NIH IRB CONSENT LIBRARY

The purpose of this guidance is to provide sample language for use with the NIH IRB Consent Form Templates. Each topic below offers sample language that may be used to describe study procedures and/or risks related to participation, as appropriate. In some cases, additional simplified language for use in an assent document is provided. Any sample language used while drafting a consent form should be modified according to the study protocol. Please note that the IRB may require additional changes after reviewing the protocol and application materials. Items are listed in alphabetical order and include:

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ALLERGIC REACTION

Risks: You might be allergic to the study drug. You could get a mild reaction, like a skin rash. Sometimes, it could be worse, like throat swelling, low blood pressure, or trouble breathing. In rare cases, a severe reaction could cause death.

ANESTHESIA

Risks: We will give you anesthesia to make you sleep during the procedure. Risks include slower breathing and breathing in saliva or stomach contents, which is called aspiration. Other risks are a drop in heart rate or blood pressure. If these happen, the doctor may put a longer breathing tube into your mouth and windpipe. They might use a machine to help you breathe and give you medicine to raise your blood pressure. Please tell us if you or any family member has had problems with sedation or anesthesia before.

ANESTHESIA IN PEDIATRICS

Include this language if children on study will be getting procedures that require general anesthesia—this language is required by CC anesthesiology.

Risks: The FDA has given a safety warning about using anesthesia in children, especially if it lasts more than 3 hours or if it is used more than once, even for a short time. Studies have shown that animals can have learning and behavior problems after getting anesthesia for a long time or repeatedly. These problems might also happen in children. So far, no problems have been found after just one short use of anesthesia. An anesthesiologist will discuss the risks and benefits of the anesthesia with you for your child in this study.

LOCAL ANESTHESIA

Risks: Biopsies can be done with local anesthesia. Possible side effects include feeling sleepy, headaches, blurred vision, muscle twitching or shivering, ongoing numbness, weakness, or a pins and needles feeling. These side effects usually go away quickly.

AUDIO-TAPING AND/OR VIDEO-RECORDING

Procedure: We will record your interview. After the interview, we will create a written transcript from the recording. Your name will not be included in the transcript. Once the transcript is done, the recording will be destroyed.

We would also like to videotape one of your sessions. The videotape will help us review and study your body language and reactions during the session. The videotape will be stored until the study is finished, and then it will be destroyed. Letting us videotape one of your sessions is optional.

Risks: See "**INVASION OF PRIVACY/BREACH IN CONFIDENTIALITY**" below.

BLINDED STUDIES

Procedure: You and the study team will not know which study drug you will get. If there is an emergency and it is important for your care, the study team can quickly find out which group you are in.

BLOOD DRAWS

Procedure: You will have blood drawn from a vein. This may require a needle stick in your arm or hand. If you already have an IV in place, we might be able to use that instead. The amount of blood we will draw is about *[specify in teaspoons/tablespoons]* at *[specify visits when there will be blood draws]*.

Risks: Blood draws may cause pain, redness, bruising, or infection where we put the needle. Some people might faint, but this is rare. We can put numbing cream on the area, so the needle won't hurt as much.

BONE MARROW ASPIRATION / BIOPSY

Procedure: We will ask you to have a bone marrow biopsy and will collect a small amount of bone marrow tissue and cells from your hip *[specify other site if appropriate for the study]*. Bone marrow is the soft material in the center of bones that makes new blood cells. The area will be numbed with lidocaine. Once numb, a large needle will be inserted through a small cut in your skin. We will then take about [*4 tablespoons or specify alternative volume as relevant*] of marrow out of your bone (this is called aspiration). We may also take a small piece of bone. We will check your pain level during the procedure, so please tell us how you are doing. We may give you more numbing medicine if needed. The procedure will take about *[1 hour]* to complete. We will call you in about [*2 days*] to see how you are doing.

Risks: The bone marrow collection and biopsy may cause pain, bruising, bleeding, and infection. Soreness may last for a couple of days. You may have more pain, bleeding, and bruising if you have both aspiration and biopsy rather than just the aspiration. If your pain is severe or if you have a fever, tell the study team right away.

BRONCHOSCOPY

Procedure: If you decide to join this study, you will have a bronchoscopy. We will pass a long tube with a light on it through your nose or mouth and into your lungs. Before we begin, we will use a numbing spray in your nose and throat. An IV (intravenous) needle with a tube attached will be put in your arm. The IV will give you medication to make you drowsy and to help you stay comfortable during the procedure. The test will take about 20-40 minutes to complete. You can go home once you're fully awake, but someone else must drive you home.

If Bronchoalveolar lavage will be performed: While the tube is in your lungs, we will do a procedure called bronchoalveolar lavage (BAL) to collect cells to look at in the lab. We do this by putting a small amount of salt water in your lungs through the tube and then pulling it back out.

If transbronchial biopsy will be performed: We also plan to collect small pieces of lung tissue during the bronchoscopy. We will do this by inserting very small tweezers ("forceps") into your lung through the bronchoscope. We will then collect several very small pieces of your lung tissue. [*If fluoroscopy will be used, add this and also include radiation language in the relevant section*] We will use x-ray pictures to see where the forceps are inside the lung while we collect the samples.

Risks: The bronchoscopy is not typically painful, but it may cause throat numbness, coughing, a sore throat, and fever. Sometimes, the bronchoscopy can cause your blood oxygen levels to drop.

We will watch your oxygen levels during the entire procedure and afterwards until you are recovered. The numbing spray may make your mouth feel funny and has an unpleasant taste. Common side effects of the drug given to you through the IV include feeling dizzy, faint, lightheaded, tired, or out of breath. We will watch you closely throughout the procedure, and we will treat any side effects that happen.

If BAL is performed: In addition to the risks of the bronchoscopy, you may have a slight fever after the bronchoscopy with BAL. This usually goes away quickly. If it does not go away, you should tell the study team or your doctor.

If transbronchial biopsy is performed: The biopsy may cause bleeding in your lung. This usually is only a small amount and will stop on its own. You may cough up small amounts of blood for a few days. Rarely, (less than 1 in 100 times) the biopsy can cause a pneumothorax. This is where the lung is punctured and may partially collapse. If this happens, we may need to insert a tube called a chest tube to re-expand your lung. A chest tube is a tube placed through your skin into the space between your lung and your chest wall. Depending on how you are doing, we may need to watch you in the hospital.

CENTRAL LINE

Procedure: Before your [*insert procedure/reason*], you may need to have a "tunneled" catheter inserted. This type of catheter is a thin, long tube made of flexible silicone rubber that is surgically put into one of the main blood vessels leading to your heart. One end of the catheter is inserted through a small cut into the main blood vessel leading into your heart. The other end of the catheter is tunneled under your skin and comes out through a second small cut in your skin.

Your doctor or nurse will explain the procedure in detail and ask you to sign a separate consent form. Before you go home, we will give you instructions on how to care for the catheter.

Risks: Many people get central catheters, and they are generally well tolerated. The most common risk is infection, which can be treated with antibiotics or by removing the catheter. Other risks include blood clots inside or near the catheter. These clots can break off and travel to the veins near your neck, face, chest, arms, or lungs (called a pulmonary embolism). If you get blood clots, your doctor will treat you, possibly with blood thinners. Uncommon side effects include swelling of the face and arm, and/or lung collapse. If your lung collapses, you might need a tube placed between your ribs to allow the lung to re-expand. Rarely, the catheter can break, or air could get inside it and travel to the veins near your neck, face, chest, arms, or lungs.

CHART REVIEW

Procedure: As part of this study, we will collect some information from your medical record. This will include your age, sex, race, height and weight, pain level, number of blood transfusions, medicines you are taking and the results of any lab or diagnostic tests.

Risks: See "**INVASION OF PRIVACY/BREACH IN CONFIDENTIALITY**" below.

COGNITIVE TESTING

Procedure: You will have tests to check your mood, memory, attention, and mental functioning. We will ask you to answer questions, take paper and pencil tests, and do a test on the computer.

This testing will take about *[specify # of minutes]* to complete.

Risks: You may feel frustrated while taking the tests. These tests are meant to be challenging. You can take breaks as needed.

Written Assent language: You will do some tests so we can find out how you pay attention to things and how you think. These tests will take about [*specify # of minutes*] to finish. You might feel nervous or frustrated, or you might even get bored with them. You can take breaks whenever you want to.

CONTRAST AGENT

Risks for IV contrast: You may feel discomfort when the contrast is injected. You may feel warm or flushed. You may get a metallic taste in your mouth or, rarely, you may vomit or feel sick to your stomach.

You could have an allergic reaction to the contrast, which may cause side effects ranging from mild itching or a rash to severe trouble breathing, shock, or, rarely, death. The contrast may also cause kidney problems. The study doctors will do a blood test to make sure it is safe for you to get the contrast.

Risks for oral contrast: You may have vomiting, nausea, cramping, bloating, constipation, or diarrhea after drinking the contrast.

CONSCIOUS SEDATION

Risks: The most common risks of conscious sedation last up to a few hours after being given can include drowsiness, feeling slow or sluggish, low blood pressure, headache, and nausea.

CT SCAN

Procedure: You will have a CT (Computed Tomography) scan at months [*specify which visits*]. The CT scanner is a donut-shaped machine that uses x-rays to make computer pictures of the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan, and you will be told to hold your breath. The scan itself will only take a few minutes, and the entire visit will take about 30 minutes [*update duration as applicable]*.

Risks: See "**RADIATION**" below & "**CONTRAST AGENT**" above.

DISCARDED TISSUE

Procedure: Normally during surgery small amounts of tissue are removed and thrown away. At the end of your surgery, instead of throwing it away, we will keep that tissue. Taking your tissue for this study will not affect your surgery. No extra tissue will be taken from you for this study.

DISCOVERY OF PREVIOUSLY UNKNOWN CONDITION(S)

Risks: As a result of the study tests, we may discover that you have a medical condition that you did not know about. If we find something, we will inform you. We will discuss the findings with you and explain your options. You may be advised to follow up with your regular doctor or other specialists for future care.

DOSE ESCALATION

Procedure: How much [*specify drug*] you get will depend on when you join the study. We will start by using a low dose when people join the study. If participants on one particular dose don't have serious side effects, the next group of participants will get a higher dose.

If you have a serious side effect, you will stop taking the drug. You will be asked to continue in the study for the rest of the visits even if you stop taking the study drug.

DXA

Procedure: You will have a DXA (Dual energy X-Ray Absorptiometry) scan to check your bone density. This scan will take place at [*X*] and will take about [*20 minutes*] to complete. During that time, you will need to lie still on a padded table while your body is scanned. We will do [*specify # of scans*] different scans: [*Specify, as applicable: 1 of your whole body, 1 of your lower back, and 1 of your forearms*].

Risks: See "**RADIATION**" below.

TRANSTHORACIC ECHOCARDIOGRAM

Procedure: You may/will [*choose appropriate language*] need to have an echocardiogram done as part of this study. An echocardiogram is a painless test that uses sound waves to take a picture of your heart. During this test, we will put some jelly on your chest. We will then place the ultrasound probe on your chest to take the picture. We may ask you to lie on your side to get a better picture. For some pictures, we may put the probe on the upper part of your abdomen and push down firmly. This can be uncomfortable. The scan takes about 30 minutes to complete.

Risks: Other than mild discomfort during the test, there are no known risks to an echocardiogram.

*Also see "**DISCOVERY OF PREVIOUSLY UNKNOWN CONDITION(S)**" above.*

ELECTROCARDIOGRAM

Procedure: An electrocardiogram (ECG) is a test that looks at the electrical activity of your heart. You will need to lie still for about 5 minutes. We will place electrodes on your chest, arms, and legs. Electrodes are small stickers attached to wires that go to the machine. The signals are recorded by the machine. If you have a lot of hair on your chest, it may hurt a little bit when we remove the stickers.

Risks: Other than having some minor skin irritation from the electrodes, there are no known risks related to the ECG.

EXERCISE TESTING

Procedure: At study visit *[X]*, you will have an exercise test. This test involves walking and running on a treadmill while hooked up to a monitor. The monitor will measure your heart rate, heart rhythm, and blood pressure. You may also be asked to wear a mouthpiece and a clip on your nose so that we can check your breathing. To start, the treadmill will be set at a slow walk speed but will change to slightly faster speeds and higher inclines (slope) every few minutes. You will be encouraged to give as much effort as you can and to keep going until you feel too tired to

continue. Once you reach that point, you can tell the study team, and they will slow down the treadmill and lessen the incline. We will ask you to keep walking on the treadmill until you are comfortable walking again. Your blood pressure, heart rate, and breathing rates will still be checked for 15 minutes after you complete the test.

Risks: The exercise test may cause muscle soreness, dizziness, shortness of breath, lightheadedness, abnormal heart rhythm, chest pain, or you might feel faint. You could also trip or fall while on the treadmill. You will be watched during the entire test by the study doctor.

FIBROSCAN

Procedure: A Fibroscan® exam is like a regular ultrasound but it only looks at the liver. It has a special probe to look at the toughness of the liver.

You will be asked to lie flat on the exam table. We will put a small amount of warm jelly on your skin. We will slide a special probe over your liver so the Fibroscan® can measure the toughness of your liver.

FLUORESCEIN ANGIOGRAPHY

Procedure: This test is done to confirm your diagnosis of *[insert disease]*. A small amount of dye will be injected into your arm. Your skin may turn pale yellow for a few hours, and your urine will turn a bright yellow-orange. This is normal and may take 2 days to wear off. We will take special pictures of the back of your eye, which will show the dye in the blood vessels of your eye. If you are allergic to fluorescein dye, please tell us. You will not be able to be in this study if you have a fluorescein allergy.

Risks: For angiography, you will get an injection (shot) in your arm of a dye that glows when exposed to certain kinds of light. You may have some discomfort from the bright lights that will be shined into your eyes to take the pictures. You may have mild discomfort from the needle that injects the dye. The dye may leak into the tissue in your arm near the needle stick, causing discomfort that lasts only a short time. It is also possible, but not likely, that you will get an infection. Some people feel dizzy and may faint during the procedure. Occasionally, people have mild nausea. You may have an allergic reaction to the dye. This can include vomiting, fever, hives/rash, itching, and trouble breathing. Very rarely, people have a serious allergic reaction to the dye. We will watch you closely during and after this procedure for any signs of side effects.

FOCUS GROUP

Procedure: You will be asked to take part in a focus group discussion led by one of the investigators. The focus group will have about *[specify #]* members. The discussion will last for about [specify duration of time]. During that time, you and the other group members will be asked questions about your opinions and experiences with *[specify topic about which data are being collected]*. We ask you to keep what is said during the group discussion confidential between the focus group members only.

Risks: See "**INVASION OF PRIVACY/BREACH IN CONFIDENTIALITY**" below.

GENE THERAPY

***Example language for* lentiviral gene transfer [tailored per protocol]:**

Procedure: Gene therapy corrects a gene mutation in your cells. In this study, we use an experimental procedure called "lentiviral gene transfer." This procedure is considered investigational, which means it has not been approved by the U.S. Food and Drug Administration (FDA). We are testing it in this study.

The gene therapy you will get on this study uses a lentiviral vector. A lentiviral vector is like a virus, but it does not make people sick. We use it because it can add its own DNA into other cells. Our lentiviral vector holds a working, "healthy" gene. When we mix it with some of your stem cells in the lab, the vector uses its own DNA to add the working gene into your stem cells. This means that your stem cells will then have a working version of the gene. Then we will infuse the stem cells back into you.

Risks: Gene therapy can cause serious complications and even death. The risk of death or other complications can vary greatly. You should discuss your individual risk with the study doctor. Your risk depends on your age, the way the gene therapy is done, the amount of damage your body may have from infections and treatments you have had in the past, and other reasons.

Lentivirus Vector

The process of making the changed T cells involves permanently transferring genetic material into your T cells. The "vehicle" or "carrier" for this transfer is a lentivirus vector, which is related to the HIV virus. The lentivirus vector cannot replicate like a virus and therefore cannot cause HIV infection or disease.

The lentivirus vector contains some proteins related to HIV. As we explain above, there is no risk of getting HIV from the vector. However, it is possible that future HIV testing may falsely indicate that you are HIV positive when you are not. Since simple screening tests could detect HIV antibodies in your blood, additional tests will need to be done to determine your true HIV status.

DNA Integration

When lentivirus vectors enter a normal cell in the body, the genetic material (DNA) of the vector is put into the normal DNA in that cell. This process is called DNA integration. Most DNA integration will not cause any harm to the cell or to you. However, there is a chance that this process could damage your healthy cells and could even make these cells become cancerous. Continued follow-up with your Study Doctor is important to check if you still have the changed T cells and to monitor for any new medical conditions.

Replication Competent Lentivirus

There is a risk when receiving changed T cells that the lentivirus can cause an infection. This is called Replication Competent Lentivirus (RCL). We do not know the risks of RCL since it has not been seen yet in participants receiving changed T cells. To lower the chance of RCL, tests will be performed on the T cells during the manufacturing process to make sure RCL is not found in them. The FDA requires that you continue to be tested for RCL after receiving the changed T cells.

After you receive the changed T cells, you will have blood tests done to test for RCL while you are in the active and long-term follow-up parts of the study. If at any time your blood test is positive for RCL, you will have additional tests to confirm the result. If it is found that you have RCL, your Study Doctor will work with you to come up with the best treatment plan for you.

For guidance as to whether or not you need to include Long Term Follow Up for investigational

gene therapy products in your protocol/consent; please refer to the FDA guidance document: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/gene-therapy-clinical-trials-observing-subjects-delayed-adverse-events

Example: **Risks and long term follow up after gene therapy (*retroviral vectors*)**

There are risks and complications that can happen months or years after gene therapy:

- **Extra gene copies:** Some people who get gene therapy develop blood cells that have more copies of the added genes than we meant to put in each cell. We do not know whether the extra genes are harmful. It is possible that these people may have a higher risk of getting leukemia or other blood disorders in the future. We will monitor this and tell you if we see any important changes.
- **Cancer and other health problems**: We are unsure if this type of gene therapy will cause you to become sick in the future. It is possible that it may cause a sickness of your blood cells or even a cancer such as leukemia. We do not know if you will develop any of these disorders, but you need to be aware of this possible risk. Children in France and England received gene therapy for a particular disease of the immune system. Most of the children were cured, but 5 children out of 22 later developed leukemia, and one child died. Experts who looked at these cases thought that the gene therapy caused the leukemia in these children. To watch you for this risk, we will test your blood during the study follow-up.
- **Failure**: Sometimes, even if the modified cells engraft in the bone marrow and you recover, the cells can fail at a later time. We will regularly monitor for failure after the gene therapy using blood tests at 1, 2, 3, 6, and 12 months after the gene therapy. If your modified cells appear stable by 1 year, it is unlikely that they would fail later, so after that, we will monitor you much less often.

Additional example: **Gene Therapy Long Term Follow up for retroviral vectors [tailored per protocol]**

Because we do not know the long-term side effects of gene therapy, we will ask you to take part in long-term follow-up for the next 15 years. The Food and Drug Administration (FDA) requires that people who get gene therapy are seen by a doctor for follow-up visits even after they complete the study.

We will ask you questions about your health and ask you to have a physical exam every year for *[insert number]* years. We will also take blood samples from you for at least one year, but maybe longer. We will take blood samples (2 teaspoons each time) right after you get the *[insert product]*, and at 3, 6, and 12 months after gene therapy.

We may also take blood samples over the next several years if you have any tests that show a retrovirus in your blood. This testing will help us learn if the cells have grown or changed in your body. For this reason, we ask that you continue to give us your current address and telephone number, even after you complete this research study.

If you return to your referring doctor after being in the study, we will ask you to have your doctor send us a copy of your physical exam and any blood samples.

When you die, no matter the cause, we may ask for consent from your family for an autopsy. This will allow us to learn important information about the safety of this gene therapy. Please talk about this with your family to inform them about this potential request.

Gene Therapy Long Term Follow up for non-retroviral vectors [tailored per protocol]

The Food and Drug Administration (FDA) requires that people who get gene therapy be monitored even after they complete the gene therapy study. Once you have finished the gene therapy study, you will be monitored for up to *[insert number of years]* years to see how well you are doing. This will be done under a separate NIH study that you have enrolled in even before enrolling in this study. At the least, you will be asked to have a routine physical exam each year for five years after gene therapy.

We will ask questions about your health, such as whether you have any new cancers or problems with your blood or immune system. You will also be asked whether you have had a hospital stay for something you did not expect. You will be asked what medicines you are taking. You will be called on the telephone for more information about your health each year for *[insert number of years]* years following the gene therapy. The FDA will have access to this information. For this reason, we ask that you continue to give us your current address and telephone number, even after you complete this research study.

GENOMIC SEQUENCING

Purpose of planned [genome, exome sequencing or other genomics-related analysis research]

Prospective participants should be given a succinct explanation of why they have been approached for the proposed study. This section should include topics such as a brief description of the underlying scientific justification for the research project, the study design, the diseases(s) or condition(s) being studied, and the immediate and long-term goals of the research project. Using simplified language that is not overly technical may help prospective participants understand the rationale for genome sequencing, exome sequencing or other genomics-related analysis.

Example Language #1:

We are asking for your permission to do *[specify type of analysis, i.e., genome and/or exome sequencing]* on your *[specify type of specimen, i.e., blood and/or tissue samples]* and to link the results to your medical and/or family history.

Your blood and tissue samples contain genes, which are made up of DNA (deoxyribonucleic acid) which serves as the "instruction book" for the cells that make up our bodies. Sequencing *[specify type of analysis, i.e., genome and/or exome]* tells us the exact order of the chemical letters in *[the tumor being studied, or blood].* Your sample(s), along with *[specify any correlations, i.e., medical and family history information]* will help us study how genes *[specify purpose of analysis].*

Example Language #2:

We will also study your DNA. DNA is in your blood and other samples.

All human beings share more than 99% of their DNA with each other. The tiny bit that is different is part of what makes each of us unique. Things like our hair color and eye color depend on the

bits of our DNA that are different between human beings. We call these our DNA changes. These changes can also tell you about your health and how your body works. They can tell you about where your ancestors may be from. We are still learning about what role DNA plays in many parts of our lives.

DNA is passed from parents to children. Half of your DNA came from your mom and half came from your dad. If you have children, each of them will get half of your DNA. In this way, your DNA also tells you about your family.

We will use many methods to study your samples. For example, we might study your DNA using whole genome sequencing. Whole genome sequencing is a way of studying almost all of a person's DNA. Every person's whole genome sequence is different. It is unique to them, like a fingerprint. Because this study will last for ten or more years, some of the methods we use may not even be invented yet.

Example Language #3:

Tumor and blood samples taken for research purposes in this study may be used to look for specific changes in the DNA of tumors. Learning about these changes could help us develop new ways to diagnose and treat cancer.

DNA (also called deoxyribonucleic acid) in the cells carries genetic information and passes it from one generation of cells to the next, like an instruction manual. While normal tissue contains the DNA (instructions) that you were born with, DNA in tumor cells has changed—or mutated—and we think that change in the DNA is what causes tumors to form and grow. RNA (also called ribonucleic acid) carries the instructions from the DNA to the parts of your cells that make proteins.

To look at your DNA and RNA, we may use what is called "DNA sequencing" or "RNA sequencing." We will do special tests in the lab to look at the order (also called a sequence) of how your DNA or RNA are put together. This is what makes you unique.

To learn which parts of the DNA or RNA have mutated, we will compare the DNA or RNA in your tumor cells to DNA or RNA from normal cells. We will then analyze the results from similar tumors to see if there are any changes in the DNA or RNA that are common to a particular type of tumor.

Secondary Findings

Investigators performing genomic analysis that can feasibly be interrogated for secondary findings, such as genome or exome sequencing, in their protocols must describe a plan for the management of such findings within the protocol and consent. For a complete description of the expectations for a return of secondary findings plan, please refer to the Guidance for the return of secondary genomic findings document.

If there will not be any analysis and reporting of secondary findings, this must be stated in the consent.

If there will be analysis and reporting of secondary findings, the informed consent must address the following elements:

- *What secondary findings will be looked for and disclosed. It is acceptable to refer to "genes that are important for your health" or something similar. You do not need to specify the specific genes, unless you think this will be meaningful to the subjects.*
    - *The ACMG list that is most current at the time the analysis is performed is the minimum that should be performed.*
    - *Additional genes over and above the ACMG list may be included if they are generally agreed upon by the expert community to be clinically important to the subject and are actionable.*
- *A description of the expectation of research subjects to keep the NIH investigators informed of current contact information and the process for them to do so.*
    - *The informed consent should make it clear that the onus is on the subject to provide the research team with updated contact information, and that if they fail to do so the NIH will not be able to contact them and return secondary findings.*
- *A statement that subjects will not receive a negative report, i.e., that they will not be notified if the result of the analysis does not show any reportable findings, unless the investigators intent is to notify all subjects regardless of the presence of secondary findings.*
- *A statement describing the timing of the planned analysis expected time frame for subject notification relative to the time of sample collection.*
    - *If it is known that the analysis may not be conducted for an extended period, this should be made clear to subjects. In particular it should be clear that the lack of any notification does not mean that there are no findings, as no analysis may yet have been performed.*
- *A description of the process by which subjects will be informed of any secondary findings*
    - *How do you intend to contact subjects?*
    - *If the original analysis will not be conducted in a CLIA certified laboratory and the investigator will contact the subject for the collection of additional samples, this should be stated.*
    - *How the information will be provided (in person visit, telephone or telehealth) and involvement of a genetic counselor (if applicable).*
- *A statement that if at any time the subject chooses not to be informed of any secondary findings, that choice will be respected.*
    - *It is not required to include opt in/opt out selections on the informed consent document. However, during the consent discussion, it should be clear that the if a secondary finding is detected, the subject is free to decline learning about it.*
- *A statement that the result will only be provided to the research subject (or parent/legal guardian if the subject is a minor, or legally authorized representative if the subject lacks decisional capacity).*
    - *In the case of minor participants, the consent should disclose whether results for adult-onset disorders will be disclosed to children or the parents of minor participants and the rationale for either choice.*
- *If applicable, a plan for return of results when to minor research participants when they reach the age of majority.*
- *If the research team wishes to have the option to inform someone other than the subject, for example a family member in the event the subject is deceased, this should be addressed*

in the consent and in addition a valid release of medical information naming that person as authorized to receive the information should be executed.

- *Any risks and benefits associated with returning secondary genomic findings*

Example Language for Secondary genetic findings – Return of results

In this study, we will use a test to look at most or all of your genes or DNA. This test might find changes in your genes that are not related to what we are studying. These are called "secondary findings." Most of the time, we do not find anything. If we looked at 100 people, we might find these changes in only about 2 to 4 people.

If we find a secondary finding that might be important for your or your family's health, we will tell you. But first, we may need to do the test again in another lab to make sure the result is correct. We might need you to give another sample for testing. Once we have the results, we will invite you to come to the NIH (at our expense), schedule a telemedicine visit, or use another way to explain the result and help you get follow-up care if needed. The NIH will not usually provide any further testing or care for this condition for you or your family.

We might not test your samples for several years. So, if you don't hear from us, it doesn't mean you don't have any important gene changes. Also, we do not know all the gene changes that cause health problems. In the future, we might learn that some gene changes we don't think are important now could cause health problems.

You can choose if you want to know about any secondary findings. You can tell us at any time that you don't want to be contacted about these findings. We will only give these results to you. If you want us to tell someone else, you must give us a signed written release.

It is very important to keep us updated on how to contact you. If we don't have your current contact information, we won't be able to reach you to collect another sample or tell you about a secondary finding. If your contact information changes, you need to let us know. *[Insert information here on how to update your contact information]*.

If you have questions or concerns about learning this kind of genetic information, please talk to someone from the study team.

Disclosure of secondary genetic findings to research participants who are minors

If we find a gene change that is known to cause a health problem in children, we will tell you so you can get care for your child. Some gene changes cause health problems only in adults. If we find a risk of an adult-onset condition in your child's genes, we will also tell you. You can choose to include your child in this discussion, or you can tell them yourself when you think it's the right time.

Risks of returning secondary genetic findings

- The test for unexpected gene changes is limited. It might not be as thorough as the clinical genetic tests you could get outside of this research study.
- If we confirm an unexpected gene change, the test result will go into your NIH medical record. These records are private, but other NIH researchers can see them.

- Learning about gene changes might affect your family members and could cause stress for you or them. Before joining the study, it might be helpful to talk with your family about whether they want to know your results.
- If we find a gene change, it might show which parent passed it to a biological child.
- We might tell you about a gene change that doesn't actually cause the health problem we think it does. This might cause you unnecessary worry or lead to extra medical tests that aren't needed and cost money.

Benefits of returning secondary genetic findings

- An unexpected gene change result may be useful because you may be able to do something about it to protect your health or to plan for your future.

Example language for Secondary genetic findings - Explanation of why results are not being returned

Language for use by protocols when the IRB determines that secondary results do not need to be returned.

In this study, we will use a test called genetic sequencing that looks at most or all of your genes or DNA. There is a small chance that we might find gene changes that are not related to this research study. We do not plan to give you any individual results from your genetic sequencing because *[insert explanation here]*. If you want to learn more about your genes, you can get clinical genetic testing through your healthcare providers.

HIV TESTING

*If your study involves testing participants for HIV at the Clinical Center, the following language is **required** per the CC epidemiology department (it may be used for other locations as applicable):*

As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV, you will (*not/still*) be able to be in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners who are at possible risk because of your HIV infection.

IMMUNOSUPPRESSION: REACTIVATION OF VIRAL INFECTIONS

Many people have had infections with different viruses without knowing it or without having symptoms. Some of these viruses can stay inactive in your body but might become active again after certain cancer treatments, including the study drug and chemotherapy.

Viruses like Epstein Barr virus (EBV), cytomegalovirus (CMV), herpes zoster virus (HZV), and Hepatitis B virus (HBV) can become active again after cancer treatment, including T-cell therapy. If the EBV virus becomes active, it may cause a condition called lymphoproliferative disease, which makes certain white blood cells multiply quickly in lymph glands or other organs. Rarely, reactivation of these viruses can lead to new cancers.

Before you join the study, we will check to see if you have had any of these viruses in the past. If the study doctor thinks any of these viruses have become active after your treatment, we will do a

blood test to confirm it and provide treatment if needed.

IPS CELLS

We may use some of your blood or skin samples to make special cells called induced pluripotent stem cells, or iPS cells. iPS cells can be used in the lab to create many other types of cells. They can help us make an unlimited supply of stem cells (cell lines) for research. Using iPS cells from your samples can help us understand your condition better. We can use your cells to find out if changes in your genes are causing your disease or to see how your cells work.

IV (INTRAVENOUS CATHETER)

Procedure: We will put a small plastic tube called an intravenous (IV) catheter into a vein in your arm using a needle.

Risks: The risks of putting an IV in your arm include temporary pain, bleeding, and bruising where the IV goes into your skin. There is a small chance that fluid might leak into the tissue near the IV, which can cause swelling and discomfort. Rarely, the IV site might get infected. If you get an infection, we may have to give you antibiotics.

INTERVIEW

Procedure: We will interview you in a private location for about *[X time]*. We will ask you questions about your experiences with *[specify topic(s)]*.

Risks: Some of the questions may be upsetting or make you feel uncomfortable. You do not have to answer any questions you do not want to answer. You can stop the interview at any time.

*Also see "**INVASION OF PRIVACY/BREACH IN CONFIDENTIALITY**" below.*

INVASION OF PRIVACY/BREACH IN CONFIDENTIALITY

Risks: Because we will collect personal, identifiable information about you, it is possible that people who are not supposed to see your information might somehow get access to it. We will take precautions to prevent this, but we cannot be completely sure it won't happen. To minimize this chance, we will label your information with a study number instead of your name or medical record number. All the information we collect about you will be securely stored, such as in locked cabinets or password-protected computer files.

LEUKAPHERESIS

Procedure: Leukapheresis is a procedure where we separate white blood cells, a type of immune cell, from your blood using a machine.

Two large needles will be placed in your veins near each elbow. These needles are the same size as those used by the Red Cross for blood donations. The needles are connected to a machine that will process your blood. During the procedure, your blood will flow from one arm to the machine and back to your other arm. The machine will remove some of your white blood cells and return the rest of your blood to your body.

Sometimes we use a central line instead of needles in your arms. A central line is a large catheter placed in your neck or under your collarbone.

To keep your blood from clotting inside the machine, we add a chemical called citrate. We also add some saline (fluid) to your blood. The amount of saline depends on your blood pressure and how long the procedure takes. Your kidneys will remove the extra saline quickly, so it won't affect you. The citrate might cause tingling in your lips and fingers. If this happens, we will give you calcium (like Tums) to stop the symptoms.

We will use standard medical procedures to collect your white blood cells. We will check your pulse, blood pressure, and temperature before and after the procedure. You will also be asked to tell us about any new symptoms, like lightheadedness, tingling lips or fingers, or shortness of breath. The procedure could last about 2-4 hours, and you will be watched for about 1 hour or more afterward. You will return for a check-up.

Risks: The risks of leukapheresis include pain, bruising, lightheadedness, dizziness, nausea, vomiting, and chills. Bruising may last up to 72 hours. You might have tingling around your mouth, fingers, or toes, or mild muscle cramps because your blood calcium may drop slightly from the blood thinner used during the procedure. These symptoms can be treated by stopping the procedure temporarily or by giving you a calcium pill.

Leukapheresis uses a completely closed sterile system. We minimize the risk of infection by cleaning your skin before inserting the needle. No infections from leukapheresis have been reported in thousands of procedures done over the last 10 years at the NIH.

Rarely, the machine can malfunction and prevent the return of your blood to your body. The amount of blood lost would be very small and is not harmful. It is also rare for people to faint, have seizures, or have air trapped in the bloodstream. Nerve damage may occur where we place the needle, but this is very rare. So far, there have been no cases of permanent nerve damage with leukapheresis at the NIH.

During leukapheresis, your platelet count may drop because platelets are collected with the white blood cells. Platelets help your blood to clot. Taking aspirin while you have a lowered platelet count may increase your chance of bleeding. Therefore, you should not take aspirin or drugs that contain aspirin for 2 weeks after leukapheresis unless your doctor approves it.

LIVER BIOPSY, PERCUTANEOUS

Procedure: The percutaneous liver biopsy will be done with you lying on your back. The doctor will clean the skin over your liver on the right side of your chest. You will be awake for the procedure. We will give you a numbing medication. When your skin is numb, the doctor will insert the liver biopsy needle into your skin. The doctor will then quickly pass the needle into and out of your liver to take the biopsy.

The biopsy itself is a quick procedure. You may or may not feel it, but some people feel slight pain when the needle enters the liver.

After the biopsy, you will be asked to roll onto your right side and lie on that side for *[specify # of hours]*. This puts pressure on the biopsy site and helps stop any bleeding. Then you will need to stay on your back in bed for *[specify # of hours]*.

LIVER BIOPSY, TRANSJUGULAR

Procedure: We will access your liver through a large vein in your neck. This procedure is done while you are sedated. We will insert a needle into a large vein in your neck area. Through this site, a thin tube (catheter) will be moved along the large veins of your chest until it reaches the veins of your liver. About *[specify amount in simple terms, such as "a small piece"]* of liver tissue will be taken using a needle. After the biopsy, you will need to stay in bed for *[specify # of hours]*.

LUMBAR PUNCTURE

Procedure: You will have a lumbar puncture (also called a "spinal tap") so we can get cerebrospinal fluid (CSF) samples at visits *[specify which visits]*. We will insert a small needle into your lower back. Then we will help you lie on your side or sit up. We will clean the lower part of your back with antiseptic, and then we will inject a small amount of local anesthetic to numb the area. Once numb, a very thin needle will be inserted into the spinal canal in your lower back (well below where the spinal cord ends). About *[specify volume, such as "a few teaspoons"]* of spinal fluid will be removed for analysis and storage. Your body usually replaces this fluid within 1-2 hours.

After the lumbar puncture (LP) is complete, you will be watched for about 30 minutes. To prevent side effects, it is important that you do not do any strenuous physical activity for 24 hours after the procedure. For example, you should not do any lifting, bending, housework, gardening, or exercising.

Risks: The lumbar puncture (LP) may cause pain where the needle goes into your skin and where the spinal fluid is taken. There is a small risk of infection or bleeding.

You may get a headache after the LP. About 1 in 3 adults report a headache after an LP. To minimize the risk of a headache, the doctor will use a small needle during the procedure. The doctor may also prescribe bed rest for one or more hours afterward. If you get a headache, it is usually mild and can be controlled with bed rest, drinking lots of fluids, and taking a pain pill, such as acetaminophen. Rarely, the headache is severe and may require additional treatment with a "blood patch." In this procedure, a small amount of your own blood is injected into the lumbar puncture site. This usually stops the headache.

A rare but serious complication of an LP is known as a medullary herniation, which can cause death. This can happen if the LP is done when the pressure inside your head is higher than normal (such as when there is a brain tumor). Increased pressure inside your head is very unlikely. We will not do the LP if there are any signs that you have increased pressure inside your head. We will also not do the LP if you have a skin infection in your lower back area, or if you have bone defects of the lower back (including severe scoliosis) which would make an LP difficult to do.

To minimize these risks, the LP will be done by a medical professional specifically trained to perform this procedure.

*Also see "**ALLERGIC REACTION**" above for risks related to the use of lidocaine.*

MAGNETIC RESONANCE IMAGING

Instructions to investigators: If more than one type of MRI scan is done during the protocol or during a single session, combine the appropriate procedure language (structural, functional, spectroscopy) into a single paragraph.

Routine or Structural MRI

Procedure: At visit *[X and Y]*, you will have an MRI (Magnetic Resonance Imaging) done at *[list location]*. An MRI makes pictures of the inside of your body using strong magnets instead of X-ray energy. At each scan, you will be asked to fill out a screening form to confirm that it is safe for you to have the scan. You will also be asked to remove any metallic objects you are wearing (such as watches, earrings, or piercings). We may ask you to change into a hospital gown.

Then you'll be asked to lie on a narrow bed that will move into the MRI scanner. *If applicable:* [Before moving you into the scanner, special padding will be placed around your head to help keep your head still.] The scanner is a long, narrow tube that is open at each end. Once you are comfortable, the table will be moved into the scanner. You will need to lie still on the table during the scan. The scan will take about *[30 minutes or specify as applicable]* to complete. You will hear normal "hammering," clicking, and squealing noises during the scan. We will give you earplugs or earmuffs to muffle the sound. You will be able to communicate with the technician running the scan the entire time. We will also give you an emergency button to squeeze at any time if you want the scan to stop.

Brain Functional MRI

Procedure: Magnetic resonance imaging (MRI) uses a strong magnetic field and radio waves to take pictures of your brain. Functional MRI (fMRI) lets us see which parts of your brain are used when you do a task.

The MRI scanner is a metal tube surrounded by a strong magnetic field. During the MRI, you will lie on a table that can slide in and out of the tube. A device called a "coil" will be placed over your head.

For your fMRI scan, you will *[insert task]*. *If applicable:* There is a computer screen that you can see when you are inside the scanner. The screen will show you task information.

You will be in the scanner for about *[insert time]* minutes/hours. During the scan, you may be asked to do the study task, or you may be asked to lie still for up to *[insert time]* minutes at a time. While in the scanner, you will hear loud knocking noises. We will give you earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff the entire time. You may ask to be moved out of the machine at any time.

Magnetic Resonance Spectroscopy

Procedure: Magnetic resonance spectroscopy (MRS) uses a strong magnetic field and radio waves to take pictures of various chemicals in your *(insert body part)* using an MRI scanner. The MRI scanner is a metal tube surrounded by a strong magnetic field. During the MRS scan, you will lie on a table that can slide in and out of the tube. We will place soft padding or a coil around your *(insert body part)*.

You will be in the scanner for about *(insert time)* minutes. You may be asked to lie still for up to *(insert time)* minutes at a time. While in the scanner, you will hear loud knocking noises. We will give you earplugs or earmuffs to muffle the sound. You will be able to communicate with the MRI staff the entire time. You may ask to be moved out of the machine at any time.

For any MRI, if applicable:

It is very important that you do not move your head or body inside the scanner. We will use padding around your *(insert body part)* to help keep it in place.

We may place a bar in your mouth to help keep your head still.

If MRI will be done combined with PET scanning

Describe both the MRI and PET procedures and add the statement:

The MRI and PET scans may be done on a combined MRI-PET scanner during the same session.

Investigational use of MRI (machine, sequences coils, and/or imaging software)

If your protocol is using MRI in an investigational manner (using research (i.e. not FDA-cleared) pulse sequences, research coils, research imaging reconstruction and analysis software, and/or an unapproved MRI scanner), use this language as applicable and see 501.Guideline for Device Classification for Protocols Using MRI:

We will use the MRI in this study for research purposes. This means that the way the MRI is making the images may be different than what is normally done in a routine clinical scan.

Revise and include ONLY the detail that is applicable to your specific study:

We plan to use *[insert correct choice(s): research pulse sequences, research coils (antennae), and research imaging reconstruction and analysis software]*. These are the parts of the machine that help make or analyze the image. These MRI research tools have not been cleared by the FDA and are considered investigational. *If applicable:* [The MRI machine that we will use is also considered investigational (not yet cleared by the FDA)]. However, all MRI scans done under this protocol will be done within the stated FDA safety parameters and meet all relevant safety guidelines.

Risks for MRI, fMRI, MRS:

You might be at risk for injury from the MRI magnet if you have certain kinds of metal in your body. It may be unsafe for you to have an MRI scan if you have:

- Pacemakers or other implanted electrical devices
- Brain stimulators
- Some types of dental implants
- Aneurysm clips (metal clips on the wall of a large artery)
- Metal prostheses (including metal pins and rods, heart valves, and cochlear implants)
- Permanent eyeliner
- Tattoos
- An implanted delivery pump
- Shrapnel fragments (pieces of metal from injuries)
- Small metal fragments in the eye (common for welders and metal workers)

You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should tell us. You will be asked to fill out an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before you enter the MRI scan room.

If you are afraid of confined (small, cramped) spaces, you may get anxious during an MRI. If you have back problems, you may have back pain or discomfort from lying in the scanner.

The noise from the scanner is loud enough to damage your hearing, especially if you already have hearing loss. We will give you hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Additional language for gadolinium enhanced MRI

Procedure: During part of the MRI we will give you gadolinium, a contrast agent, through an intravenous (IV) catheter (small tube). It will be done for *(Use the applicable wording*: research *OR* both research and medical) uses.

Only use this language if pregnancy risks are not discussed elsewhere in the consent: We do not know if MRI with contrast is completely safe for a developing fetus. Therefore, all women who could become pregnant will have a pregnancy test done no more than 24 hours before each MRI scan with contrast. We will not do the scan if your pregnancy test is positive.

Risks: Gadolinium-based contrast agents (GBCAs) used in MRIs are generally safe, but there are some risks to consider:

- **Side effects**

Common side effects include headache, nausea, dizziness, and a cold feeling at the injection site. Less common side effects include itchy skin rash and severe allergic reactions.

- **Gadolinium retention**

Most of the gadolinium contrast will leave your body in the urine. However, small amounts of gadolinium can remain in the body for months or years, and can be detected in the brain, skin, kidney, bone, and lymph nodes. When you get the scan, we will give you additional information called a "Medication Guide". If you ask, we will give you individual information about any remaining gadolinium we see on your scans.

- **Nephrogenic systemic fibrosis (NSF)**

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)." NSF can cause skin contractures and internal organ damage. The risk of NSF is believed to be low for patients with less severe kidney disease, but it can still occur.

Additional language for 7T scanner

Risks: In this study, we are using an MRI scanner that has a strong 7 Tesla magnet. Because of the strong magnetic field, some people briefly experience:

- Muscle twitching
- Eye discomfort
- Dizziness
- Mild nausea
- Headache

- A metallic taste in their mouth
- A sensation of flashing lights

Many of these effects are caused by moving too quickly in the magnetic field, so you will be asked to walk slowly to the MRI table. Once you lie down, we will move the table slowly into the scanner. You can ask us to stop the scan at any time if you feel too uncomfortable. There is no evidence that scanning using a high magnetic field is dangerous. However, we do not know if there are any long-term effects.

Language regarding incidental MRI findings

Note: If you use this language, this paragraph should be placed in the consent section in the return of results to participants

A credentialed radiologist *(or neuroradiologist)* will read your MRI scan. They might find unexpected findings on your MRI scan or from other tests we perform. We may not know the significance or importance of some findings, which could make you anxious. We will only inform you about any findings that require further evaluation or care. We are not able to evaluate or treat these conditions at NIH. If needed, we will refer you to a healthcare provider.

NASAL WASH

Procedure: We will do a nasal wash at study visits [*specify which visits*]. To do this, a small amount of salt water will be put into each side of your nose and then suctioned out.

Risks: The nasal wash may cause sneezing and minor irritation of your nose and throat.

OPTICAL COHERENCE TOMOGRAPHY(OCT)

Procedure: A machine will measure the thickness of your retina by taking pictures of your eyes. [*If applicable:* OCT will be repeated during the study to see whether retinal thickening is getting worse, getting better, or staying the same.]

Risks: There are no known medical risks to measuring retinal thickness using OCT or having pictures taken of the eye.

ORAL GLUCOSE TOLERANCE TEST

Procedure: An Oral Glucose Tolerance Test (OGTT) will be done during visits *[X and Y]* to measure the levels of glucose (sugar) and insulin in your blood. We will give you specific instructions for your diet the day before the testing. The instructions will be tailored to you. Generally, the test will include the following procedures:

- Drink only water. Have no other foods or liquids after 10 pm the night before the test and on the morning of the test. This is called "fasting."
- We will insert an intravenous (IV) needle and thin tube in your arm so that we can take blood multiple times without having to "stick" you each time. The needle will stay in your arm for the entire test.
- We will ask you to drink *[specify what they will drink]*.
- We will take some blood about every ½ hour from the IV over 4 hours.

Risks: Fasting before the OGTT may make you feel light-headed or dizzy. You may also feel weak,

hungry, nervous, or restless towards the end of the test because your blood glucose levels may drop. The risks of putting an IV in your arm may include temporary pain, bleeding, or bruising where the IV enters your skin. There is a small chance of fluid leaking into the tissue near the IV. There is a small chance the IV might get infected. We will give you antibiotics if you get an infection. Rarely, the IV may need to be removed, and we will have to insert a second one.

PAYMENT

If your study provides payment to participants, required language for your consent is found in the relevant consent template. Below is the language in Spanish that must be included if payment to an individual could equal or exceed $2000 (not including reimbursement for parking, meals, etc. based on receipts) in a calendar year.

La compensación del estudio puede considerarse ingreso gravable y debe declararse al Servicio de Impuestos Internos (IRS). Se le enviará un formulario "Form 1099-Other Income" si el total de los pagos que recibe por participar en la investigación supera el límite que debe declararse como ingreso gravable en el año calendario en el que participó. Si tiene preguntas, comuníquese con el Programa de voluntarios de investigaciones clínicas escribiendo a CC-PRPLRVSSupport@cc.nih.gov.

PET SCAN

Procedure: You will have a PET (Positron Emission Tomography) scan at visits *[Y and Z]*. The PET scanner is a donut-shaped machine that uses X-rays combined with a dose of radioactive material (tracer) to make computer pictures showing the inside of your body.

Before the scan, we will give you an injection (shot) of radioactive material into a vein in your arm. After the shot, you will need to wait for about 1-2 hours for the material to be absorbed by your body. After this time, you'll lie on a narrow, padded table. We will position your body for the scan. The scan itself is painless and won't make noise. During the scan, you will need to lie very still. The scan will take about another 30 minutes to complete.

Risks: See "**RADIATION**" below and "**CONTRAST AGENT**" & "**IV (INTRAVENOUS CATHETER)**" above.

PLACEBO

Procedure: A placebo looks like the study drug but doesn't include any medicine.

RESEARCH-RELATED INJURIES—PREP ACT

Required Informed Consent Language if applicable

If your study uses a COVID-19 covered countermeasure, substitute the following language in the research injury section of the informed consent document. For NIH studies that are conducted at NIH sites other than the Clinical Center, please adapt the first paragraph to be consistent with your site-specific language already approved by OHSRP.

The NIH Clinical Center will give you short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care will be given to you by the NIH, the NIH Clinical Center, or the Federal Government.

A Declaration under the Public Readiness and Emergency Preparedness (PREP) Act was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a subject participating in clinical studies using COVID-19 countermeasures. Because this study is covered by the PREP Act Declaration, covered persons, such as the manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States).

If you believe that you may have been harmed because of this research study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program. This is a program set up by the United States Government. Information about this program can be found at https://www.hrsa.gov/cicp/about/index.html or by calling 1-855-266-2427.

PRIVACY LANGUAGE FOR STUDIES CONDUCTED OUTSIDE OF THE CLINICAL CENTER

Required Informed Consent Language if applicable

Situations arise in which subjects are enrolled into an NIH protocol, but they do not receive the usual Certificate of Confidentiality and Privacy Act notifications. This may occur in the following situations:

1. *The research is approved for an oral consent process with a waiver of documentation of consent (also known as a waiver of signature);*
2. *The research utilizes an online consent process with an IRB waiver of documentation of consent;*
3. *The research is approved with a standard written consent process, but the subject is not ever registered with the Clinical Center (CC) and therefore the standard CC consent privacy language is not appropriate, and there is not alternative approved language included.*

In these cases, if any identifiable private information will be collected and stored, the prospective subject must receive a privacy notice and be informed of the NIH Certificate of Confidentiality policy. The language below should be used as follows to meet this requirement.

1. *Adding the language below to a written statement mailed to an off-site subject when not a CC-registered subject; or*
2. *Reading the language below to a subject if the consent process is entirely oral (by phone or otherwise), In this case, the person obtaining consent must offer to send a written copy of the privacy statement below to the subject via mail or electronic means. Note this option should only be used if the subject will not be registered with the CC and there is no plan to mail or otherwise provide a written consent document to the subject.*
3. *Adding the language below to a written statement online for online research when not a CC-registered subject;*

4. *Including the language below in the informed consent document provided to a subject that will not ever be registered at the CC, unless alternative approved Privacy Act notice language is already included in the consent.*

Certificate of Confidentiality

To help us protect your privacy, NIH has a Certificate of Confidentiality (Certificate). With this Certificate, researchers may not release or use information about you except in certain cases.

NIH researchers must not share information that may identify you in any legal proceedings, such as if a court requests it with a subpoena.

The Certificate does not protect your information when it:

1. is shared with people connected with the research. For example, information may be used for internal reviews by NIH; or
2. is required by law to be disclosed. For example, information may be shared with the FDA or with public health agencies.
3. is for other research if allowed by other regulations;
4. is shared with your consent.

Researchers may provide your information when you say it is okay. The Certificate does not keep you from sharing your own information.

The Certificate will not prevent telling authorities about harm to yourself or others. Examples are child abuse and neglect.

Privacy Act

The Privacy Act helps keep your NIH research information confidential. In some cases, it is different from the Certificate. Under 42 U.S.C. § 282, NIH is authorized to collect the data for this study. This data is covered by an NIH Privacy Act System of Records Notice: 09-25-0200, Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH). Sometimes the Privacy Act allows sharing your information without your permission. An example is if Congress requests it.

Information may also be shared for some research. It can be given to some federal and state agencies. It can be used for HIV partner notification, or for infectious disease, abuse, or neglect reports. It may be shared with tumor registries, or for quality or medical reviews. It may also be shared if NIH is involved in a lawsuit or event of a suspected or confirmed breach. However, NIH will only release information about you if allowed by both the Certificate and the Privacy Act. If you do not want to share your information with us, then you cannot participate in this study.

Privacy Act (in Spanish)

La Ley de Privacidad ayuda a mantener la confidencialidad de la información de investigación que los NIH tienen sobre usted. En algunos casos, difiere del Certificado. En virtud del código 42 U.S.C., sección 282, los NIH pueden reunir datos para este estudio. Estos datos están cubiertos por un Aviso del Sistema de Registros conforme a la Ley de Privacidad de los NIH: 09-25-0200, Estudios de investigación clínica, básica y basada en poblaciones de los Institutos Nacionales de la Salud (NIH). A veces, la Ley de Privacidad permite divulgar su información sin su autorización, por ejemplo, si el Congreso la solicita.

La información también se puede divulgar para algunas investigaciones. Se puede entregar a algunas agencias federales y estatales. Se puede usar para informar a las parejas sexuales en caso de infección por el VIH o para notificar enfermedades infecciosas, abuso o negligencia. Se puede comunicar a registros de tumores, o para control de calidad o revisiones médicas. También se puede transmitir si los NIH están involucrados en alguna demanda o incidente de violación de seguridad sospechada o confirmada. No obstante, los NIH solo divulgarán información suya si lo permiten tanto el Certificado como la Ley de Privacidad. Si no desea entregarnos su información, no puede participar en este estudio.

PRIVACY LANGUAGE FOR STUDIES CONDUCTED AT THE CLINICAL CENTER (SPANISH)

If you are conducting your study at the NIH Clinical Center, or using Clinical Center resources in any way (e.g. iMed), then you are required to use the version of the Privacy Act language that is found in the relevant consent templates. Below is the translation of that content into Spanish.

La Ley de Privacidad ayuda a mantener la confidencialidad de la información médica que los NIH tienen sobre usted. En algunos casos, difiere del Certificado. En virtud del código 42 U.S.C., sección 282, los NIH pueden reunir datos para este estudio. Estos datos están cubiertos por Avisos del Sistema de Registros conforme a la Ley de Privacidad de los NIH: 09-25-0200, Estudios de investigación clínica, básica y basada en poblaciones de los Institutos Nacionales de la Salud y 09-25-0099, Investigación clínica: expedientes médicos de pacientes. A veces, la Ley de Privacidad permite divulgar su información sin su autorización, por ejemplo, si el Congreso la solicita.

La información también se puede divulgar para algunas investigaciones. Se puede entregar a algunas agencias federales y estatales. Se puede usar para informar a las parejas sexuales en caso de infección por el VIH o para notificar enfermedades infecciosas, abuso o negligencia. Se puede comunicar a registros de tumores, para control de calidad y revisiones médicas. También se puede transmitir si los NIH están involucrados en alguna demanda o incidente de violación de seguridad sospechada o confirmada. No obstante, los NIH solo divulgarán la información de los expedientes médicos si lo permiten tanto el Certificado como la Ley de Privacidad.

PREGNANCY

Note that the NIH IRB requires each of these elements in the ICF rather than specific language. If the sponsor's suggested ICF language contains all these required elements, addition of NIH sample language is not required, although sponsor language may be revised/edited during the IRB review process.

Required Elements

- *Description of rationale for preventing pregnancy during study, and which subgroups are excluded*
- *Description of pregnancy testing requirements (women able to become pregnant only)*
- *Description of duration and type of contraception required*
- *Description of actions taken in event of pregnancy*

- *Description of any potential risks to future fertility if noted in protocol*

Description of rationale for preventing pregnancy during study, and which subgroups are excluded

Women: Example Language

- ***Known human teratogen**: [Study drug]* is known to increase the risk of birth defects and miscarriage when taken during pregnancy. There may also be risks for breastfed children. To reduce the risk of harms, women who are pregnant, planning a pregnancy, or breastfeeding cannot be in studies using *[study drug]*.
- ***Teratogen in animal studies, human effects unknown**:* In animal studies, *[study drug]* increased the risk of some birth defects. We do not know whether these harms could also happen in humans. To reduce the risk of any harms, women who are pregnant, planning a pregnancy, or breastfeeding cannot be in studies with *[study drug]*.
- ***Unknown risks**:* The effects of *[study drug]* on a developing pregnancy or breastfeeding infant are unknown. To reduce the risk of harms, women who are pregnant, planning a pregnancy, or breastfeeding cannot be in studies using *[study drug]*.
- ***No risks**:* Although *[study drug]* is generally considered safe to use during pregnancy, the changes your body goes through during pregnancy may affect some of the things we are measuring in this study. Therefore, women who are pregnant or planning a pregnancy cannot be in this study.

Men: Example Language

- ***Known risk with paternal exposure**:* A higher risk of certain birth defects has been seen in pregnancies where the father was taking *[study drug]* at the time the pregnancy began. Therefore, men who are trying to become fathers cannot be in studies using *[study drug]*.
- ***Unknown risk, no concern about seminal transmission:*** We do not know whether pregnancies that began while the father was taking *[study drug]* are at higher risk for birth defects, miscarriages, or other bad outcomes. To reduce the risk of any harms, men who are trying to become fathers cannot be in studies of this drug.
- ***Unknown risk, concern about seminal transmission:*** We do not know whether pregnancies that began while the father was taking *[study drug]* are at higher risk for birth defects, miscarriages, or other bad outcomes. In addition, *[study drug]* may be present in semen and a partner may be exposed to the study drug during sexual activity. To reduce the risk of any harm, men who are trying to become fathers cannot be in this study.

Description of Pregnancy Testing Requirements *(women who can become pregnant only)*

Description should include:

- Who is required to be tested?
- If blood test required, risk of false positive/indeterminate blood test
- If additional testing required, description of type, frequency, and consequences of positive result

Example Language

If you could possibly become pregnant (you have not completed menopause or haven't had surgery that makes it impossible for you to become pregnant) and if you have a partner who is able to

father children, a *[blood/urine]* pregnancy test will be done. The pregnancy test must be negative for you to stay in the study.

If serum pregnancy test used: In women [*insert age*] and older, blood pregnancy tests may sometimes give a false positive or "indeterminate" (unsure) result. If that happens, we may need to do additional tests to make sure you can still be in the study.

If additional tests required: You will also have additional *[blood/urine]* tests at some study visits, as described above. The additional tests must also be negative for you to stay in the study.

Description of Duration and Type of Required Contraceptive Methods

Description should include:

- *Statement that complete abstinence from sex (vaginal intercourse) for the study-specified duration of contraception is acceptable.*
- *Duration of need for abstinence or contraception, including starting time and ending time*
- *Specific methods which (a) meet the protocol-specified level of effectiveness and (b) are compatible with the study population (for example, combination oral contraceptives are contraindicated in many populations because of increased risk of venous thrombotic events).*
- *Statement that the study team will assist with any required changes to contraceptive methods.*
- *Statement of possibility of pregnancy even with highly effective methods and need to notify study team.*
- *For males,*
    - *If specified by protocol and appropriate for clinical population, statement that donation of sperm is prohibited for same duration as contraception requirement.*
    - *If concern is seminal transmission, a statement that condoms are required for all types of sex if partner is currently pregnant or breastfeeding.*
- *"Highly effective methods" (<1% failure rate)*
    - *"Typical use"*
        - *Partner vasectomy*
        - *Bilateral tubal ligation*
        - *IUDs*
        - *Progestin implants (Implanon)*
    - *"Perfect use" (acceptable with some sponsors, FDA, ICH/EU guidance)*
        - *Other hormonal methods (OCPs, injections, patches, rings)*
- *"Effective Methods"*
    - *Any of the above, or*
    - *Barrier (condom, diaphragm, cervical cap) plus spermicide*
- *If protocol specifies dual methods, specific combinations (e.g., barrier method plus other method) must be specified. A list of all methods and statement that two must be used is not acceptable.*

Women: Example Language

You and your partner must agree to one of the following for the entire study, and for *[X time]* after your last dose of the study drug:

- Stop having sex (vaginal intercourse), or
- Use a highly effective method of contraception (birth control). These methods include:
    - Partner vasectomy (making sterile)
    - Bilateral tubal ligation
    - Intrauterine devices (IUDs)
    - Hormonal implants (such as Implanon)
    - Other hormonal methods (birth control pills, injections, patches, vaginal rings)

If you and your partner are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness needed for this study. Because no birth control method is 100% effective, you should tell your study doctor immediately if you think there is any chance you could be pregnant.

If protocol requires ongoing pregnancy testing: You should tell your study doctor right away if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test.

Men, No Concern about Seminal Transmission: Example Language

If you have a partner who could possibly become pregnant (has not completed menopause, or hasn't had surgery that makes it impossible for them to become pregnant), you and your partner must agree to one of the following for the entire study, and for *[X time]* after your last dose of the study drug:

- Stop having sex (vaginal intercourse), or
- Use a highly effective method of contraception (birth control). These methods include:
    - Vasectomy
    - Bilateral tubal ligation
    - Intrauterine devices (IUDs)
    - Hormonal implants (such as Implanon)
    - Other hormonal methods (birth control pills, injections, patches, vaginal rings)

If you and your partner are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness needed for this study. Because no birth control method is 100% effective, you should tell your study doctor immediately if you think there is any chance your partner could be pregnant.

You should not donate sperm during the study and for *[X time]* after your last dose of study drug.

Men, Concern about Seminal Transmission, Pregnancy Risk Only: Example Language

If you are able to father children and your partner could possibly become pregnant (has not completed menopause, or hasn't had surgery that makes it impossible for them to become pregnant), you must agree to either abstain completely from vaginal intercourse for the duration of the study and for *[X time]* after your last dose of the study drug, or use a condom every time you have vaginal intercourse, even if you have had a vasectomy (because vasectomy does not

prevent transmission of the drug in semen). Because no birth control method is 100% effective, you should tell your study doctor immediately if you think there is any chance your partner could be pregnant.

If your partner is currently pregnant, breastfeeding, or becomes pregnant during the study, you must use a condom for all types of intercourse to prevent transmission.

You should not donate sperm for the duration of the study and for *[X time]* after your last dose of the study drug.

Men, Concern about Seminal Transmission to Partner: Example Language

During sex, your partner could be exposed to the study drug, which could possibly have harmful effects. Therefore, you must agree to use a condom every time you have any type of sex, even if you have had a vasectomy (because the study drug could still be present in your semen). If your partner cannot possibly become pregnant, you must still use a condom to ensure the study drug does not affect your partner or a breastfed baby.

You should not donate sperm during the study and for *[X time]* after your last dose of the study drug.

Description of Actions Taken in Event of Pregnancy

Description should include:

- *Specific actions (stopping drug, study withdrawal, etc.)*
- *Any follow-up of pregnancy in either subject or subjects' partner*

Women, Example Language

If you do become pregnant during the study, your study doctor will stop the study drug and notify the sponsor. You will be followed for the entire pregnancy so we can learn about the study drug's potential effects on pregnancy outcomes.

Men, Example Language

You should notify your partner about being in this study and the potential risks to pregnancies that begin while you are taking the study drug. If your partner does become pregnant during the study, you should tell your study doctor, and your partner should notify their doctor. We will ask for your partner's permission to collect information about the pregnancy so we can learn about the study drug's potential effects on pregnancy outcomes.

Description of Any Known or Suspected Potential Risks to Future Fertility (if appropriate)

Description should include:

- *Whether risks are known or unknown*
- *Discussion of options for fertility preservation, if available*

Women, Example Language

The study drugs used in this study may affect your ability to become pregnant in the future. There may be fertility preservation options available, which your study doctor will discuss with you.

Men, Example Language

The study drug used in this study may affect your ability to father children in the future. There may be fertility preservation options available, which your study doctor will discuss with you.

Reproductive Risks

Women, Example Language

We do not know the effect of *[study drug]* on the risk of birth defects, miscarriage, or other bad outcomes when taken during pregnancy or while breastfeeding. To reduce the risk of any harmful effects, women who are pregnant, trying to become pregnant, or breastfeeding cannot be in studies using *[study drug]*.

If you could possibly become pregnant (you have not completed menopause or haven't had surgery that makes it impossible for you to become pregnant) and if you have a partner who is able to father children, we will do a blood pregnancy test. The pregnancy test must be negative for you to stay in the study. In people *[insert age]* and older, blood pregnancy tests may sometimes give a false positive or "indeterminate" (unsure) result. If that happens, we may need to do additional tests to make sure you can still be in the study. You will also have additional pregnancy tests at some study visits, as described above, and they also must be negative for you to stay in the study.

You and your partner must agree to one of the following for the entire study, and for 30 days after your last dose of the study drug:

- Stop having sex (vaginal intercourse), or
- Use a highly effective method of contraception (birth control). These methods include:
    - Partner vasectomy
    - Bilateral tubal ligation
    - Intrauterine devices (IUDs)
    - Hormonal implants (such as Implanon)
    - Other hormonal methods (birth control pills, injections, patches, vaginal rings)

If you and your partner are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness needed for this study. Because no birth control method is 100% effective, you should tell your study doctor right away if you think there is any chance you could be pregnant, even if you have had a recent negative pregnancy test.

If you do become pregnant during the study, your study doctor will stop the study drug and notify the sponsor. You will be followed for the entire pregnancy so we can learn about the study drug's potential effects on pregnancy outcomes.

Men, Example Language

We do not know whether pregnancies that began while the father was taking the study drug are at higher risk for birth defects, miscarriages, or other bad outcomes. To reduce the risk of any harms, men who are trying to become fathers cannot be in studies using the study drug.

If you can father children and your partner could possibly become pregnant (has not completed menopause, or hasn't had surgery that makes it impossible for them to become pregnant), you and your partner must agree to one of the following for the entire study, and for 90 days after your last dose of the study drug:

- Stop having sex (vaginal intercourse), or
- Use a highly effective method of contraception for the same length of time. Highly effective methods include:
    - Vasectomy
    - Bilateral tubal ligation
    - Intrauterine devices (IUDs)
    - Hormonal implants (such as Implanon)
    - Other hormonal methods (birth control pills, injections, patches, vaginal rings)

If you and your partner are not currently using one of these methods, your study doctor will discuss options with you, given your medical condition, your personal preferences, and the level of effectiveness needed for this study. Because no birth control method is 100% effective, you should tell your study doctor immediately if you think there is any chance your partner could be pregnant.

You should not donate sperm for the entire study and for 90 days after your last dose of the study drug.

Written assent example language

We will give you a pregnancy test if you can become pregnant.

You cannot be part of the study if you are pregnant. If you think you might be pregnant, tell us right away.

We will tell you the results of your pregnancy test in private. If your life is in danger or if we think you might have been hurt, we might need to tell your parent(s) or guardian(s). But otherwise, we will not tell them unless you say it's okay.

Even if we do not tell your parent(s) or guardian(s), they might guess you are pregnant. We would have to tell them you cannot be in the study. If you think you are pregnant and do not want your parent(s) or guardian(s) to know, you might not want to join the study.

When appropriate: You must use birth control or not have sex during the study.

QUESTIONNAIRES

Procedure: We will ask you to answer [*specify number*] questionnaires that will take about [*specify duration of time*] to complete. The questionnaires will ask you about [*Add relevant information here. For ex: the symptoms you're experiencing, your ability to complete everyday activities and will test your memory and concentration.*]

Risks: Some of the questions in the questionnaire may be upsetting or make you feel uncomfortable. You can skip any of the questions you do not want to answer. You can stop at any time.

Also see "**INVASION OF PRIVACY/BREACH IN CONFIDENTIALITY**" below.

RADIATION

Non-Therapeutic Radiation

Investigators: Please note, this language below is required, not suggested, language if this is applicable to your protocol. Please do not alter it in any way.

Scans, tests, and procedures that involve radiation that are specified in the protocol are considered by the IRB to be research. If the scan, test, or procedure is dictated solely by the clinical needs of the participant, then this is considered clinical and should not be included in the protocol or the consent. The IRB has no regulatory authority over the practice of medicine and can only review proposed research and associated risks.

***Note** that for pediatric participants (<18 years old), RSC review is required if these participants are healthy volunteers or if the annual effective dose will be ≥ 0.5 rem.*

*Use the appropriate reproductive risk language under the "***PREGNANCY***" section.*

A. Consent language required when the Effective Dose (ED) is < 0.3 rem (non-therapeutic radiation)

During this research study, you may be exposed to radiation from [*list all sources of radiation that are required by the protocol*] each year. This is considered a low exposure. The risk of this exposure is too low to be reliably measured. [*For pediatric participants add the following here:* The amount of radiation you will get is less than the NIH Radiation Guidelines of 0.5 rem per year for children.]

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The radiation you will get by being in this study is less than the average yearly background radiation in the United States.

B. Consent language required when the Effective Dose (ED) is ≥ 0.3 rem and ≤ 5 (non-therapeutic radiation)

During this research study, you may be exposed to radiation from [*list all sources of radiation that are required by the protocol*] each year. The amount of radiation exposure from these procedures is equal to about [*insert effective dose (ED) value, in rem*]. A rem is a unit of radiation absorbed by the body. [*For pediatric participants*[1] *add the following here:* This amount of radiation is [less than/the same as/greater than] (*select appropriate language based on the ED*) the NIH Radiation Guidelines of 0.5 rem per year for children.]

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The [*insert type of scan, e.g., PET, CT*] that you get in this study will expose you to roughly the same amount of radiation as [*insert estimate in years based on background radiation dose of 0.3rem /year. e.g. for total dose of 0.6 rem, insert "2 years' worth" here*] of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a

[1] Pediatric participants (<18 years of age) who are healthy volunteers or who will receive an ED of at least 0.5 rem will be reviewed by the RSC.

very large amount of extra radiation.

C. Consent language required when the Effective Dose (ED) is > 5 rems (non-therapeutic radiation)

During this research study, you may be exposed to radiation from [*list all sources of radiation that are required by the protocol*] each year. The amount of radiation exposure from these procedures is equal to about [*insert effective dose value, in rem*]. A rem is a unit of radiation absorbed by the body.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States gets a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." This study will expose you to more radiation than you get from everyday background radiation. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The [*insert type of scan, e.g., PET, CT*] that you get in this study will expose you to roughly the same amount of radiation as [*insert estimate in years based on background radiation dose of 0.3rem /year. e.g. for total dose of 6 rem, insert "20 years' worth" here*] of background radiation. Being exposed to too much radiation can cause harmful side effects such as an increase in the risk of cancer. The risk depends on how much radiation you are exposed to. Please be aware that about 40 out of 100 people (40%) will get cancer during their lifetime, and 20 out of 100 (20%) will die from cancer. The risk of getting cancer from the radiation exposure in this study is *X* out of 100 (Y%) [*Calculate X based on 0.1% per rem. e.g. for total dose of 6 rem, "insert 0.6 out of 100 (0.6%)"]* and of getting a fatal cancer is *A* out of 100 (B%) [*The PI should calculate A based on .05% per rem. e.g. for total dose of 6 rem, "insert 0.3 out of 100 (0.3%)*].

Therapeutic Radiation

For assistance drafting risk language specific to a therapy, researchers should contact:

- *Radioactive therapy drugs (I-131, Lu-177, etc.): the Clinical Authorized User (CAU) signing off on the protocol. A CAU is required for all clinical administrations of radioactive materials.*
- *Radiation Oncology therapies (TBI, SBRT, HDR): Kevin Camphausen or Freddy Escorcia*
- *Additional guidance may be found at https://drs.ors.od.nih.gov/rsc/Pages/forms_index.aspx*

Risks and side effects related to radiation therapy include:

- *Likely: [List of risks and side effects]*
- *Less likely: [List of risks and side effects]*
- *Rare, but serious: [List of risks and side effects]*

Overall radiation risk:

During a year in this research study, *[choose most appropriate: you, your tumor, your 'target organ']* you may be exposed to *[insert therapeutic radiation dose in Gy or rad]* of radiation from *[indicate radiation therapy source-TBI, SBRT, the radioactive drug, I-131, etc.]*. You will also get a much smaller amount of radiation from scans used to plan your treatment and measure your progress. [*Optional statement: Additionally, tumor biopsies may be done by a specialist using a*

CT scanner to guide the biopsy needle into the tumor to ensure accuracy.] The total scans include *[insert list of scans and procedures]*. The amount of radiation from these scans adds minimal additional risk to the higher radiation doses you would get during treatment. *[If applicable include the following: This radiation has been reviewed by the NIH Radiation Safety Committee and deemed appropriate for this study.]*

Radiation reviewed by the RDRC

During your participation in this radioactive drug research study, you may be exposed to radiation from [*list all sources of radiation that are required by the protocol*] each year. The amount of radiation exposure from these procedures is equal to about [*insert effective dose (ED) value, in rem*]. A rem is a unit of radiation absorbed by the body. The US Food and Drug Administration (FDA) has set an annual radiation limit of 5 rem for participants for this type of research. The dose you will get in this study is below the limit and is not expected to be harmful.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. The average person in the United States receives a radiation exposure of 0.3 rem per year from these sources. This type of radiation is called "background radiation." No one knows for sure whether exposure to these low amounts of radiation is harmful to your body.

The [*insert type of scan, e.g., PET, CT*] that you get in this study will expose you to roughly the same amount of radiation as [*insert estimate in years based on background radiation dose of 0.3rem /year. e.g. for total dose of 0.6 rem, insert "2 years' worth" here*] of background radiation. Most of the time, this amount of extra radiation is not harmful to you. However, scientists believe that being exposed to too much radiation can cause harmful side effects. This could include getting a new cancer. We estimate that this could happen in about 1 out of every 1000 people who get a very large amount of extra radiation.

RANDOMIZATION

Procedure: If you join this study, you will be assigned by chance (like flipping a coin) to one of two- groups. Group 1 will get *[X]* and Group 2 will get *[Y]*. There is an equal chance that you will be assigned to either group. [*If applicable, include*: Neither you nor your doctor will be able to choose or to know which group you are assigned to.]

You will be randomized into one of *[specify number]* study groups. Randomization means that you are assigned by chance (like pulling a number from a hat) into one of the groups described below. [*If applicable, include*: Neither you nor your doctor will be able to choose or to know which group you are assigned to.]

If you are in Group 1, you will…

If you are in Group 2, you will…

If you are in Group 3, you will…

SALIVA SAMPLE

Procedure: We will give you a saliva collection tube with a mini cotton swab that you will swirl around the inside of your mouth and put the cotton swab back in the collection tube.

SKIN BIOPSY

Procedure: We will numb an area of your skin with a shot of local anesthetic, which might cause a little burning discomfort. Then, we will remove a small piece of skin about the size of a pencil eraser using a special tool. Skin biopsies are generally safe procedures. Bleeding usually stops quickly, and the risk of infection is very small. You will get a scar at the biopsy site, but it usually heals well and stays flat. Up to *XX* skin biopsies may be done at one time, with a maximum of *XX* skin biopsies allowed per *XX* months.

Risks: You will be given a local anesthetic for this procedure. There might be a small burning feeling from the shot of anesthetic. You could have some bruising where the needle went in. There might be minor bleeding or redness near the biopsy site. A skin biopsy will leave a scar, and we can't say for sure what the scar will look like.

There is a very small chance that a scar could become raised and hard, called a "keloid." If this happens, we might be able to treat it to make it softer and flatter. Very rarely, the biopsy site might get infected. If it does, you might need to use an antibiotic ointment or take antibiotic pills for a few days. You must watch the site and let us, or your regular doctor, know if it looks infected.

STEM CELL TRANSPLANT

Procedure: Doctors collect stem cells from people with healthy immune systems (donors) and give the cells to people with weak immune systems (recipients). Stem cells are special cells found in the blood and in bone marrow inside bones. Stem cells make all the different cells in the blood, including the blood cells that fight infection and make up the immune system. After a stem cell transplant, if the new healthy stem cells survive and grow inside the recipient, the stem cells could fix the recipient's immune system.

Stem cell transplants can be challenging:

- One challenge is finding a donor. Recipients need a donor who is a good "match" with them to have the best chance of a successful transplant. The donor could be a sibling or family member or someone unrelated. If there is not a donor available who is a good match, the stem cell transplant could have higher risks.
- Another challenge is that stem cell transplants can have serious complications. For example, the recipient's own immune system could fight or "reject" the donor's cells, or the donor's cells could attack the recipient's body. These complications can be life-threatening.

Because of these challenges, some people are not eligible to have a stem cell transplant, or they choose not to have it because the risks are too high, even though it could cure them.

STOOL SAMPLE

Procedure: We will give you a stool sample collection kit and instructions to collect the stool. You will give your sample to the study team for testing and storage.

TRANSCRANIAL MAGNETIC STIMULATION (TMS)

Procedure: Transcranial Magnetic Stimulation (TMS) uses a brief, pulsed magnetic field to affect brain activity. During the TMS session(s), a device called a "coil" will be placed on your head. A brief electrical current will then pass through the coil and create a magnetic field. You will hear a

click, and you may feel a tapping or pulling sensation on your skin under the coil. You may feel a twitch in your face, neck, arm, or leg muscles. You will be given hearing protection that must be worn during TMS because the clicking noise can be loud enough to damage your hearing. We may ask you to tense certain muscles or do simple actions or tasks during TMS.

Electromyography (EMG), Electroencephalography (EEG), or Magnetic Resonance Imaging (MRI) may be used with TMS to measure the effects of TMS on your brain and body. The TMS session will take about *[insert time in minutes/hours]*. This study involves *[insert number]* sessions. You will always be able to talk with the study staff during the TMS session. You may ask to stop the session at any time.

Single Pulse or Paired Pulse TMS: When TMS pulses are given one or two at a time, several seconds apart, this is called "Single Pulse" or "Paired Pulse" TMS. These types of TMS let us study your brain's reaction to the pulses. It can also tell us about the role of a brain region in certain behaviors or how the brain is connected. During the TMS session(s) you will get about [insert number] [pulses/pairs of pulses].

Repetitive TMS (rTMS): A series of repeated TMS pulses can lead to brain and behavior changes even after you stop getting TMS. This type of TMS is called "repetitive TMS" or "rTMS" and can be used to study the brain or as a treatment. During the rTMS session(s) you will get [insert number] pulses of rTMS. The pulses will be given *[insert number]* times every second for a total of *[insert number of pulses]* over *[seconds/minutes]*.

Sham TMS: Sham (fake) TMS is a type of TMS that looks, sounds, and feels like active TMS but doesn't include any active pulses.

Double Blinded Study: Neither you nor the study team will know whether you are getting active or sham (fake) TMS. If there is an emergency and it is important for your care, the study team will find out quickly whether you got active or sham TMS.

Risks:

It may not be safe for you to get TMS if you have certain kinds of metal in your body including:

- Metal staples or screws in the head or neck
- Pacemakers or other implanted electrical devices
- Brain stimulators
- Aneurysm clips (metal clips on the wall of a large artery)
- Cochlear implants
- An implanted delivery pump
- Shrapnel fragments. Welders and metal workers may have small metal fragments in the eye.

It may also not be safe for you to get TMS if you have a history of certain medical conditions or if you are taking certain drugs. You will be asked to complete a screening form before you get TMS. This screening form will be updated at each session. If you have questions about metal in your body or other potential risks mentioned on the screening form, you should let us know.

TMS may give you a headache. The TMS pulse may also activate nerves or muscles in your head

and neck that may cause pain or discomfort in or around your head or neck. If you have any pain during or after TMS, you can take medicine to make it feel better.

The clicking noise that the machine makes is loud enough to damage hearing, especially if you already have hearing loss. We will give you hearing protection. If your hearing protection comes loose during the session, tell us right away.

Very rarely, TMS has led to seizures (abnormal activity in the brain that can cause muscle spasms and can happen with or without losing consciousness). [*If rTMS is applied, include the following:*] Also rarely, rTMS may lead to a short-term change in your ability to remember, your ability to pay attention, or your mood. If these effects happen, they do not usually last long and will go away without treatment. [*Add additional specific patient-related rTMS risks as applicable (e.g., suicidal ideation, mania, worsening of clinical symptom severity, etc.)*].

Safety Plan: A safety plan is in place, and a licensed clinician will be available during each TMS session in case you have a seizure or other side effect. There may be other risks that we don't currently know about. There are no known long-term risks of TMS.

Only include this content if pregnancy risks are not addressed elsewhere in the consent: The effects of TMS on a developing fetus are not known. You will not be able to have TMS if you are pregnant. Women who can get pregnant will have a pregnancy test before their TMS sessions.

Investigational Use of TMS: We will be using the TMS System and the coil for research purposes. This means that we are using it to study brain function, not to treat patients. However, all sessions done under this protocol will follow safety guidelines. There is no increased risk in the use of these research techniques compared with clinical uses. The use of the TMS system and coil for research has not been approved by the FDA and is considered investigational.

WITNESS SIGNATURE

If your protocol includes potential enrollment of non-English speaking subjects, blind and/or illiterate subjects, your consent document must include a block for a witness signature. There is a mandatory note that is below the witness signature line in the consent template. Below is the "note" content in Spanish that can be used in Spanish translations of the consent document.

NOTA: El testigo debe dominar con fluidez el idioma del participante y el del investigador. El intérprete también puede ser el testigo; sin embargo, el investigador que obtiene el consentimiento no puede ser el testigo. Debe documentarse el uso de un intérprete en el expediente médico o de investigación. Consulte la Política 301 para ver más detalles.

WASHOUT PERIODS/WITHDRAWING CURRENT MEDICATION

Procedure: You will need to stop taking the medication you normally take for your condition about *[specify # of days]* before you can start taking the study drug. You will not be able to start taking your normal medication again until after you have completed or left the study. [if applicable: Based on your randomization assignment, you may get no active medication (placebo) or] the study drug may not be a dose that will help your condition. As a result, you may have an increase in symptoms, including *[specify symptoms]*. If your symptoms worsen or make you uncomfortable, talk to the study doctor about leaving the study.

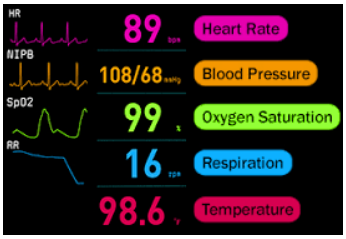
X-RAY

Procedure: As part of your regular care, you will have x-rays of your [*specify body part*] taken at [*specify visits/timeframes for x-rays*] after your *[insert procedure]*. For this study, we will ask you to have additional x-rays done at [*specify visits/timeframes for x-rays*].

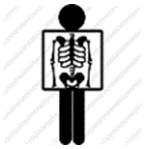
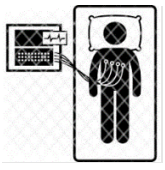
Risks: See "**RADIATION**" above.

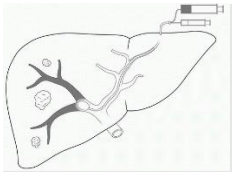
PROCEDURE TABLE

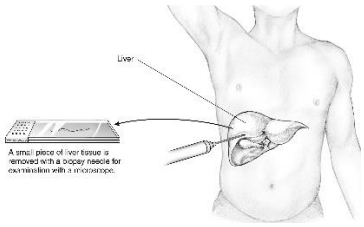
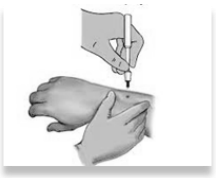
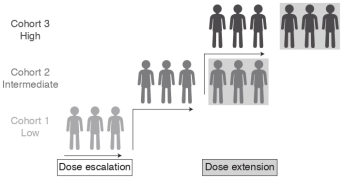
Procedure Name	Procedure Description
 **Chart Review**	**Write short, simple (6-8th grade reading level) description here.**
 **Medical History Review**	**Write short, simple (6-8th grade reading level) description here.**
 **Physical Exam**	**Write short, simple (6-8th grade reading level) description here.**
 **Eye Exam**	**Write short, simple (6-8th grade reading level) description here.**
	**Write short, simple (6-8th grade reading level) description here.**

Procedure Name	Procedure Description
Eye Exam	
 **Vital Signs**	**Write short, simple (6-8th grade reading level) description here.**
 **Blood Draws**	**Write short, simple (6-8th grade reading level) description here.**
 **Blood Draw**	**Write short, simple (6-8th grade reading level) description here.**
 **HIV Testing**	**Write short, simple (6-8th grade reading level) description here.**
 **Saliva (Spit) Samples**	**Write short, simple (6-8th grade reading level) description here.**

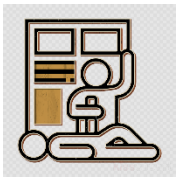
Procedure Name	Procedure Description
 **Cheek Swab**	**Write short, simple (6-8th grade reading level) description here.**
 **Hair Sample**	**Write short, simple (6-8th grade reading level) description here.**
 **Urine Sample**	**Write short, simple (6-8th grade reading level) description here.**
 **Stool Sample**	**Write short, simple (6-8th grade reading level) description here.**
 **Pregnancy Testing**	**Write short, simple (6-8th grade reading level) description here.**
 **Photographs**	**Write short, simple (6-8th grade reading level) description here.**

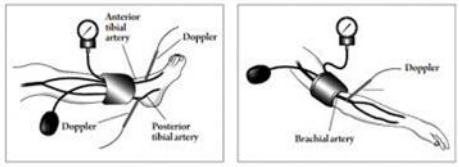
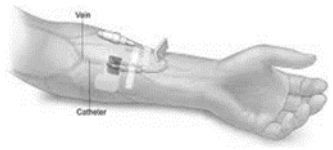
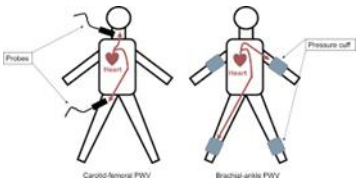
Procedure Name	Procedure Description
 **Pictures of your face and body**	**Write short, simple (6-8th grade reading level) description here.**
 **Radiologic Imaging**	**Write short, simple (6-8th grade reading level) description here.**
 **MRI**	**Write short, simple (6-8th grade reading level) description here.**
 **MRI with Gadolinium Contrast**	**Write short, simple (6-8th grade reading level) description here.**
 **Electrocardiogram (ECG)**	**Write short, simple (6-8th grade reading level) description here.**
 **Electrocardiogram (ECG) & ECG Monitoring**	**Write short, simple (6-8th grade reading level) description here.**

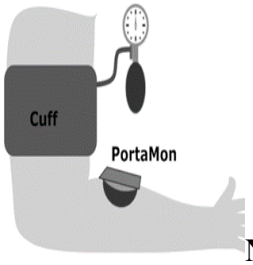
Procedure Name	Procedure Description
 **Bike Stress Test**  **Stress Echocardiogram (after bike)**	**Write short, simple (6-8th grade reading level) description here.**
 **Treadmill**	**Write short, simple (6-8th grade reading level) description here.**
 **Echocardiography**	**Write short, simple (6-8th grade reading level) description here.**
 **Six Minute Walk Test**	**Write short, simple (6-8th grade reading level) description here.**
 **Liver Biopsy**	**Write short, simple (6-8th grade reading level) description here.**

Procedure Name	Procedure Description
 **Percutaneous Liver Biopsy**	**Write short, simple (6-8th grade reading level) description here.**
 **Skin biopsy**	**Write short, simple (6-8th grade reading level) description here.**
 **Study Drug**	**Write short, simple (6-8th grade reading level) description here.**
 **Study Drug Diary**	**Write short, simple (6-8th grade reading level) description here.**
 **Medication Safety**	**Write short, simple (6-8th grade reading level) description here.**
 **Dose Escalation**	**Write short, simple (6-8th grade reading level) description here.**

Procedure Name	Procedure Description
 **Inpatient Admission**	**Write short, simple (6-8th grade reading level) description here.**
 **Injections**	**Write short, simple (6-8th grade reading level) description here.**
 **Ultrasound**	**Write short, simple (6-8th grade reading level) description here.**
 **Stomach Ultrasound**	**Write short, simple (6-8th grade reading level) description here.**
 **Lumbar Puncture**	**Write short, simple (6-8th grade reading level) description here.**
 **Questionnaire**	**Write short, simple (6-8th grade reading level) description here.**
 **Questionnaire**	**Write short, simple (6-8th grade reading level) description here.**

Procedure Name	Procedure Description
 **Surveys/Tests**	**Write short, simple (6-8th grade reading level) description here.**
 **Lifestyle Changes**	**Write short, simple (6-8th grade reading level) description here.**
 **Follow-Up Visits**	**Write short, simple (6-8th grade reading level) description here.**
 **Safety Follow-up**	**Write short, simple (6-8th grade reading level) description here.**
 **Fibroscan®**	**Write short, simple (6-8th grade reading level) description here.**
 **Adrenal Insufficiency (AI) Teaching**	**Write short, simple (6-8th grade reading level) description here.**

Procedure Name	Procedure Description
 **Pulmonary Function Test**	**Write short, simple (6-8th grade reading level) description here.**
 **Cardiopulmonary Exercise Test**	**Write short, simple (6-8th grade reading level) description here.**
 **Ankle Brachial Index and Digit Measurement**	**Write short, simple (6-8th grade reading level) description here.**
 **Brachial Vein Endothelial Sampling**	**Write short, simple (6-8th grade reading level) description here.**
 **Pulse Wave Velocity – SphygmoCor**	**Write short, simple (6-8th grade reading level) description here.**
 **Skin Biomechanical Measurements – DermaLab**	**Write short, simple (6-8th grade reading level) description here.**

Procedure Name	Procedure Description
Suction Cup Probe	
 **Non-invasive tissue oxygenation using Near-Infrared Tissue Spectroscopy (NIRS)**	**Write short, simple (6-8th grade reading level) description here.** **** Please do not use this image if you are using a NIRS head cap.**

OHSRP thanks our colleagues at NIDDK and NHLBI for sharing these images for use across the IRP.