Lead Site Principal Investigator: <PiFullName> **Version Date: June 24, 2020**
Lead PI Institution/Hospital: <PiLocation>
Study Title: Human Mesenchymal Stromal Cells for the Treatment of Acute Respiratory Distress Syndrome

Part 1 of 2: MASTER CONSENT

Name of participant: _____ Age: _____

You are being invited to take part in a research study. This study is a multi-site study, meaning it will take place at several different locations. Because this is a multi-site study this consent form includes two parts. Part 1 of this consent form is the Master Consent and includes information that applies to all study sites. Part 2 of the consent form is the Study Site Information and includes information specific to the study site where you are being asked to enroll. Both parts together are the legal consent form and must be provided to you.

When reading this form, please note that the words "you" and "your" refer to the person in the study rather than to a legally authorized representative who might sign this form on behalf of the person in the study.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

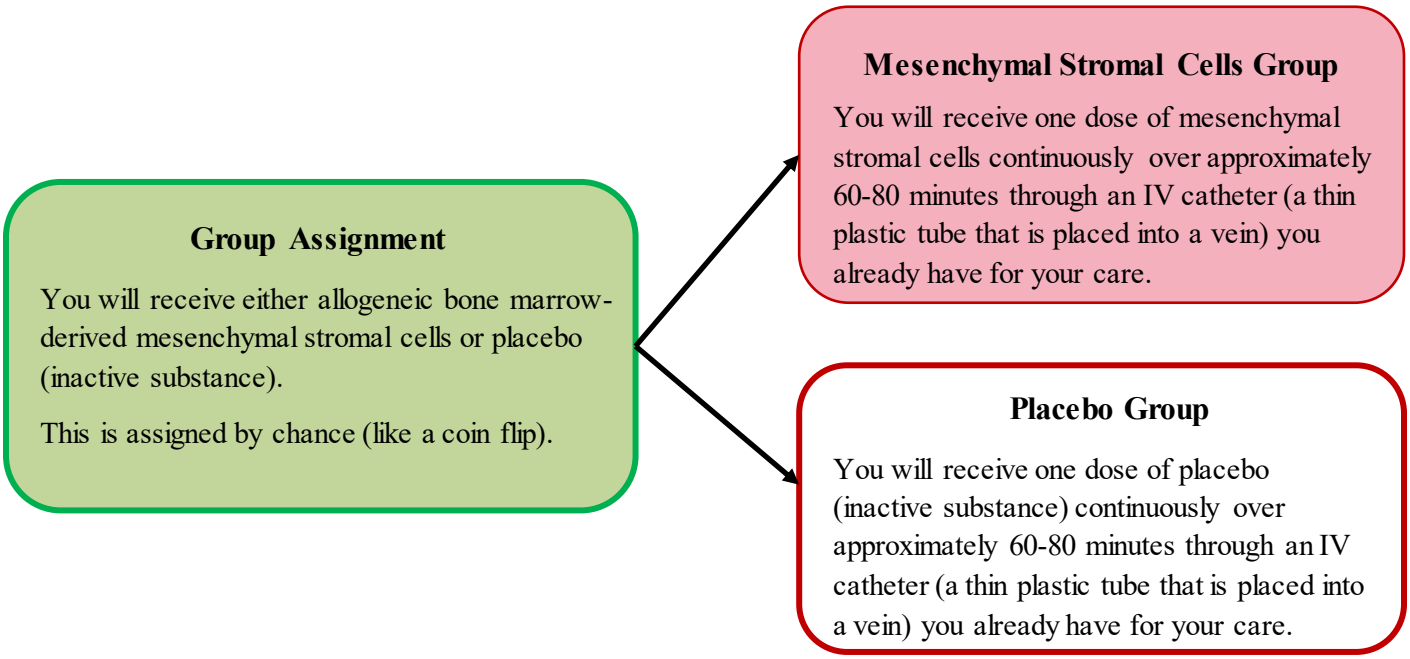
What is the purpose of this study?
You are being asked to take part in this study because your lungs are badly injured – you have Acute Respiratory Distress Syndrome (ARDS). This is a type of lung injury makes it hard to breathe and get enough oxygen. Your doctors are using a breathing machine to help you breathe and get more oxygen.

This study is funded by the Department of Defense. The study is being done to find out if early treatment with an experimental treatment can have any effects, good or bad, on you and your lung injury. The experimental treatment is an infusion of allogeneic bone marrow-derived mesenchymal stromal cells, which are a special type of human cells. Based on studies in animals, bone marrow-derived mesenchymal stromal cells appear to have the ability to decrease injury and increase healing in the injured lung, but their ability to have this effect in humans with lung injury is unknown. The cells used in this trial have been taken from normal humans and processed in a laboratory so they can be used in patients. If you have religious beliefs that disallow you from receiving blood or tissue you should not participate.

If you agree to join the study, you will be assigned by chance (like a coin flip) to one of two groups. One group will receive the allogeneic bone-marrow derived mesenchymal stromal cells, the other group will not. Both groups will get all other common lung injury treatments, and will get the same medical treatment given to patients who are not in the study. If you do not join this study, your doctors will care

for you as they normally would. Leaving the study will not affect your medical care, and you can still get your care from your hospital.

What will happen and how long will you be in the study?
We will ask up to 120 people with your type of lung injury to join this study at 7 hospitals. The University of California, San Francisco is the Clinical Coordinating Center for this trial.



Everyone in the study:

- ☑ We will monitor you closely for two hours before the study product infusion, during the infusion and 6 hours after the start of infusion to make sure that your medical condition is stable.
- ☑ We will monitor your blood pressure and the level of oxygen in your blood using a catheter placed in an artery.
- ☑ We will check your breathing machine settings. If not already being used, your breathing machine will be adjusted using a lung protective strategy in order to make sure that you will receive the beneficial effects of lung protection while you are in this study.
- ☑ We will do blood tests to monitor you while you are in this study for up to 14 days. Blood will be drawn through a catheter you already have in your vein or your artery. We will use the blood test results that your regular doctor gets for your care whenever available. This will reduce the amount of blood we need to take for the study.

- ☑ We will collect blood samples at 6 different times: the start of the study, and then after 6 hours, 12 hours, 24 hours of the start of study product infusion, and after 2 and 3 days (approximately five tablespoons of blood total). We will collect urine (pee) samples at 3 different times: the start of the study, and then 24 hours and 2 days. We will store these samples for years for studies of lung injury and other conditions. These samples will not contain your name or identifying information, only a coded study number.

  Your samples and information about you may be shared with others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

  Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, University of California, and/or others. If this happens, there are no plans to provide money to you.
- ☑ We will place a thin tube (catheter) past the end of your breathing tube and rinse part of your lung after 2 days. We will rinse with about three tablespoons of sterile salt water. Your lung will quickly take up (absorb) the rest of the rinse. This is called a mini bronchoalveolar lavage (mini-BAL) and is a common procedure that is often done to diagnose pneumonia. Doctors, nurses and respiratory therapists commonly place a catheter past the end of a breathing tube to suck out secretions from the lungs.
- ☑ With the exception of the study infusion, both groups will receive the same medical care for lung injury.
- ☑ While you are in the hospital, we will look at your medical records or check on you to see how you are doing. We will collect information like your blood pressure, heart rate, medical history, and test results, and whether there is any signs of infection or failure of your organs. We will also record measurements from your breathing machine.
- ☑ After you leave the hospital, we will contact you by telephone at 28 and 60 days after the start of study product infusion, as well as 6 months to see how you are doing and feeling. Each call will be less than 15 minutes. Contact information will be collected for you and up to 2 family members and/or friends. If you go to another health care facility, we may contact you or the health care facility to find out how you are doing.

Your participation in this study is complete after the 6-month phone call. It is possible that other researchers studying lung injury may contact you in the future regarding potential participation in other studies and to see how you are doing.

Side effects and risks that you can expect if you take part in this study:

a. The risks of the mesenchymal stromal cell study product are similar to the risks of a blood transfusion. During the infusion, you may have symptoms like a rise in heart rate or a fall in blood pressure or a fall in oxygen level in your blood. These changes may require changes to your medications or to the ventilator. You may have an allergic reaction which could result in hives, rash, difficulty breathing, low blood pressure, or severe blood circulation and breathing problems. Finally, the stromal cell product is prepared sterilely, but rarely these products become contaminated with bacteria and viruses and you can have a serious bacterial infection from the stromal cell product.
b. Arterial lines (the thin plastic tube placed in your artery) are placed routinely in patients with the Acute Respiratory Distress Syndrome. Rare but known risks include infection, reduced blood flow to the hand or leg resulting in pain, and even more rarely, damage to the skin and muscles or an abnormal connection between the artery and a nearby vein.
c. The mini-bronchoalveolar lavage is a routine procedure in patients who are on a breathing machine. During the procedure, you may cough when we rinse the lung or suck fluid from the lung. Rare but serious risks include low blood oxygen levels, bleeding and collapsed lung (pneumothorax). To decrease these risks, the procedure will be done with 100% oxygen and only if your overall condition, lung function and the ability of your blood to clot are stable.
d. Participation in research may cause you to lose some privacy. Your health information will be handled as confidentially as possible.
e. We do not know if your risk of dying from your lung injury will be changed by choosing to be in this study.
f. There are no major risks associated with drawing blood. We will usually take blood from tubes that are already in your vein or artery. If you do not have a tube in a vein or artery, then we will get the blood with a needle and you may experience minor discomfort, bruising or soreness. Sampling from a needle very rarely causes infection. Blood draws will be done by a trained professional to minimize risk.

Risks that are not known:

Because this treatment is experimental, there may be risks that we do not know about at this time.

Good effects that might result from this study:

We do not know if you will benefit from being in this study. Your participation in this study will help us learn more about Acute Respiratory Distress Syndrome and may help other patients in the future. You will not receive any benefit from the tests done on your blood, urine or mini-BAL (lung fluid)

samples. These tests may help us learn more about lung injury and the best treatments for it, and may help us develop new products or tests. These may have value and may be developed and owned by the study staff and/or others. If this happens, there are no plans to provide money to you.

Other treatments you could get if you decide not to be in this study:
Taking part in this study is completely voluntary, which means you can choose whether or not you want to take part. You will receive the care you need whether or not you join the study. If you decide not to join this study, your doctors will care for you as they normally would.

Reasons why the study doctor may take you out of this study:
The study doctor may take you out of this study if new information about lung injury becomes known, if it is best for you, or if the study is stopped by the Department of Defense, the Food and Drug Administration (FDA), the Data and Safety Monitoring Board (DSMB) or the Vanderbilt University Institutional Review Board.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

If you decide to stop being in the study, the study doctor may ask you if you are willing to have some follow up study care or tests. If you stop being in the study, we will store your blood and urine samples unless you request them to be destroyed. We will continue to collect information from your medical record unless you ask us not to. We will give you any new information that may affect your decision to stay in the study.

Clinical Trials Registry:
A description of this clinical trial is available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:
University of California, San Francisco – San Francisco serves as the Coordinating Center for this trial and may share your study information, without anyone knowing it is related to you specifically, to others or use it for other research projects not listed in this form.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Department of Defense
- The Food and Drug Administration (FDA)
- The Vanderbilt University Institutional Review Board (IRB)
- The Data and Safety Monitor Board (DSMB) and Research Monitor as entities

The Coordinating Center at the University of California San Francisco – San Francisco, <PiFullName> and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

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Part 2 of 2: STUDY SITE INFORMATION

Site Name:	<SiteName>
Site Principal Investigator:	<SitePiFullName>
Site Principal Investigator Contact:	<IcfPhoneNumber>

This part of the consent form includes information about the site that is asking you to participate in this study and is specific to participation at your site only. Before making your decision, both the site-specific information and the general study information should be reviewed with you. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Payments for your time spent taking part in this study or expenses:
You will not be paid for taking part in this study.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the rest of the care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at (415) 476-1814.

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Who to call for any questions or in case you are injured:
If you should have any questions about this study or if you feel you have been hurt by being a part of this study, please feel free to contact <SitePiFullName> at <IcfPhoneNumber>. For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Medical Center Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Authorization to Use/Disclose Protected Health Information
You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

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STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Participant

Participant's Name (Print): _____

Signature (if able to consent): _____ Date: _____/_____/_____

Surrogate

Legal Representative (Print): _____

Relationship to Participant: _____

Signature:_____ Date: _____/_____/_____

Witness

(If required) Witness's Name (Print):_____

Signature: _____ Date: _____/_____/_____

Witness to: ☐Discussion ☐Signature

Interpreter

(If required) Interpreter Name (Print):_____

Signature: _____ Date: _____/_____/_____

Study Representative Statement

I have explained the purpose of the research, the study procedure, the possible risks and discomforts, the possible benefits, and have answered all questions to the best of my ability.

Study Representative's Name (Print): _____

Signature:_____ Date: _____/_____/_____

Time Consent Obtained: ____:_____ AM / PM

You will receive a copy of this form after it has been signed and dated.

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CONSENT FOR DNA/RNA TESTING ON STORED SPECIMENS

The purpose of this study is to store samples of your blood. The purpose is to look for the genetic factors (DNA/RNA) that may cause or relate to your lung injury or other diseases.

Description of the Procedures: An extra 1 teaspoon of blood prior to study product infusion and additional 1 teaspoon of blood on day 2 after the initiation of study product infusion will be drawn and stored for genetic testing purposes. The blood will be taken with other laboratory test samples so you will not get an extra needle stick. Your blood sample will be processed and may be tested and shared for research genetic testing. The sample will be sent to a repository at the University of California San Francisco – San Francisco (UCSF). The purpose of sending your blood samples to the Repository is to make samples available for future research by investigators not involved in this study.

Confidentiality of Your Blood Samples: We will freeze your samples and store them for years for future studies. We will protect your privacy and give all samples coded study numbers. Only your hospital study team will know your coded study number identity, which will be kept secure. The stored blood samples will not contain your name or identifying information.

How Long Will the Samples Be Stored: The samples will be stored for an unknown period time (maybe years). The samples may be thrown away at any time when they are no longer needed. The results of tests run on your samples will not be recorded in your records and neither you nor your doctor will be told of the results. No one else, including relatives, doctors, or insurance companies can get the stored samples or results. Your samples will be used only for research and will not be sold or used directly to produce commercial products.

Risks: One possible risk might be the release of your name which could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job. You are currently protected from genetic discrimination by employers or insurance companies through the Genetic Information Nondiscrimination Act (GINA 2008). To protect you from this risk we will keep the link between the samples and your personal ID as secure as possible. This link will only be kept by the local study team. The UCSF repository and future researchers will not have access to any of your personal information so they will not know who you are or be able to contact you.

Benefits: You will not receive any direct benefit from your samples. Information obtained from the tests may provide useful information, about the causes, risks, and prevention of ARDS and other diseases, may help other patients.

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Voluntary Participation/Right to Withdraw Your Permission for Genetic Testing: Your decision to join this study is completely up to you (completely voluntary). Your decision will not change the quality of the care you receive. You are still eligible to join the study described in the other consent form even if you do not want your samples stored for genetic testing. At any time, you may ask to have your sample destroyed. You should contact <SitePiFullName> in writing (<SitePiAddress>) to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

Costs or compensation of study: There will be no costs to you or compensation.

Consent

Please **initial** Yes or No line and sign your name, to show you have freely given your answers and consent:

My blood sample may be stored for future genetic research in ARDS. Yes ____ No ___

My blood sample may be stored for future genetic research involved with other medical conditions for example, obesity, diabetes, cancer, heart disease, Alzheimer's disease, etc). Yes ____ No ___

_____ _____/_____/_____
Signature (subject or surrogate) Date

_____ _____ ____ / ____ / ____
Signature of Person Obtaining Consent Printed Name and Title of Person Date

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CONSENT FOR CONTINUED RESEARCH PARTICIPATION

You have been taking part in a research study entitled Human Mesenchymal Stromal Cells for the Treatment of Acute Respiratory Distress Syndrome. This study is funded by the Department of Defense. Consent for your participation was obtained from your legal representative because you were unable to provide consent at that time. We are now asking for you to consent to continue being in the study. Your continued participation is entirely voluntary, which means you can decide whether or not you want to be in this study. If you decide not to continue in this study, it will not affect your relationship with your doctor or with your treating hospital and will not result in any penalty or loss of benefits to which you are otherwise entitled. If you stop being in the study, we will continue to store your samples (blood, urine and rinse samples of your lung) unless you request they be destroyed. We will continue to collect information from your medical record unless you ask us not to.

STATEMENT OF VOLUNTARY CONSENT

I have read this form and the attached consent or have had them read to me. I have been told what to expect if I take part in this study, including risks and possible benefits. I have had a chance to ask questions and have had them answered to my satisfaction. I have been told that the people listed in this form will answer any questions that I have in the future. By signing below, I am volunteering to continue to be in this research study.

Participant's Name (Print):

_____

Signature: _____ Date: ____/____/_____

- My blood sample may be stored for future genetic research in ARDS. Yes ____/No ____
- My blood sample may be stored for future genetic research involved with other medical conditions (for example, obesity, diabetes, cancer, heart disease, Alzheimer's disease, etc). Yes ____/No ____

Witness

(If required) **Witness's Name** (Print):_____

Signature: _____ Date: _____/_____/_____

Witness to: ☐ Discussion ☐ Signature

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Interpreter

(If required) Interpreter Name (Print):_____

Signature: _____ Date: _____/_____/_____

Study Representative Statement

I have explained the purpose of the research, the study procedure, the possible risks and discomforts, the possible benefits, and have answered all questions to the best of my ability.

Study Representative's Name (Print): _____

Signature:_____ Date: _____/_____/_____

Time Consent Obtained: ____:_____ AM/PM

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits.

You have been given a copy of this consent form and of the Experimental Subject's Bill of Rights to keep.