INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**University of Minnesota / "Randomized Controlled Trial of Losartan for Patients with COVID-19 Requiring Hospitalization"**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

This form is for use in a research study that may involve participants who may or may not have the capacity to consent to take part in the study. When the participant cannot legally consent to take part, pronouns "you" and "your" should be read as referring to the participant rather than the person (legally authorized representative) who is signing this form for the participant. In cases where the participant's representative gives consent, the participant should be informed about the study to the extent possible given his/her understanding. During the course of the study, if the participant regains the capacity to consent, informed consent will be obtained from the participant and the participant offered the ability to leave the study if desired.

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you have either tested positive for COVID-19 (novel coronavirus), and you are in the hospital for care.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you. You will not be penalized or lose benefits you are otherwise entitled to.
- You can ask all the questions you want before you decide.

Why is this research being done?

The virus COVID-19 uses a specific protein on the surface of your cells to enter the cell. This protein is important to protect your lung from circulating hormones. COVID-19 blocks this protein and damages your lungs. In this study, we want to see if giving you a study drug (called Losartan) that can block this lung damaging hormone helps reduce problems with breathing while you recover from COVID-19. Losartan is approved by the U.S. Food and Drug Administration (FDA) to treat high blood pressure and diabetic kidney disease in patients with type 2 diabetes and high blood pressure. Losartan has not been approved to treat COVID-19 or its symptoms. The use of this drug in this study is considered experimental.

How long will the research last?

We expect that you will be in this research study for up to 90 days. You will receive study drug for 10 days unless you are sent home from the hospital, whichever comes first.

What will I need to do to participate?

You will be asked to have a physical exam, provide blood samples, nose or mouth swab samples, answer daily questions about symptoms or side effects, and take your study drug daily. You will be randomly assigned to receive either Losartan or a placebo (a liquid mixture that looks just like Losartan but doesn't have any active drug in it). You have a 50:50 chance of taking either liquid mixtures during this study, like flipping a coin. Neither you nor the study staff will know what you are taking, but they can find out if they need to.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

Risks of Losartan include:

- Feeling tired, weak, or dizzy (more common, 2-3 out of 100 people)
- Diarrhea (less common)
- Chest pain (more common, 1-2 out of 100 people)
- Low red blood cell count (less common)

- Low blood pressure (more common)
- Worsening kidney function (less common)
- Abnormal levels of electrolytes (minerals in your blood, less common)
- Allergic reaction (less common)

Blood draws may cause pain, bleeding, or bruising where the needle pokes your skin. There is a small risk of infection at the needle site, and sometimes people feel lightheaded or faint during a blood draw. The team will try to draw your blood from IVs you already have, but might need to perform a needle stick.

There is also a small risk that someone who is not part of the study team might see information collected about you for this research. We store your data securely to try to avoid this.

You will be emailed a PDF copy of this signed and dated consent form. There may be risks of loss of privacy and confidentiality if the PDF copy of this consent form is viewed and/or stored on a personal electronic device (PED), especially if that PED is shared with other users or is lost, hacked, or subject to a search warrant or subpoena. Also, the PDF copy of the consent may not be able to be permanently removed from a PED.

Since the use of this study drug is experimental, there may be other risks that are unknown. Additionally, there may be unknown risks to a pregnancy, embryo, or fetus if you become pregnant.

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, if you receive Losartan and if this study drug works, you might need less oxygen or mechanical ventilation.

What happens if I do not want to be in this research?

You do not have to participate in this research. Instead of being in this research study, you can continue to receive supportive care in the hospital.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 220 people here will be in this research.

What happens if I say "*Yes, I want to be in this research*"?

If you decide you want to be in this research, you will participate for 90 days. You will receive study drug for 10 days or until you are sent home from the hospital, whichever comes first. During your hospital stay, you can expect the following procedures:

- You will have a physical exam to determine if you are eligible for this study. If you are a woman who is able to become pregnant, you will also have a pregnancy test.
- If you are eligible for this study, you will be randomly assigned to receive either Losartan or a placebo. You have a 50:50 chance of receiving either study treatment, like flipping a coin. You will not know which study treatment you are receiving; study staff will not know but if they need to find out during an emergency, they can.
- You will have the following done while you are in the hospital, beginning as soon as you sign and date this consent form:

  - Study staff will ask you some questions about symptoms or side-effects daily
  - You will have a blood draw of about two tablespoons on day 1, and a tablespoon plus one teaspoon of blood on days 2, 4, 6, 8, 10, and 15.
  - You will have a swab of samples taken from your nose or mouth on days 1, 4, 8, 10 and 15.
  - You will be given study drug (either Losartan or placebo) twice a day while in the hospital for up to 10 days.
  - You will be asked to return to the clinic for a blood draw for follow up creatinine and potassium levels (about 2 tablespoons of blood) around 15 days after you enroll in the study, in addition to a nose or mouth swab sample on day 15. If you are still in the hospital this visit can occur while you are in the hospital.
  - If you're discharged from the hospital before 7 days have passed since you started the study treatment you will be sent home with a pulse oximeter to test your blood oxygen levels. Study staff will also follow up with you via phone calls to collect the pulse oximeter readings.
- You have the choice to have your samples of blood and saliva stored for future research. You can choose if you want to give that permission at the end of this consent form.
- You have the choice to join the blood concentration (PK) substudy. This looks at blood concentrations of the study drug over 24 hours starting at your first dose. If you participate in this substudy it will be about the same amount of blood drawn, but samples will need to be taken at 4 time points on the first day of the study.

Around day 30 and 90, the study team may contact you by phone to complete end of study assessments.

What happens if I say "Yes", but I change my mind later?

If you take part in this research study, and want to leave, you should tell us. Your choice not to be in this study will not negatively affect your right to any present or future medical care, your academic standing as a student, or your present or future employment.

We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

If you decide to leave the research study, study staff will ask you if it is okay to conduct a final study visit for safety testing.

If you stop being in the research, information about you that has already been collected may not be removed from the study database. You will be asked whether the study doctor can collect information from your routine medical care, such as your medical records after you leave the study. If you agree, you will be asked to sign and date an additional consent form (Clinical Data Collection after Withdrawal Consent Addendum) and HIPAA authorization to document your agreement to participate in ongoing data collection.

Can I be removed from the research?

It's possible that we will have to ask you to leave the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Losartan has additional risks to a fetus or baby. Women who are pregnant or breastfeeding are not eligible

to participate in this study. Women of child bearing potential must already be using highly effective contraception and continue to use it until the study is completed.

Will it cost me anything to participate in this research study?

- There will be no cost to you for any of the study activities or procedures.
- There will be no cost to you for the lab tests, drugs, and follow-up visits that are done for research purposes only and are not part of your regular care.
- You will have to pay for basic expenses like any childcare, food, parking, or transportation related to study activities.
- You or your insurance company will have to pay for all costs for medical care not related to participation in this study, including copayments and deductibles. You will have to pay for any costs your insurance does not cover. If you have any questions about these costs, or what out-of-pocket expenses you may have to pay, you should contact your insurance company. If you do not have health insurance, you will have to pay all costs for your medical care just as you would if you did not take part in this study.
- If you need treatment for side effects while you are on the study, you or your insurance will need to pay for this treatment.

What happens to the information collected for the research, including my health information?

We try to limit the use and sharing of your information, including research study records, any medical records and any other information about you, to people who have a need for this information. But we cannot promise complete confidentiality.

Overview

If you participate in this study, your information, including your health information, will be used and shared for purposes of conducting this research. As described later in this Consent Form, your information may also be used and shared for publishing and presenting the research results, future research, and any optional elements of the research you agree to in this Consent Form, which may include creating audio and video recordings of you. If you sign this Consent Form, you are giving us permission to use and share your health information for these purposes, and if we are using your medical records, you are giving permission to any health care providers who are treating you to share your medical records with us.

What health information will be made available?

Health information about you to be used and shared for the research includes those items checked by the research team below:

☒ Your medical records, which may include records from hospital and clinic visits, emergency room visits, immunizations, medical history and physical exams, medications, images and imaging reports, progress notes, psychological tests, EEG/EKG/ECHO reports, lab and pathology reports, dental records and/or financial records. These records may be used and shared for as long as this research continues.

☒ Information collected as part of this research study, including research procedures, research visits,

and any optional elements of the research you agree to, all as described in this Consent Form. This information might not be part of your medical record, and may include things like responses to surveys and questionnaires, and information collected during research visits described in this Consent Form.

What about more sensitive health information?

Some health information is so sensitive that it requires your specific permission. If this research study requires any of this sensitive information, the boxes below will be marked and you will be asked to initial to permit this information to be made available to the research team to use and share as described in this Consent Form.

☐ My drug & alcohol abuse, diagnosis & treatment records _____ (initial)

☐ My HIV/AIDS testing records _____ (initial)

☐ My genetic testing records _____ (initial)

☐ My mental health diagnosis/treatment records ____ (initial)

☐ My sickle cell anemia records _____ (initial)

Who will access and use my health information?

If you agree to participate in this study, your information will be shared with:

- The University of Minnesota research team and any institutions or individuals collaborating on the research with us;

- Others at the University of Minnesota and M Health/Fairview who provide support for the research or who oversee research (such as the Institutional Review Board or IRB which is the committee that provides ethical and regulatory oversight of research at the University, systems administrators and other technical and/or administrative support personnel, compliance and audit professionals (Such as the Quality Assurance Program of the Human Research Protection Program (HRPP)) , individuals involved in processing any compensation you may receive for your participation, and others);

- The research sponsor(s), any affiliates, partners or agents of the sponsor(s) involved in the research, organizations funding the research, and any affiliates, partners or agents of the funding organization(s) involved in the research;

- Organizations who provide accreditation and oversight for research and the research team, and others authorized by law to review the quality and safety of the research (such as U.S. government agencies like the Food and Drug Administration, the Office of Human Research Protections, the Office of Research Integrity, or government agencies in other countries); and

- Organizations that process any payments that may be made to you for participating in this study, and any other individuals or organizations specifically identified in this Consent Form.

Additional sharing of your information for mandatory reporting

If we learn about any of the following, we may be required or permitted by law or policy to report this information to authorities:

- Current or ongoing child or vulnerable adult abuse or neglect;
- Communicable, infectious or other diseases required to be reported under Minnesota's Reportable Disease Rule;
- Certain wounds or conditions required to be reported under other state or federal law; or
- Excessive use of alcohol or use of controlled substances for non-medical reasons during pregnancy.

How will my information be used in publications and presentations?

We may publish the results of this research in scientific, medical, academic or other journals or reports, or present the results at conferences. Information that makes it easy to identify you (such as your name and contact information, SSN and medical records number) will not be part of any publication or presentation. If you have an extremely unique or rare condition that is not shared by many others, it is possible that some people may be able to determine your identity even without these identifiers.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the agency which is funding this project or for information that must be disclosed in order

to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of, for instance, child abuse or neglect, harm to self or others, and communicable diseases.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

What will be done with my data and specimens when this study is over?

Your data and/or samples may be used for any future research after this study is complete. The future research will be look at the virus and your health status during the study.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include your name or any other direct identifiers such as your contact information. The Web site may include a summary of the results of this research. You can search this Web site at any time.

Will I receive research test results?

Most tests done on samples in research studies are only for research and have no clear meaning for health care. The investigator(s) will not contact you or share your individual test results.

Will anyone besides the study team be at my consent meeting?

You may be asked by the study team for your permission for an auditor to observe your consent meeting. Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (for example, name, date of birth) or confidential information about you. The auditor will not observe your consent meeting without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00042757.

To share feedback privately with the University of Minnesota Human Research Protection Program (HRPP) about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner to you or your insurance company. If you think that you have suffered a research related injury, let the study doctor know right away. By signing this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.
Due to the coronavirus public health crisis, the federal government has issued an order that may limit your ability to recover damages if you are injured or harmed while participating in this COVID-19 clinical study. If the order applies, it limits your ability to recover damages from the University, researchers, healthcare providers, study sponsor, manufacturer or distributor involved with the study. However, the federal government has a program that may provide compensation to you or your family if you experience serious physical injuries or death due to this study. To find out more about this "Countermeasures Injury Compensation Program" go to
https://www.hrsa.gov/cicp/about/index.html or call 1-855-266-2427.

Will I be compensated for my participation?

«Compensation»

Participant or Legally Authorized Representative Phone Number:
_____

Participant or Legally Authorized Representative Email Address:
_____
_____

Is the Legally Authorized Representative signing consent?
O Yes
O No

Are you signing this consent in person (at the hospital with study staff) or remotely?
O Yes
O No

All of my questions have been answered, and I have been given the opportunity to decline this research.
O Yes
O No

Signature Block:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed and dated document.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Legally Authorized Representative (if applicable)

_____ _____
Signature of Legally Authorized Representative Date

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

Signature Block for Witness:

WITNESS STATEMENT:

The participant or legally authorized representative (LAR) was unable to read or sign this consent form because of the following reason:

☐ The participant/LAR is illiterate

☐ The participant/LAR is visually impaired

☐ The participant/LAR is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____

For the Consent of Non-English Speaking Participants or LARs when an Interpreter is used:

As someone who understands both English and the language spoken by the participant or LAR, I represent that the English version of the consent form was presented orally to the participant of LAR in their own language, and that they were given the opportunity to ask questions.

_____ _____
Signature of Interpreter Date

_____
Printed Name of Interpreter

OR:

Statement from a Non-Interpreter:
As someone who understands both English and the language spoken by the participant or LAR, I represent that the English version of the consent form was presented orally to the participant or LAR in their own language, and that they were given the opportunity to ask questions.

_____ _____
Signature of Individual Date

_____
Printed Name of Individual

Signature for Optional Future Scientific Research

We are asking you to take part in this optional future scientific research because you have already agreed to take part in the main study, named above. You are now being asked to give permission for your biologic samples to be used for future scientific research which may include examining your genes. This future research will examine how individuals respond to COVID-19 infection.

Your biologic samples will be stored indefinitely. You have the right to change your mind at any time about participating in this optional research. And your biological samples will be destroyed if you ask. Any information gained from your biological samples before you change your mind will not be destroyed.

This portion of the study is optional.

All of your rights as a research participant are covered in the main study Consent Form This form only provides additional information for you to decide if you want to give your permission for this future scientific research. You may stay in the main study even if you decide not to take part in this future research. Before you consent to give your sample for future research, please read this form. Ask as many questions as you need to before you decide if you want to take part.

Your signature documents your permission to take part in this optional research. You will be provided a copy of this signed document.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Legally Authorized Representative (if applicable)

_____ _____
Signature of Legally Authorized Representative Date

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

Signature for Optional Blood Concentration (PK) Substudy

We are asking you to take part in this optional substudy because you have already agreed to take part in the main study, named above. You are now being asked to give permission for 4 additional blood samples over 24 hours from the first dose of study drug. This will examine how the study drug concentration in blood changes over 24 hours.

Your biologic samples will be stored indefinitely. You have the right to change your mind at any time about participating in this optional research. And your biological samples will be destroyed if you ask. Any information gained from your biological samples before you change your mind will not be destroyed.

This portion of the study is optional.

All of your rights as a research participant are covered in the main study Consent Form This form only provides additional information for you to decide if you want to give your permission. You may stay in the main study even if you decide not to take part in this blood concentration study. Before you consent to give your samples, please read this form. Ask as many questions as you need to before you decide if you want to take part.

Your signature documents your permission to take part in this optional research. You will be provided a copy of this signed document.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

_____
Printed Name of Legally Authorized Representative (if applicable)

_____ _____
Signature of Legally Authorized Representative Date

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent