other medical treatment will not be changed by your participation in this research.

Research Subject Advocate:

The National Institutes of Health supports a Research Subject Advocate or RSA for the research study that you are being asked to join. The RSA, Dr. Tomas Silber, is here to answer your questions or concerns about taking part in this research. Dr. Silber does not work for the doctors who are doing this research and they do not pay him. He is here only to help and protect you during any research.

You may contact Dr. Silber at any time. This can be done before you decide to take part in the research, during the study, or even after you finish the study. You can call Dr. Silber at 202-476-3066 or reach him by e-mail at tsilber@cnmc.org.

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AFTER CAREFUL CONSIDERATION, I HAVE DECIDED THAT MY BLOOD SAMPLE, WITHOUT NAME OR OTHER IDENTIFYING INFORMATION (BIRTH DAY, MEDICAL RECORD NUMBER, ETC), CAN BE USED FOR:
(please choose one and initial next to your choice):

☐ Research ONLY on the focus of this study. (Initials) _____
OR

☐ Research on the focus of this study and for additional research ONLY on metabolic syndrome. (Initials) _____
OR

☐ Research on the focus of this study as well as for general research on metabolic syndrome and other diseases. (Initials) _____

CONSENT/AUTHORIZATION:

I am the participant or I am authorized to act on behalf of the participant. I have read this information and will receive a copy of this form after it is signed.

By signing this form, you agree that you have talked to your doctor about the study and understand it, and you want to be in the study. You agree that we have talked to you about the risks and benefits of the study, and about other choices. You may decide to stop being in this study at any time and no one will mind and nothing will change about your medical care other than not being in the study. Copies of this form will be:

(1) Kept in the study file by the Principal Investigator;
(2) Put in your medical record; and
(3) Given to you to keep.

Please call the Principal Investigator, Dr. Eric P. Hoffman, at 202-476-6011 if you have any questions.

Printed Name of Participant: _____
Medical Record Number: _____
Printed Name of Parent(s)/Guardian(s): _____

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Signature of Participant: _____ Date: _____
(Participant must be 18 years of age or older)

Signature of Parent(s)/Guardian(s): _____ Date: _____

[Note: Signature of both parents required if more than minimal risk and no direct benefit, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child]

Signature of 2nd Parent/Guardian: _____ Date: _____
(ONLY when applicable)

Witness (to signatures): _____ Date: _____
(may be investigator)

Translator's Signature (if, applicable): _____
Language: _____

AFFIDAVIT OF PERSON OBTAINING CONSENT: I certify that I have explained to the above individual(s) the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised.

Printed Name of Individual Obtaining Consent: _____

Title: _____ Signature: _____ Date: _____

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