Partners HealthCare System
Research Consent Form

Subject Identification

General Template - Drug Clinical Trial
Version Date: August 2016

Protocol Title: A Phase II Trial of Inhaled Carbon Monoxide for the Treatment of Acute Respiratory Distress Syndrome (ARDS)

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Site Principal Investigator: Diana Barragan Bradford, M.D. (MGH)

Description of Subject Population: Adults in the ICU with ARDS who are mechanically ventilated

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.

Some of the people who are eligible to take part in this study may not be able to give consent to take part because of their medical condition. Instead we will ask the person's authorized representative to give consent. Throughout the consent form, "you" always refers to the person who takes part in the study.

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 study to find out if inhaled carbon monoxide (CO) can help people with acute respiratory distress syndrome (ARDS). We also want to find out if inhaled CO is safe to use without causing too many side effects in critically ill patients.

Inhaled CO is not approved by the U.S. Food and Drug Administration (FDA). This means that inhaled CO is considered "investigational" and can only be used in research studies.

About 130 healthy volunteers, subjects with chronic obstructive pulmonary disorder (COPD), and idiopathic pulmonary fibrosis, have received inhaled CO as part of research studies so far. We have previously treated 12 sepsis patients with ARDS who were randomly assigned to receive either inhaled CO or placebo air. A total of 8 patients were treated with inhaled CO and 4 patients were treated with placebo gas. We did not find any differences in side effects between the two groups.

This research study will compare inhaled CO to placebo. The placebo gas looks exactly like inhaled CO, but contains no CO. During this study, you may get placebo instead of inhaled CO. Placebos are used in research studies to see if the results are due to the study drug or due to other reasons.

We are asking you to take part in this research study because you have ARDS and you need to be on a mechanical ventilator to help you breathe. ARDS is a life-threatening lung condition that prevents enough oxygen from getting into the blood. There are no specific therapies available to treat ARDS itself at this time. However, treatments are available to treat the underlying condition that leads to ARDS, such as infection, in addition to supportive care treatments to help protect the lung from additional injury while you are on the ventilator.

A total of up to 32 subjects will take part in this research study. About 25 subjects will take part at Brigham and Women's Hospital (BWH) and Massachusetts General Hospital (MGH).

The Department of Defense (DoD) is paying for this research study to be done.

How long will I take part in this research study?

It will take 3 days to complete the study drug administration portion of this research study. You will have an initial screening evaluation. If you are eligible to take part in this study, we will give you the study drug (CO or placebo air) once a day for 3 days. After study drug completion, we will follow you for clinical outcomes for 6 months. During this time, we will call you about 3 times.

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 Evaluation

The Screening Evaluation will take about one hour. At this time, we will review some tests and procedures that have been performed as part of your medical care 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:

- Review your medical history.
- Review your physical exam, including height, weight and "vital signs" (blood pressure, temperature, heart and breathing rates).
- Review your chest X-ray.
- Review an electrocardiogram (ECG). This test checks the electrical activity of your heart. This is done by placing 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 5 minutes.
- Review blood tests. Blood will most likely be taken from a catheter already placed into your vein or artery by your healthcare team. This will include a test for pregnancy, if you are a female able to become pregnant. Pregnant women cannot take part in this research study.
- Review the amount of hemoglobin and lactate in your blood using a blood sample.
- Review arterial blood gas (ABG) tests. An ABG test measures the levels of oxygen and carbon dioxide in your blood to see how well your lungs are working. In most instances, this sample will be drawn from a catheter which has already been placed in your artery by the medical team caring for you. In some circumstances, if you do not have an arterial catheter, a sample of blood will be taken from the artery inside your wrist. You will have your arm extended and hand resting on a small pillow. The place where the needle is put will be cleaned. The performing provider may give you an injection of local anesthetic to numb the area. A needle will be placed into the artery inside the wrist and a sample of blood will be taken. A bandage will be placed over the place where the needle went in. Pressure will be applied to this area for ten minutes after the needle is removed.

Assignment to a Study Group

If you still qualify for the study, we will assign you by chance (like a coin toss) to the inhaled

CO group or the placebo group, which is air. You and the study doctor cannot choose your study group. You will have an equal chance of being assigned to the inhaled CO group as the placebo group.

You will not know which study group you are in, but the study doctor and a respiratory therapist who will administer the study drug will know what study group you are in.

If you agree to be part of the study we will make adjustments to the settings of your ventilator, following best practice guidelines for use of ventilators in ARDS.

The device we will use to deliver CO, the Carbon Monoxide Ventilator Delivery System (COventDS) will be plugged into your ventilator. The device was built for this study and the FDA cleared its investigational use for this purpose only.

Study Drug Administration Period (Days 1-3)

These visits will take about three hours.

Taking the Study Drug (CO or Placebo)

We will give you the study drug for 90 minutes daily for 3 consecutive days. **Day 1** will be the first day you start receiving the study drug.

On days 1-3 *before* you receive the study drug, we will perform tests to see if you still qualify for the study drug treatment:

- Check your vital signs
- Perform an electrocardiogram
- Draw a blood sample to measure your lactate and hemoglobin level
- Check the level of carbon monoxide in your arterial or venous blood using a co-oximeter
- Perform a blood gas test using blood from your artery (ABG) or vein (VBG)

If you still qualify for the study, we will give you the study drug over a period of 90 minutes. During the 90 minute administration of the study drug, we will:

- Monitor your vital signs continuously
- Check the level of carbon monoxide in your blood using a pulse co-oximeter (this is a non-invasive device which is attached to your finger) at 20 min, 60 min, 75 min, 90 min, and 3 hours after the study drug is administered

- Draw your arterial or venous blood to check the level of carbon monoxide in your blood using a co-oximeter at 20 min, 60 min, 75 min, 90 min, and 3 hours after the study drug is administered
- Check the oxygen and carbon dioxide in your blood from an arterial blood gas (ABG) test using a blood sample from your artery after the study drug has been completed (90 min). If an ABG is not available, a VBG will be obtained

Days 1 to 3

Additional blood samples will be drawn daily before and after the study drug on Days 1-3 of the study. These blood samples will be for:

- Safety Tests
- Biomarker Testing- This testing is being done to evaluate changes in certain biochemical characteristics of your blood. These tests are for research purposes only. Therefore, you will receive no results from the biomarker tests.
- Genetic Testing- This testing is being done to understand which individuals will respond well or poorly to the study drug. To do this, we would like to look at your genes. Genes contain the material passed from parent to child that determines the make-up of the body and mind. (For example, some genes control the color of your hair or eyes). Genes are contained in your DNA (deoxyribonucleic acid). Most DNA is the same among human beings.

We will also collect urine samples before and after the study drug on Days 1-3. These urine samples will be for Biomarker Testing. In most cases, urine will be collected from an indwelling catheter which has previously been placed by your clinical team as part of your routine care. If you do not have an indwelling catheter, we will ask you to provide urine samples in sterile collection cups.

We may perform one additional chest X-ray during the study drug administration period, if not performed by the clinical team.

<u>After You Complete the Study Drug Administration Period</u>

After you complete the study drug administration period, your inpatient medical team will continue all other aspects of your ongoing medical care.

<u>Study Day 5</u>

On study day 5, we will:

- Draw blood for Biomarker Testing

- Collect a urine sample for Biomarker Testing. In most cases, urine will be collected from an indwelling catheter which has previously been placed by your clinical team as part of your routine care. If you do not have an indwelling catheter, we will ask you to provide urine samples in sterile collection cups.

Study Day 7

On study day 7, we will:

- Perform an electrocardiogram
- Perform a blood gas test using blood from your artery (ABG) or vein (VBG)
- Perform a chest X-ray if not performed by the clinical team as part of your routine care

Study Days 14 and 28

On study day 14 and day 28, if you are still in the hospital, we will draw your blood to measure the bilirubin in your blood if not drawn by your doctors as part of your usual care. Bilirubin is produced in your body by the breakdown of red blood cells and is processed by the liver. It gives us information about how well your liver and gallbladder are functioning.

In total, we will draw about 6 tablespoons (less than 1/2 cup) of blood during the entire course of this research study. We may draw an additional 2 tablespoons during the course of the study if not drawn by the clinical team taking care of you.

Throughout the study, blood drawn for this research study will most likely come from indwelling catheters, however if you no longer have these catheters, blood will be taken from a vein in your arm (venipuncture). You will have your arm extended and the place where the needle is put will be cleaned. A needle will be placed into the vein in your arm and a sample of blood will be taken. A bandage will be placed over the place where the needle went in. Pressure will be applied to this area for 10 minutes after the needle is removed. In most cases, additional blood will be drawn for this study at the same time your clinical team has blood drawn as part of your routine care and no additional venipuncture will be required.

Leftover Samples

As part of your routine care, your doctor may obtain additional blood samples and fluid from lung washings from you for testing. After the tests for your medical care are completed, part of your samples may be left over. Normally these leftover samples would be thrown away. We are asking you to allow us to collect this leftover plasma and fluid from lung washings for biomarker testing.

If you choose to allow your leftover samples to be stored for future research, we will store the leftover samples as described below.

Follow-up Period

28-day Check-in
On Day 28, we will check your medical record to see if you are still in the hospital. If you have left the hospital, we will call you to see how you are doing. The phone call will last about **2 minutes.**

60-day Check-in
On Day 60, we will check your medical record to see if you are still in the hospital. If you have left the hospital, we will call you to see how you are doing. The phone call will last about **2 minutes.**

6 month Follow-up Call
Six months after your initial participation, we will call you and ask you some questions that will assess your memory and cognitive function. The phone call will last about **10 minutes**.

We will ask you and/or your surrogate to provide contact information so we can reach you after you leave the hospital. If we are unable to contact you, we may look in publicly available databases.

In case you are transferred to another medical facility before you complete the follow-up period, we will ask you to sign a medical release form so that we can contact the staff there to find out how you are doing at Day 28, Day 60, and 6 months after your enrollment into the study.

Stopping the Study Early

If you decide to stop taking part in the study for any reason, we will do some follow up testing. This will include:

- Review your medical history
- Record vital signs (if before day 3)
- Perform an electrocardiogram (if before day 7)
- Perform a chest X-ray (if before day 7)
- Do an arterial or venous blood gas test (if before day 7)
- Measure the amount of lactate in your blood using a blood sample (if before day 3)
- Measure the bilirubin in your blood (if before day 14)

Also, the study doctor may take you out of the study without your permission. This may happen because:

- The study doctor or your inpatient medical doctor think it is best for you to stop taking the study drug
- You start certain treatments for ARDS that may interfere with the study drug administration
- Your blood tests show levels of study drug that are too high to continue with the study
- The Sponsor decides to stop the study
- We stop doing the study for safety or other reasons

If this happens, the study doctor will explain why you need to stop taking part in the study. We will ask you to complete a final study visit as described above.

Review of Medical Records from Hospital Admissions or Emergency Department Visits

Partners has an electronic system that lets your study doctors know if you are admitted to a Partners Hospital, or if you visit a Partners Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects, you experience while you are taking part in the study.

Sending Study Information to Research Collaborators Outside Partners

We will send your study information and/or samples to researchers working with us at Duke University and Weill Cornell Medicine. We will label all your study materials with a code instead of your name. The key to the code connects your name to your study information and samples. We will keep the key to the code here at Partners and will not share it with our research collaborators. No one outside of Partners will know which study information or samples are yours.

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of whole genome studies. These central banks will store your genetic information and give them to other qualified and approved researchers to do more studies. We do not think that there will be further risks to your privacy and confidentiality by sharing your whole genome information with these banks. However, we cannot predict how genetic information will be used in the future. The data will be sent with only your code number attached. Your name or other directly identifiable information will not be given to central banks. There are many safeguards in place to protect your information while they are stored in repositories and used for research.

Storing Samples and Health Information at BWH/MGH for Future Use

We would like to store some of your samples and health information for future research related to critical illness and lung disorders. We will label your samples and health information with a code instead of your name. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password protected computer file. The samples may be shared with other Partners institutions, as well as non-Partners academic institutions. Any samples sent outside of Partners will not contain information that could identify you.

Do you agree to let us store your leftover samples and health information for future research related to carbon monoxide, ARDS, sepsis, trauma and burn injuries, critical illness or other lung diseases?

☐ Yes ☐ No Initials_____

If later you change your mind and want your samples destroyed, contact the study doctor.

Future Genetic Research

In addition to the current research, we would like to do future DNA (deoxyribonucleic acid) research on your leftover samples. 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 which 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.

The DNA tests are being done for research purposes only and will not be used for your medical care. You and your doctor will not be told the results of the test(s) done on your DNA blood sample. The test results will not be put in your medical record.

We will label your samples and health information with a code instead of your name. The key to the code connects your name to your samples and health information. The study doctor will keep the key to the code in a password protected computer file. We will store your blood sample at Partners for the genetic testing. Your blood sample as well as any electronic information associated with you will be labeled with a study ID number. The blood sample will be kept safe in a locked freezer and will only be accessed by the study doctors.

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.

We may also perform a whole genome analysis on your DNA sample. Usually researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and may be used by researchers to study links to carbon monoxide treatment, ARDS, sepsis, trauma and burn injuries, critical illness or other lung diseases. The samples may be shared with other Partners institutions, as well as non-Partners academic institutions. Any samples sent outside of Partners will not contain information that could identify you.

You can still take part in the main part of the study and not have your leftover samples stored and used for future genetic studies. The choice is yours.

Do you agree to let us use your leftover samples for future genetic research?

☐ Yes ☐ No Initials_____

If later you change your mind and want your samples destroyed, contact the study doctor.

Study Information Included in 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).

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

Study Monitoring

Research staff will have access to your study records. Your records may also be reviewed by groups who watch over this study to see that we are protecting your rights, keeping you safe, and following the study plan. These groups include:

- The Department of Defense (DoD) and its study monitors,
- The US Food and Drug Administration (FDA),
- The Partners Human Research Committee

• The US Office for Human Research Protections (OHRP)

We will do our best to protect your private information.

Use of Your Social Security Number

As part of this research we will collect your social security number. This information will be stored separately from the other data collected in the study. It will not be sent to the main coordinating center. It will be used to get in touch with you for follow-up visits while you are in the study. We will also use this information to help locate you, in case we cannot reach you. This may include using the Social Security Death Master File, National Death Index, general internet searches, and obituary postings.

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

Risks of Taking Inhaled CO

CO has been used in several research studies with healthy volunteers. In previous studies, exposure to the dose you will be given for up to 8 hours did not cause any significant bad outcomes.

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

- Headache
- Fast heart beat
- In cases of overdose people can have nausea, vomiting, seizures, problems thinking, coma, cardiopulmonary arrest, and death. These doses are much higher than the one you will be given. In our study, we will give you a low dose of the gas for a short period of time.

We will monitor you closely while we give you CO. We will look for signs and symptoms of toxicity and will check your blood levels to see how much CO your body is absorbing. We will not allow the levels to come close to a dangerous level. If this does happen for an unforeseen reason, we will stop giving you the study drug until your levels return to an acceptable range.

There may be other risks of inhaled CO that are currently unknown.

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. If you think you are having an allergic reaction, notify the study doctor right away.

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

The effect of inhaled CO on an embryo or fetus (developing baby still in the womb), or on a breastfeeding infant, is 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 menstrual 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. Methods of surgical sterilization include having had a hysterectomy (removal of the uterus), bilateral oophorectomy (removal of both ovaries), a tubal ligation (having your tubes tied), and transvaginal occlusion (plugging the opening of the tubes with a coil). All other female subjects must have a negative pregnancy test before starting the study drug.

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 and for at least one month after your last dose of study drug.

Acceptable birth control methods for use in this study are:

- hormonal methods, such as birth control pills, patches, injections, vaginal rings, 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 might be pregnant during the study, you must tell the study doctor immediately. If you become pregnant, you must stop taking the study drug and 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.

If you are sexually active and able to father a child, you must agree to use one of the birth control methods listed below. You must use birth control for the entire study and for at least 90 days after your last dose of study drug.

Acceptable birth control methods that you can use in this study are:

- condoms with spermicide (a foam, cream, or gel that kills sperm)
- abstinence (no sex)

Acceptable birth control methods that your partner(s) should use 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)

If your female partner becomes pregnant, the study doctor would like to follow the outcome of the pregnancy. You should notify us immediately if your partner becomes pregnant. We will work with you and your female partner to provide contact information to the study doctor. She may be asked to sign a release of medical information form that gives her doctors permission to provide information to the study doctor. You will not have to stop taking the study drug or stop taking part in the study if your partner becomes pregnant.

Risks of Taking CO with Other Medications

For your safety during this study, we will review your medications including:

- new medications prescribed by your own doctor
- other medications sold over-the-counter without a prescription
- dietary or herbal supplements

Only a small number of people have taken inhaled CO. Therefore, we don't know about all the side effects that can happen when taking inhaled CO with other drugs.

Risks of Modified Ventilator Settings

This study requires the study team to ensure that your ventilator settings are similar to those recommended by the ARDS Network (ARDSNet) in order to ensure all subjects have similar settings. The ARDS Network is the world's largest organization that studies ARDS. It has published best practice guidelines for the use of ventilators in ARDS. These settings have been evaluated in large trials across the globe and are considered safe. This may represent a deviation from the settings currently being used, however we will communicate with your treating physicians to determine if there is any increased risk in moving to these standards. If your treating physician deems that you are not able to use these settings because of your particular illness we will not include you in the study.

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 Blood Draws for Arterial Blood Gas Tests (ABG)

You may feel lightheaded, faint or dizzy while the blood is being taken from your artery. You may develop a small bruise or infection at the site of the puncture. On rare occasions the needle may damage a nerve or an artery causing the artery to become blocked. A blocked artery can prevent blood from flowing to the hand, which can lead to damage. Because the arterial blood gas procedure can be slightly more painful than drawing blood from a vein, we may give you an injection of local anesthetic to numb the area.

Risks of Radiation Exposure

If not performed by your medical team, we may perform chest X-rays. These chest X-rays are the same as the chest X-rays performed for clinical care and individually, each chest X-ray exposes you to a small amount of radiation. The cumulative radiation exposure from these X-ray tests is considered small and is not likely to adversely affect you or your disease. However, the effects of radiation add up over a lifetime. It is possible that having several of these X-ray tests may add to your risk of injury or disease.

Risks of Genetic Testing

Information about taking part in a genetic study may influence insurance companies and/or employers regarding your health status. If you do not share information about taking part in this study with others, you will reduce these risks. We will not place information about the results of the study tests in your medical record. In addition, all study information and samples will be coded and will only contain your study code number.

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

You may not benefit from taking part in this research study. You may benefit from the way in which your ventilator is managed, which has been shown to help other patients with ARDS. If you receive inhaled CO, it is possible that your ARDS will improve while you are taking it. However, this is not guaranteed.

Because inhaled CO is not approved by the FDA, your doctor cannot prescribe it after you finish the study.

Others with ARDS may benefit in the future from what we learn in this study**.**

What other treatments or procedures are available for my condition?

You do not have to take part in this research study to be treated for ARDS. There are currently no proven effective medical therapies for ARDS. While there are currently no alternative available approaches to treat ARDS itself, there are treatments available to treat the underlying disease (eg. infection). In addition, there are supportive treatments for ARDS, including different positioning and methods to protect the lung from further injury while you are on the ventilator. Sometimes, doctors use a skeletal muscle relaxant to allow rest and better breathing on the breathing machine. Sometimes, doctors use other inhaled medications to relax the blood vessels in the lung which may improve the oxygen level in the blood, although studies have not definitively proven benefit in ARDS.

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 I be paid to take part in this research study?

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples are used for this purpose.

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

Study funds will pay for the costs of the study drug. You or your health insurer will be responsible for the cost of your mechanical ventilation because this would be needed for your care even if you are not in the study.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

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.

Rebecca Baron, MD, is the person in charge of this research study at BWH. You can call her at 617-525-6642, Monday through Friday from 9 AM to 5 PM. Outside of normal business hours,

Dr. Baron can be reached 24 hours/day 7 days/week by calling 617-732-5500 and asking to have her paged.

Diana Barragan Bradford, MD, is the person in charge of this research study at MGH. You can call her at 617-726-3030, Monday through Friday from 9 AM to 5 PM. Outside of normal business hours, Dr. Barragan Bradford can be reached 24 hours/day 7 days/week by calling 617-724-5700 and asking to have her paged.

If you have questions about the scheduling of appointments or study visits, call Rebecca Baron at 617-525-6642 (BWH) or Diana Barragan Bradford at 617-726-3030 (MGH).

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 857-282-1900.

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: Department of Defense

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 of Guardian or Authorized Representative for Adult:

I give my consent for the person I am authorized to represent to take part in this research study and agree to allow his/her health information to be used and shared as described above.

_____

Print Name (check applicable box below)

- ☐ Court-appointed Guardian
- ☐ Health Care Proxy
- ☐ Durable Power of Attorney
- ☐ Family Member/Next-of-Kin

_____ _____ _____

Signature Date Time (optional)

Relationship to Subject:_____

Assent

Statement of Person Giving Assent

- 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, and my questions have been answered.

Signature of Adult:

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

_____ _____ _____

Adult 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 of Non-English Speaking Subjects Using the "Short Form" in the Subject's Spoken Language

Statement of Hospital Medical Interpreter

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

_____	_____	_____
Hospital Medical Interpreter	Date	Time (optional)

OR

Statement of Other Individual (Non-Interpreter)

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

_____	_____	_____
Name	Date	Time (optional)

Witness to Consent of Subjects Who Cannot Read or Write or are Physically Unable to Talk or Write

Statement of Witness

I represent that the consent form was presented orally to the subject in the subject's own language, that the subject was given the opportunity to ask questions, and that the subject has indicated his/her consent and authorization for participation by (check one box as applicable):

☐ Making his/her mark above

☐ Other means _____
(fill in above)

_____ _____ _____
Witness Date Time (optional)

Consent Form Version: 4/28/2022