

SIREN Informed Consent Forms

The Sponsor/Investigator of C3PO does not allow edits to this central IRB approved main consent form for this multicenter trial. This is to ensure equity of the language across the enrolling sites. Your site may add site-specific content in a single contained section below the universal text if necessary. This section is limited to information that pertains specifically to your local institution.

Please note the process for submitting informed consent forms for C3PO as sites submit ceding applications to local IRBs. All SIREN informed consent forms are approved by the Advarra Central IRB (ER-CIRB) with the parent protocol. The informed consent form is a completely locked down form, to be used consistently across C3PO sites. Please submit this form to your local IRB as is, without making any site specific changes. The current ER-CIRB approved form to be used is located in the C3PO Toolbox and the Getting Started page.

Where local site and study team contact information needs to be included, this will populate directly into the form after the site application is submitted to and approved by the ER-CIRB. In very limited circumstances, when institutionally required language is requested by the IRB, there is potential to add a separate site specific section at the end of the form prior to the signature page. However, for the time being, please submit the form as is. Additions will only be considered per a request from the IRB, and will be discussed on a case by case basis. Should this request from the IRB be made, please provide at the earliest time the additional requested language in a separate document for review by the SIREN CCC. Please do not edit or insert language into the body of the trial-wide approved ICF.

Please note that while HIPAA language is already included in the body of the consent form, a separate local HIPAA form is acceptable for use, so long as it is signed and dated by subject.

We understand that this process differs from how the ICF review process has operated for other trials. We are happy to help as we move along with this process; please let us know if we can be of assistance. Please also note the below statement from Advarra regarding this process for SIREN trials.

As you know, Advarra is the single IRB for the SIREN network trials. If your organization has a negotiated process in place with Advarra specifically as it pertains to the Informed Consent language, please note that the established process that has been in place with your site and Advarra is suspended for the SIREN network's trials. SIREN has their own IC process which Advarra will follow for these specific trials. Any non-SIREN trials will follow the established process you already have in place with Advarra.

If you have any questions regarding this please contact C3PO-contact@umich.edu.

Thank you for your attention with this matter,

Best regards,

Advarra Institutional Services Team & SIREN



NIH SIREN
Emergency
Trials
Network



C3PO
Clinical Trial of COVID-19
Covalescent Plasma in
Outpatients

CONSENT FOR CLINICAL RESEARCH STUDY AND AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

**Sponsor / Study
Title:**

The National Heart, Lung and Blood Institute (NHLBI) and The National Institute of Neurological Disorders and Stroke (NINDS)/ “Clinical-trial of COVID-19 Covalescent Plasma in Outpatients (C3PO)”

**Principal
Investigator:
(Study Doctor)**

«PiFullName»

Telephone:

«lcfPhoneNumber»

Address:

«PiLocations»

Key Information

You have been diagnosed with COVID-19 illness. You may be eligible to participate in a research study. This form includes information to help you decide whether you wish to participate in the study. The purpose of the research study is to learn whether a possible treatment for people with milder COVID-19 illness can prevent them from getting much sicker. The possible treatment being studied is convalescent plasma. **Convalescent plasma (CP) is made from blood taken from persons who have recovered from COVID-19.** CP contains proteins that can fight the COVID-19 infection (antibodies). It is unknown if being given CP will help, hurt, or be the same as not getting CP.

People who choose to be in this study are assigned at random, that is, by chance, to receive an infusion of CP or placebo. The placebo is water mixed with minerals and multivitamins in order to look like CP. The CP or placebo will be given only once. You will not know if you are given CP or placebo, but this can be revealed if medically necessary.

Blood samples will be drawn before the infusion, one hour after the infusion, and once on day 15 and 30 of being in the study.

We will call or email people who chose to be in the study six times to see how you are doing. This will happen every other day after the infusion for two weeks. We will also call to arrange follow up at 15 and 30 days. We will also review medical records of people in the study. About 600 people will take part at about 30 hospitals in the United States.

You taking part in the study will help doctors learn the best way to treat patients in this and future pandemics. You may or may not directly benefit from being in the study. Some people may benefit directly if they get CP and if it treats COVID-19. Taking part also has risks. Some risks are currently not known. Known risks of receiving CP include fever, rash, itching, allergic reactions, injury to the lungs and excess fluids.

Taking part in this study is entirely voluntary. If you decide not to take part, you will receive the usual medical care for COVID-19 illness given here. There is no penalty for choosing not to take part. You can withdraw from the study at any time.

Medical records and data collected in the study will remain as confidential as possible. Your records may be viewed by the study team here or from the study coordinating centers, by the Institutional Review Board, or by those providing Federal Government funding, oversight and regulation of the study.

You will not be paid for taking part in the study. You may receive compensation for travel and expenses. There is no cost to taking part in the study. Charges for all standard medical care will be billed in the same manner regardless of whether you take part.

Please contact us for any questions about the research, your rights, or other research related concerns.

- Please carefully read this form, additional detail about each item just described is found below.
- Please listen to the study team explain the study and this form to you.
- Please ask questions about anything that is not clear.

If you consent, you will be asked to sign and date this form.

What is the purpose of this research study?

Convalescent plasma (CP) is made from blood taken from persons who have recovered from COVID-19. CP contains proteins that can fight the COVID-19 infection (antibodies). The purpose of the research study is to learn whether giving CP to people with milder COVID-19 illness can prevent them from getting much sicker. Prior studies from previous pandemics show that CP may help persons with infectious diseases recover from their illness. However, it is not known whether giving CP to persons with mild COVID-19 illness can prevent progression to severe illness that requires hospital admission. This study is designed to answer this question. CP for COVID-19 illness is investigational, which means it has not been approved by the U. S. Food and Drug Administration (FDA) to improve recovery or lessen symptoms from COVID-19. It is unknown whether adding CP to the usual care that persons with mild COVID-19 illness receive is the same, better or worse than usual care.

Blood samples will be collected to help the study doctors learn whether getting CP increases blood levels of antibodies to the COVID-19 virus.

How long will you be in the study? How many people will be in the study?

Taking part in this study can last up to 30 days. We will enroll about 600 people from about 30 hospitals across the United States. This research study is designed so that nobody is excluded from taking part on the basis of sex, race, or national origin.

What is Convalescent Plasma (CP) and what does it involve?

Convalescent plasma (CP) is made from blood taken from persons who have recovered from an infectious illness. Plasma is the clear yellow fluid part of blood. Plasma contains proteins called antibodies that can help with fighting infections. When a person gets infected with COVID-19, the body's defense system produces antibodies which fight the COVID-19 virus. The antibodies may also protect them from becoming infected with the virus again. Some people who have recovered from COVID-19 illness have donated their blood in case it can be used to help others with COVID-19 get better. This blood is processed and the plasma portion is separated from the red blood cells. This clear yellow portion has the antibodies to the COVID virus, and is called CP for short. It is removed and stored for future use, such as for use in this study.

Who can take part in this study?

People who can take part in this study are those who come to the emergency department with symptoms and get a test indicating COVID-19 illness. To take part in the study you cannot be so sick already that you need to be admitted to the hospital today. To take part, you also have to be at some increased risk of getting sicker over the next two weeks. You may be at increased risk if you are over 50, obese, or have heart disease, lung disease, kidney disease, diabetes, sickle cell disease or a depressed immune system. Those with COVID-19 symptoms for more than 7 days, those who have had recent transfusions or prior bad reactions to a transfusion, or who cannot tolerate getting intravenous fluids (fluids directly into a vein) cannot take part.

What will happen to you in this study?

- You will receive usual treatment for COVID-19 illness, no matter to which study group you are assigned.
- We will draw up to a teaspoon of blood (5 ml) to check your blood type to make sure that any CP we give you is compatible with your blood type according to the usual practice at your hospital and local blood bank. We may draw two separate samples of blood (two needlesticks, and two teaspoons, 10 ml, total) in order to confirm your blood type.
- In the unusual case that no CP is available that is compatible with your blood type, you will not be able to participate in this research. In that case, we will not perform any further research activities. You will continue to receive usual treatment.
- You will be randomly, that is by chance, (like the flipping of a coin), assigned to receive either CP or placebo. The placebo is water mixed with minerals and vitamins that is not known to help fight COVID infection, and has no pharmaceutical ingredient for this condition. The CP or placebo infusion will be given only once. This single dose is given only on the day of enrollment. The total volume of the infusion you will receive is about 250 ml or less (about the size of a can of soft-drink).
- On the day of enrollment, we will also collect a tablespoon (15 ml) of blood prior to the study infusion and one hour after the infusion.
- Information from your medical records will also be collected.

- Your contact information and the contact information for one or more family members, close friends, or caregivers will be collected so we can perform telephone interviews and send you emails during the study.
- We will contact you by telephone, text, or email six times to see how you are doing. This will happen every other day after the infusion for two weeks. We will ask about your symptoms, if you have had any additional medical problems, and if any contact information has changed. These phone calls or email responses will take about 10 minutes each. If you are unable to answer because of your medical condition, we will ask a family member or close friend or caregivers that you designate to report how you are doing.
- We will also call to arrange follow up visits at 15 and 30 days after the infusion of CP or placebo. At these follow up visits we will draw one tablespoon (15 ml) of blood and ask you questions about how you are doing.

Authorization to store your blood for future research?

We would like your permission to store samples of blood taken for future infectious disease studies. If you agree, your blood could be stored for a long time, even if you were to die.

After temporary storage at the local hospital, blood samples will be sent to a repository for long-term storage. Only a unique code will be used to identify your information and blood sample. Blood samples may be provided to researchers at academic institutions, hospitals, national repository and biotechnology/pharmaceutical companies. De-identified (all identifying information has been removed) clinical data may be provided to the researchers requesting blood samples. These researchers may perform analysis of the blood samples you provided.

All blood tests are done only for research purposes. No results of these blood tests will be returned to you. If you decide not to give your permission for long-term storage of your blood samples, you can still participate in this study. We will ask you to indicate whether or not you give your permission at the end of this form.

How may your data and samples be shared?

The National Heart, Lung, and Blood Institute requires your data to be securely stored in a national repository per the NIH Data Sharing Policy (BioLINCC, BioData Catalyst) where it can also be accessed by researchers in a de-identified manner (meaning the researchers will not know that the data or samples came from you). Should you agree to share your samples, these will also be shared in a national repository. For more information, see the following websites.

<https://biolincc.nhlbi.nih.gov/home/>
<https://biodatacatalyst.nhlbi.nih.gov/>

If you agree to long-term storage of blood samples, they may be provided to researchers at academic institutions, hospitals, and biotechnology/pharmaceutical companies. Your biospecimens collected during this study may be used for commercial profit (even if identifiers are removed) and **you will not share in this profit.**

What are the possible risks and discomforts?

Risks of participation include risks related to being given CP or risks of being given placebo, risks related to blood collection, and risks to being involved in research.

Uncommon (1-5% chance) reactions from being given CP that usually are not dangerous:

- Fever
- Chills
- Itching
- Rash or hives
- Headache
- Bruising

Rare (less than a 1% chance) but more serious reactions to being given CP Kidney problems

- Trouble breathing
- Worsening of heart failure
- Allergies and other immune system reactions. Some symptoms of allergic reactions are rash, wheezing and difficulty breathing, dizziness and fainting, swelling around the mouth, throat or eyes, a fast pulse or sweating

Very rare (less than 1 in 1,000,000) but possibly life threatening risks of being given CP:

- Getting an infectious disease like hepatitis or HIV/AIDS or a bacterial infection
- Blood clots
- Lung injury
- Death

Unknown risks of being given CP:

- There may be other unknown risks of CP of which we are not aware. COVID-19 has been reported to affect blood clotting, but we do not know how this changes with CP.

Risks of being given placebo:

If you receive placebo, it will not help you recover from COVID-19. Getting placebo will not affect your symptoms. Your symptoms may improve or get worse just as they would without placebo.”

- Risks from blood collection Blood may be collected from an indwelling tube (IV catheter, intravenous, or in the vein) that is usually placed in participants already as part of standard of care. A rare risk is infection of this IV catheter from sampling (occurs in less than 1% or less than 1 out of 100 participants). If an IV catheter is not available or if necessary for other reasons, blood will be drawn with a needle. This can cause slight discomfort, bruising and infection at the site. Fainting is an infrequent risk from blood drawn by using a needle.

Risks to confidentiality from taking part in research:

- Breach of confidentiality is a rare risk of participation in research studies (fewer than 1 in 10,000).
- If you request it, 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 you look at or store the PDF copy of this consent form on your personal electronic device (PED). These risks increase if the 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.

The researchers have taken steps to minimize these risks. The study team will monitor closely for these possible risks, discontinue CP and treat complications if needed. As with any research study, there may be additional risks that are unknown or unexpected.

What is the possible benefit?

You may or may not benefit from being in this study. However, your participation will help researchers learn if CP is found to prevent mild COVID-19 illness from progressing to severe illness.

What is the alternative to participating in this study?

Taking part is voluntary. The alternative to participating in the trial is usual care. If you decide not to take part in the study, you will still receive usual care. The kind of usual care for COVID-19 illness offered may depend on the treating hospital, opinion of the doctors caring for you, and other medical problems you might have. There may also be other investigational treatments that may be available. Because the response to COVID-19 is evolving so quickly, your study doctor or regular healthcare provider can explain your options to you. There is no penalty for choosing not to take part. You may withdraw from the study at any time, by your choice. Choosing not to take part or choosing to withdraw will not alter the usual care available. Nor does it alter or waive any legal rights or benefits to which you are entitled.

It is important to note that it is possible to stop CP or placebo infusion after it has begun, but continue to remain in the study, by continuing to provide follow-up information. You will be asked if you are willing to continue in the follow-up portion of the study, even if you have stopped the CP or placebo infusion.

What if new information becomes available?

We will provide you in a timely manner with new information that may affect your willingness to continue your part in the study. You may be contacted about future studies available. We may also contact you with periodic updates about the study, and when the study is completed to share the results from this study. You may be contacted about future studies, and it is likely that researchers will want to contact you in order to get information about how you are doing after recovering from this illness (long term follow up).

AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

How will personal information be protected?

The study doctor and his/her collaborators will consider your personal information confidential to the extent permitted by law. "Personal Information" means any information that can be used to identify you, including name or initials, date of birth, gender, ethnic origin and medical and health-related information such as blood tests, diagnostic images and imaging results, the results of physical examinations, medical history and hospital records. We will keep your study information in a secure location during and after the study. Only the members of the study team and the persons and entities listed below will have access to your medical information for this study.

The intervention that you receive as part of this study (convalescent plasma or placebo) may be recorded in your medical record. Your study doctor and clinical care providers will be able to see this information in your medical record.

Your information collected for the study may be stored electronically or on paper. The information stored on the computer is kept in password protected files that are maintained on password protected computers. The information stored on paper is stored in a locked file cabinet in a locked office. Only the members of the study team and the persons and groups listed below will have access to the participants' medical information for this study.

The government agencies responsible for making sure that studies are conducted and handled correctly, and other organizations involved in this research study may look at your study records in order to perform their duties. These include:

- The US Food and Drug Administration (FDA),
- The US Office for Human Research Protections,
- The US National Heart Lung and Blood Institute,
- Researchers from University of Pittsburgh,
- Researchers from Stanford University,
- Representatives from the Strategies to Innovate Emergency Care Clinical Trials Network (SIREN) Clinical Coordinating Center at the University of Michigan,
- Representatives from the Data Coordination Unit at the Medical University of South Carolina,
- The research ethics review board - Advarra IRB (an independent ethics committee that reviewed the ethical aspects of this study to help protect the rights and welfare of study participants),
- And/or other agents of the study who will be bound by the same provisions of confidentiality.

Information from this study will be submitted to the FDA because the study is conducted under an Investigational New Drug Application approved by the FDA.

To help us protect your privacy, this research is covered by a Certificate of Confidentiality from the United States National Institutes of Health. With this Certificate, the study doctors may not disclose research information that may identify you in any United States Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, or be used as evidence, for example, if there is a court subpoena, in the US, unless you have consented for this use. Research information, documents, or blood samples 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), or 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.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the United States FDA. A Certificate of Confidentiality does not prevent you from voluntarily releasing information about themselves or their involvement in this research. If you want research information released to someone, 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.

The study doctor is required by law to protect your health information. By signing and dating this document, you authorize the study doctor to use and disclose your health information, as described in this section, in order to conduct this research study.

You have the right to revoke this authorization, at any time, and can do so by writing to the study doctor at the address on the first page. Even if you revoke the authorization, the study doctor and/or sponsor may still use health information they have collected about you, if necessary for the conduct of the study. However, no new information will be collected.

Your authorization does not have an expiration date unless indicated elsewhere.

You do not have to sign and date this information and consent form, but if you do not, you will not be able to take part in this research study.

Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share the information with others without your permission, if permitted by laws governing them.

Although every effort will be made to maintain confidentiality of your medical and health records, absolute confidentiality cannot be guaranteed. We will use a study number rather than your name on study records where we can. Your name and other facts that might point to you will not appear when we present this study or publish its results. Viewing or storing this electronic informed consent form on a personal electronic device may allow information you provide on this form (such as your name and email address) to be inadvertently shared with others if the device is lost, hacked, or otherwise compromised.

If you are transferred to another facility prior to the end of their participation in this study, your signature and date on this document authorizes the study doctor (principal investigator (PI)), sub-investigator(s), or members of the Executive Committee of this study to access your medical records at the new facility, if necessary.

We will keep any records that we produce private to the extent we are permitted or required to do so by law.

By signing and dating this consent form, you consent to the collection, access, use and disclosure of your information as described above. State law or the enrolling institution may require an additional separate form on which you can authorize sharing of your health information. If so, you will have to sign both forms for your authorization to be valid.

Will you have to pay anything?

There is no cost to participating in the study. Neither you nor your insurer will be charged for the convalescent plasma or its administration, or the blood tests required as part of the study. Charges for all standard medical care will be billed in the same manner regardless of participation. Funds are not available to cover the costs of any ongoing medical care and you remain responsible for the cost of non-research related care. For questions about your medical bill relative to research participation, contact the study doctor listed on this form.

Will you be paid for being in the study?

No. You will not be paid for being in the study. You may be compensated for up to \$25 for your time and travel for the day 15 and day 30 study visits.

What if you are injured as a result of being in this study?

If you are injured or become ill from participating in the study, medical treatment will be available at this institution or elsewhere consistent with the care provided for any medical problem. Payment for this care will be billed the same as any other care for any medical problem. If the hospital at which you were enrolled has any additional answers to this question, this information is found at the bottom of this form.

In the event that you suffer injury as a result of participation in this research study, neither the granting agency (National Heart Lung and Blood Institute), the treating institution, or the researchers plan to offer compensation.

Due to the coronavirus public health crisis, a new public health declaration, called the Public Readiness and Emergency Preparedness Declaration (PREP), was issued by the Department of Health and Human Services on March 10, 2020. This declaration limits the legal rights of a participant in a COVID-19 clinical study that uses a drug, device or vaccine designed to treat, diagnose, cure or prevent COVID-19. This includes the study product, convalescent plasma, used in this study. Subjects using CP in this study will have limits on their right to sue the manufacturers, the study sponsor, healthcare providers and others for significant injuries and adverse reactions.

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.

You still have all of your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages.

Is there anything else I need to know?

Continued participation in this study is entirely voluntary. You may withdraw from the study at any time and for any reason without penalty or loss of any benefits to which they are otherwise entitled. Information and samples collected prior to the withdrawal of your participation will remain in the study. The researcher may discontinue your participation if the study is discontinued or suspended or for other reasons, regardless of your consent.

Doctors caring for you during this emergency department visit may also be researchers in this study. If so, the study doctors are interested both in your medical care and in the conduct of this research. There is no obligation to participate in any research study just because it is offered by one of your treating doctors.

Whom to contact about this study

During the study, if you experience any medical problems, suffer a research-related injury, or if you have questions, concerns or complaints about the study, please contact the study doctor 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 participants. If you have any questions about your rights as a research participant, 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:
Pro00044489.

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

CONSENT STATEMENTS

PARTICIPANT'S CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not give up any of my legal rights by signing and dating this consent document. I will receive a copy of this signed and dated consent document.

May we store your blood samples for use in a future research study to learn more about infectious diseases?

Check here if we may store your blood for future research

Participant's Printed Name

_____/_____/_____ ____:____AM/PM
Participant's Signature Date Time

Study Doctor/Designee Name Title

_____/_____/_____ ____:____AM/PM
Study Doctor/Designee Signature Date Time