Protocol Title: Psychophysiological and Cognitive Biomarkers of Ketamine's Antidepressant Effects

Principal Investigator: Dawn F. Ionescu, M.D.

Site Principal Investigator:

Description of Subject Population: Adults with Treatment-Resistant Depression

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Partners HealthCare System is made up of Partners hospitals, health care providers, and researchers. In the rest of this consent form, we refer to the Partners system simply as "Partners."

If you have any questions about the research or about this form, please ask us. Taking part in this research study is up to you. If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

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.

Why is this research study being done?

We are doing this research to study ways to predict who will have an antidepressant response to ketamine. We will use different types of tests before and after giving ketamine in order to answer this question.

One of the tests utilizes a brief electric shock, which is applied to your fingers. The shock is highly annoying but not painful. The purpose of the electric shock is to help us to measure your startle response, which might be a helpful predictor for ketamine's antidepressant effects.

This is a pilot study. Pilot studies are done on a small group of subjects to learn if a larger study would be useful.

Ketamine is approved by the U.S. Food and Drug Administration (FDA) to be used with other drugs for anesthesia and as a pain reliever during procedures. However, ketamine is **not** approved by the FDA to treat depression.

We are asking you to take part in this research study because you have treatment-resistant depression (TRD) with or without anxiety. This means you have tried an antidepressant in the past that has not helped your depression.

Subjects in this study will receive one dose of ketamine *in addition to* your current antidepressant medication(s). It is very important that you take your medications exactly as your doctor has prescribed them.

We hope to enroll about 70 patients with depression in this study at Massachusetts General Hospital (MGH).

The National Institute of Mental Health is paying for this research to be done.

How long will I take part in this research study?

It will take you about 4-5 weeks, at most, to complete this research study. During this time, we will ask you to make 4 study visits. All of these visits will be at MGH.

What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Screening - Visit 1
The screening visit will take up to 3 hours. This visit will take place at the MGH Depression Clinical and Research Program. During this visit, we will do some tests and procedures to see if you qualify to take part in this research study. The study doctor will review the results of these tests and procedures. If you don't qualify, the study doctor will tell you why.

At this visit, we will:

- Ask about your medical history
- Give you a physical exam, including height, weight and "vital signs" (blood pressure, temperature, and heart rate)

- Ask you about your age, sex, and ethnic origin
- Ask you to take a brief hearing test
- Draw a blood sample
- Test your urine for certain drugs
- Test your urine for pregnancy, if you are a female able to become pregnant. Note: pregnant women cannot take part in this research study
- Give you an ECG (electrocardiogram)
- Give you some questionnaires to fill out about your general health and well-being, quality of life, mental health, emotional health, and mood.
- We may ask for your permission to contact the physician who currently prescribes your antidepressants

Urine Drug Screen
During this study, we will test your urine for certain drugs, including illegal drugs such as cocaine and marijuana. If your urine shows you have taken any of these drugs, you can't be in this study. The results of the urine drug test will not become part of your hospital medical record. These test results will, however, remain part of your research study record.

Blood Sample

Will my blood sample be used for genetic research?

Yes. We plan to do genetic research on the DNA in your blood sample. DNA is the material that makes up your genes. All living things are made of cells. Genes are the part of cells that contain the instructions that tell our bodies how to grow and work, and determine physical characteristics (such as hair and eye color). Genes are passed from parent to child. Genetic research is an important part of the investigation into the causes of depression and individual responses to antidepressant medications. The causes of depression are believed to be the result of combinations of inherited genes and possible various exposures to the environment. You may still participate in this study even if you choose not to provide blood samples for future genetic research.

Your samples may be used to create a living sample (called a "cell line") that can be grown in the laboratory. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you.

Do you agree to let us store your samples for future genetic research related to depression and other health disorders?

☐ Yes ☐ No Initials_____

Metabolic and Serum Biomarkers for Future Use

We would like to store some of your samples to study metabolic and serum biomarkers. Metabolites and biomarkers are naturally occurring substances found in blood. One component of blood is serum, which stores these substances. Future research may lead to new methods of diagnosing disease by measuring levels of metabolites and/or biomarkers in a person's blood, tissue, or urine. You may still participate in this study even if you choose not to provide blood samples for future metabolic and serum biomarker research.

Your samples may be used to create a living sample (called a "cell line") that can be grown in the laboratory. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you.

Do you agree to let us store your blood samples for future research related to metabolic and biomarkers?

☐ Yes ☐ No Initials_____

How long will my samples be kept?

The researchers will keep your sample until it is all gone, becomes unusable, or until the researchers or sponsor decide to discard the sample.

How much blood will be drawn during this study?

A total of 76-88 mL (5-6 tablespoons) of blood will be taken throughout the entire study.

ECG (electrocardiogram)

This test checks the electrical activity of your heart. We will place several small, sticky pads on your chest, arms, and legs. Each pad has a wire attached. The wires connect to a machine that makes a recording of your heart rhythm. This painless test takes about 15 minutes.

<u>Pre-Ketamine and Post-Ketamine Testing Visit - Visit 2 and Visit 4</u>
At this visit, we will ask you to complete baseline testing. Specifically, we will be asking you to complete computer-based behavioral tasks and a task that involves a brief electric shock on your left wrist.

Do not consume caffeine or nicotine within 1 hour of the experiments; do not consume alcohol within 24 hours of the experiments.

At this visit, we will:

- Ask you questions about side effects or health problems since your last visit
- Give you some questionnaires to fill out about your general health and well-being, quality of life, mental health, emotional health, and mood
- Test your urine for pregnancy, if you are a female able to become pregnant
- Complete computer-based behavioral tasks (cognitive reward task and task that involves differentiating patterns of objects).
- Complete a startle task that involves electric shock
- Draw a blood sample at the last visit

Electric Shocks
We will use a half-second annoying (but not painful) electric shock, administered on your left wrist. Two small electrodes will be attached to your left wrist The electrodes are made of a small piece of metal that is attached to a cable. The cable is connected to a battery-powered stimulator. The electric shock feels like an annoying tingling sensation.

We will first find the level of shock that you consider highly annoying, but not painful. To do this, we will begin at a low level that you will not be able to feel very much, if at all. We will slowly increase the shock levels with your permission. We will ask you to tell us when you find the level of the current to be highly annoying, but not painful. During the rest of the research study, the level of current that you will experience will not be higher than this level.

Electric shock is used to create a startle response. We will be measuring how hard your eye blinks ("startle") after the shocks. You will also be sitting in front of a computer screen, and we will ask you to complete tasks while under the threat of shock.

During the experiment, we will be monitoring how your body responds to the threat of shock. In order to do this, we will place small stick-on recording electrodes to the surface of your chest (near your right collar bone), your left arm, and to the surface of your hands. Each electrode has a wire attached. The wires connect to a computer that will measure your emotional reaction to the videos you see.

<u>Ketamine Infusion - Visit 3</u>
You will receive a single, low dose (0.5mg/kg over 40 minutes) of ketamine at this visit. We will do the infusion at the Clinical Research Center at MGH. This visit will happen 1-2 days after Visit 2.

For safety reasons, you must have nothing to eat or drink for 8 hours before this study visit.

At this visit, we will:

- Ask you questions about side effects or health problems since your last visit
- Record your vital signs
- Test your urine for pregnancy, if you are a female able to become pregnant
- Give you some questionnaires to fill out about your general health and well-being, quality of life, mental health, emotional health, and mood
- Insert an IV catheter (small, flexible tube) into an arm vein with a needle. We will use the catheter to give you the ketamine
- Place an oxygen monitor on your fingertip (to measure the amount of oxygen in your blood) during the ketamine infusion
- Do an electrocardiogram (ECG). An ECG checks the electrical activity of your heart. We will place several small, sticky pads your chest. Each pad has a wire attached. The wires connect to a machine that records your heartbeat
- Give you a ketamine infusion
- Draw a blood sample after ketamine
- Ask you questions from questionnaires

Ketamine Administration Procedures

Before the study visit, we will ask you to fast (have nothing to eat or drink, except water) after midnight before the day of the ketamine.

Do not consume alcohol or opiates/narcotic analgesics (such as morphine, hydromorphone, oxycodone, fentanyl) the night before the ketamine infusion or the day of the infusion. Benzodiazepines (such as lorazepam, alprazolam, clonazepam) should be avoided the night before the ketamine infusion and the day of the infusion. Do not consume caffeine or nicotine that morning.

Ketamine will be dosed based on your weight, at a dose of 0.5 mg/kg (a mg/kg is a unit of drug dosage). An experienced medical doctor will administer your infusion (about 40 minutes). To do this, we will place an intravenous (IV) line into a vein in your forearm. An IV is a flexible plastic tube that is connected to a needle. You may relax comfortably in bed while we give you an infusion of study drug through the IV. Your IV will stay in place for 1 hour after the infusion in case we need to give you other medications.

The medical doctor will stay with you for the entire infusion, along with a research nurse and a trained research assistant. A trained research staff member will be asking you a series of questions about how you are feeling. We will record your vital signs, your mood and anxiety levels, and any side effects you experience for up to 4 hours after the start of the infusion.

To record your vital signs during the ketamine infusion, you will need to wear:

- A blood pressure cuff (to monitor your blood pressure at regular intervals)
- A 3 or 5-lead electrocardiogram (ECG). An ECG checks the electrical activity of your heart. We will place several small, sticky pads your chest. Each pad has a wire attached. The wires connect to a machine that records your heartbeat.
- An oxygen monitor on your fingertip (to measure the amount of oxygen in your blood)
- We can use an oxygen face mask (fits over your nose and mouth) or nasal cannula (two small plastic tubes that are placed in both nostrils) to deliver oxygen therapy at 4 to 6 liters per minute, as needed. Oxygen therapy is a treatment that provides you with extra oxygen, a gas that your body needs to work well.

We will also get a blood sample for post-ketamine genetics and biomarkers. After we give you the ketamine and the up to 4 hour monitoring period is over, we will make sure that the effects of the study drug have worn off enough for you to go home. **You must have a responsible adult available to escort you home when you have completed the study.** This responsible adult escort must be present regardless of the mode of transportation you choose (i.e., even if you take a cab or the bus). If you do not know anyone who can help you, and you are not able to work with a medical escort service to take you home, then you cannot take part in this study.

Stopping the Study Early

You may withdraw from this study at any time, even in the middle of an experiment. We will make sure you stop the study safely. The study doctor will speak to you about follow-up care, if needed.

The study doctor may have to take you out of the study. This may happen because of several different reasons, such as a decline in your physical or mental health ("worsening of your condition") or missing too many study visits.

What Study Information May Become Part of Your Electronic Medical Record?

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs, vital signs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

Will I be contacted about future studies?

We have a particular interest in studying depression. We may want to contact you again in the future by letter or telephone if the researchers think you may qualify for a follow-up study. Is it okay to contact you in the future? Please indicate your choice with your initials next to the appropriate answer.

Yes:_____ No:_____

Best way to contact you:

_____

_____

_____

What are the risks and possible discomforts from being in this research study?

Risks of Taking Ketamine

Taking ketamine may cause you to have one or more of the side effects listed below.

Common side effects of ketamine are:

- fast, irregular heartbeat
- increased blood pressure
- clear dreams that may seem real
- confusion
- irritated feeling when waking up
- floating sensation (feeling "out-of-body") lasting from minutes to hours
- breathing problems, coughing
- nausea, vomiting
- twitching, muscle jerks, and muscle tension
- increased saliva (spit)
- increased thirst
- headaches
- metallic taste
- constipation
- blurry or double vision

Rare side effects of ketamine are:

- allergic reactions, like skin rash
- pain at infusion site
- ulcerations (open sores) and inflammation (swelling or irritation) in the bladder
- hallucinations (seeing or hearing things that are not really there)
- euphoria (a feeling of extreme happiness)
- involuntary eye movements
- low mood or suicidal thoughts

In one published review of ketamine's safety and tolerability in depression research, four out of 204 ketamine administrations had to be discontinued because of new or worsening physical or psychiatric symptoms (including the sensation of being "out of body," confusion, agitation, and paranoia) within the first 10 to 80 minutes after receiving ketamine. In all studies these symptoms disappeared within 110 to 240 minutes (about 2 to 4 hours). Three of the six studies also reported mild increases in blood pressure and heart rate, but this was only for 1 out of 10 or fewer of the subjects. All of the subjects' blood pressures and heart rates returned to normal within minutes.

We do not know the risk of side effects due to drug interactions between ketamine and the drugs that you are already taking is. There may be risks of ketamine that are currently unknown.

In the published studies there were no reports of severe or long-lasting side effects. If you experience any severe side effects or need to stay in the General Clinical Research Center for longer than 4-5 hours, the study doctors will send you to the Emergency Department where the emergency doctors will evaluate you.

We may give you medications to help with side effects during the administration. These medications are: labetalol for blood pressure or high pulse; lorazepam for agitation; haloperidol for delirium; glycopyrrolate for excessive spit or arrhythmia; ondansetron for severe nausea; acetaminophen for headache; and ibuprofen for headache. We will only give these medications if deemed medically necessary in the clinical judgment of the medical doctor.

If you experience any side effects once you are at home, please call the doctor in charge of this study, or the covering psychiatrist. She/he may instruct you to take a dose of your medications to help with the side effects, or may tell you to go to your local Emergency Room.

Risk of Allergic Reaction

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious, and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. An allergic reaction would typically occur shortly after receiving the ketamine, before you go home. However, if you think you are having an allergic reaction at home, call the study doctor right away. **If you are having trouble breathing, call 911 immediately.**

Risks of Electric Shocks

The electric shocks that you will receive will be uncomfortable but not painful or dangerous. You may stop the electric shocks at any time.

Risks of the IV

The risks of having an IV placed in your vein include:

- mild discomfort where the IV is placed
- bruising (black and blue marks at the site of puncture) where the IV is placed
- bleeding (usually less than a tablespoon of blood) where the IV is placed
- dizziness
- fainting (rare)

Risks of Blood Draws

You may have a bruise (a black and blue mark) or pain where we take the blood samples. There is also a small risk of infection, lightheadedness, and/or fainting.

Risks of Genetic Testing

Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

Taking part in a genetic study may also have a negative impact on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk.

Risks to an Embryo or Fetus, or to a Breastfeeding Infant

The effect of ketamine on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, are unknown and may be harmful. Because of these unknown risks, women cannot take part in this study if they are:

- Pregnant
- Trying to become pregnant
- Breastfeeding

If you are a menopausal woman and have not had a period for the past 12 months or more, you will not need to have a pregnancy test. Also, if you have had any well-documented method of surgical sterilization, you will not need to have a pregnancy test. The documented methods of surgical sterilization include having had a hysterectomy (removal of the uterus with or without the ovaries), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), or transvaginal occlusion (plugging the opening of the tubes with a coil).

If you are a menopausal woman and have not had a period for the past 12 months or more, you will not need to have a pregnancy test. Also, you will not need to have a pregnancy test if you have had a hysterectomy (surgical removal of your uterus and/or ovaries). All other female subjects must have a negative pregnancy test before starting the study medication.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study.

Acceptable birth control methods for use in this study are:

- hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- intrauterine device (IUD)
- abstinence (no sex)

If you miss a period, or think you or your partner might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking part in the study. The study doctor may ask for your permission to collect information about the outcome of your pregnancy and the condition of your newborn.

Risks of Receiving Ketamine While Taking Other Medications

For your safety during this study, call your study doctor BEFORE you take any:

- new medications prescribed by your own doctor

- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Protection Against Risk

Since your depression puts you at risk for suicidal thoughts or behaviors, we will ask you to provide information about a friend, family member, or primary doctor who will be your emergency contact.

If at any time during the study, you develop serious thoughts about suicide or harming yourself, you should immediately contact Dawn Ionescu, M.D. You can reach Dr. Ionescu directly at 617-643-0491. Dr. Ionescu (or her physician coverage if she is away) can be paged by calling the MGH page operator at 617-726-2000.

In some cases, you may be referred for emergency psychiatric evaluation and treatment with the MGH Acute Psychiatric Service or the nearest emergency department. You may be withdrawn from the study if emergency treatment is necessary.

If we learn information from you during this study that indicates intent to seriously harm others or yourself, we may share that information with third parties, including public safety or law enforcement authorities, and may take other precautions to protect against such harm.

Safety Caution

If you need to seek medical care for any reason during the study (between the screening visit and Visit 2), we ask that you inform your study doctor. There may be possible treatment interactions if you are prescribed other medications. Generally, we recommend patients inform their doctors regarding the study immediately upon deciding to participate in this study.

Discomforts

Some of the questions on the questionnaires may make you feel uncomfortable. You can skip the questions that make you feel uncomfortable.

Loss of Confidentiality

Any time information is collected about you there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential. However, this cannot be

guaranteed. Some answers you give in the study might put you at risk if other people find out. To keep what you say private, your study records will be coded; in other words, we will assign you a number to identify your information, instead of using your name. We will protect your records by keeping all your materials in locked file cabinets or secure password-protected computer files. Only research staff will have access to your private information. Any information kept on the computers is only available to research staff.

Other Risks

There may be other side effects that are unknown at this time.

What are the possible benefits from being in this research study?

You will not benefit from taking part to the study. The study may benefit other people with depression by furthering our understanding of depression and predictors of ketamine.

What other treatments or procedures are available for my condition?

There are approved treatments available for your depression, including psychotherapy, antidepressant medications, and electroconvulsive therapy (ECT).

Can I still get medical care within Partners if I don't take part in this research study, or if I stop taking part?

Yes. Your decision won't change the medical care you get within Partners now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

Taking part in this research study is up to you. You can decide not to take part. If you decide to take part now, you can change your mind and drop out later. We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should I do if I want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will the results of research tests be reported to me?

No. The research tests are being done for research purposes only. You will not receive the results of these research tests. The information created by this study will not usually become part of your hospital record.

Will I be paid to take part in this research study?

If you complete all parts of the study, you will be paid up to $200. The payment Schedule is as follows: $20 for the Screening Visit (Visit 1), and up to $60 for the remaining 3 visits. At Visits 2 and 4, you will be asked to participate in a task that involes the ability to make money based on your responses. The money you make from this task will be calculated into your total payment. We will also pay for the cost of your parking during the study visits; in the case of Visit 3 (the ketamine administration visit), we will pay for the parking for your chaperone.

What will I have to pay for if I take part in this research study?

Study funds will pay for the study drug and other study-related procedures.

Charges for any ongoing or routine medical care you receive outside this study will be billed to you or to your insurance company in the usual way. You will be responsible for any deductibles or copayments required by your insurer for your routine medical care.

What happens if I am injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the next section of this consent form.

If I have questions or concerns about this research study, whom can I call?

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Dawn F. Ionescu, M.D. is the person in charge of this research study. You can call her at 617-643-0491 M-F 9-5, or you can page her 24/7 by calling the MGH page operator at 617-726-2000 with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call Chelsea Dale at 617-724-2936 M-F 9-5.

If you want to speak with someone **not** directly involved in this research study, please contact the Partners Human Research Committee office. You can call them at 617-424-4100.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research

Also, if you feel pressured to take part in this research study, or to continue with it, they want to know and can help.

If I take part in this research study, how will you protect my privacy?

During this research, identifiable information about your health will be collected. In the rest of this section, we refer to this information simply as "health information." In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so.

In this study, we may collect health information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable health information and why they may need to do so:

- Partners research staff involved in this study
- The sponsor(s) of this study, and the people or groups it hires to help perform this research
- Other researchers and medical centers that are part of this study and their ethics boards
- A group that oversees the data (study information) and safety of this research
- Non-research staff within Partners who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- The Partners ethics board that oversees the research and the Partners research quality improvement programs.
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Federal and state agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other US or foreign government bodies that oversee or review research)
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- Other:

Some people or groups who get your health information might not have to follow the same privacy rules that we follow and might use or share your health information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your health information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your health information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your information for any mailing or marketing list. However, once your information

is shared outside Partners, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifying information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

Subject	Date	Time (optional)
Signature	Date	Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: 07/05/2016