INFORMED CONSENT FORM

(FOLLOW-UP ENDING DAY 90)

Sponsor / Study Title:	**University of Minnesota / "An International Multicenter, Adaptive, Randomized Double-Blind, Placebo-Controlled Trial of the Safety, Tolerability and Efficacy of Anti-Coronavirus Hyperimmune Intravenous Immunoglobulin for the Treatment of Adult Hospitalized Patients at Onset of Clinical Progression of COVID-19"**
Protocol Number:	**INSIGHT 013/ITAC**
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 and dating 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.

Key information:

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.

We are asking you to join a research study about COVID-19. It is your choice whether or not you want to join. This form gives you information about the study that will help you make your choice. You can discuss this information with your regular doctor or family or anyone else you would like before you make your choice. Your choice will not affect the care you are getting for COVID-19.

What is the research question?

We are trying to find out if giving anti-coronavirus hyperimmune intravenous immunoglobulin (hIVIG) can help people in the hospital with COVID-19 have fewer bad effects from COVID-19, get better faster, and get out of the hospital faster. Anti-coronavirus hIVIG contains antibodies against the virus that causes COVID-19. We think this will help your body fight COVID-19 better, but we are not sure and so we are doing this study. We are asking you to join the study because you are in the hospital with COVID-19.

What do you have to do if you decide to be in the study?

The study staff at your hospital will make sure it is safe for you to be in the study. They will check your medical history. They will look at routine medical test results that you are probably already having done regularly in the hospital.

If you agree to be in the study, we will randomize you to one of two study groups. It will be up to chance, like flipping a coin, and you will have an equal chance (50/50) of getting either hIVIG or a saline placebo (a salt solution with no active study drug). Your study doctor will not decide which of these you will get, and neither you nor your study doctor or study staff will know what study treatment you are getting. However, your study doctor can find out which group you are in if there is an emergency.

You will get the usual supportive care for COVID-19 recommended by your hospital, just as you would if you do not join the study. In addition, the study will supply an antiviral study drug called remdesivir, unless there is a medical reason that you should not get remdesivir. Remdesivir has been shown in other studies to improve recovery from COVID-19 in persons who have been hospitalized. Remdesivir has an “emergency use authorization” in the US and many other countries. This means that the regulatory authorities are allowing its use while the company that makes it is applying for FDA approval, because there are so few drugs available to treat COVID-19.

You will get the study treatment (hIVIG or placebo) once, on the day you join the study. You will get it by a drip through a tube attached to a needle in your arm (intravenously, or IV). It will take about 1-2 hours, though it may sometimes take longer depending on how your body reacts to the infusion. This infusion together with the use of remdesivir is the only thing in the study that is experimental. Everything else is part of routine medical care for someone in the hospital with COVID-19. There are no treatments for COVID-19 that are approved by the U.S. Food and Drug Administration (FDA), only best supportive care.

You will get remdesivir once a day intravenously (IV) for up to 10 days while you are in the hospital, as part of this study.

You will also need to agree not to participate in any other COVID-19 study for the first 7 days you are in this study.

You will be in the study for 90 days. We will check on your health every day while you are in the hospital, and at regular intervals once you leave the hospital.

We will collect the following information at these times:

Up to 1 day before you get study treatment	**Day 0 (the day you get study treatment)**	**Day 1, Day 2, Day 3, Day 28**	**Day 5 and Day 14**	**Day 7**	**Day 90**
• Informed consent • Blood tests to check your health • Check to see how you are feeling • Pregnancy test • Your medical history	• Infusion of study treatment • If you are taking certain other medicines • Blood for future research (18 mL, about 2 tablespoons) • Nasal swab for future research	• How you are feeling • Blood for future research (18 mL, about 2 tablespoons)	• How you are feeling	• How you are feeling • If you are taking certain other medicines • Blood tests to check your health • Blood for future research (18 mL, about 2 tablespoons)	• Blood for future research (18 mL, about 2 tablespoons)

Day 90 is the last day you will be in the study.

We may need to get some information from your medical record. By signing and dating this consent, you also agree to let us get information for this study from your medical record. You will be asked to sign a separate HIPAA form for this purpose as well.

We will send the information we collect to the University of Minnesota (UMN) in the US where it will be stored and analyzed. In this information, only a code number, your year of birth, and a 3-letter code that you or the study staff chooses will be used on your information. We never give information that could identify you, such as your name, address, birth date, or medical record number, to anyone outside this site. The study staff at this site is responsible for keeping your identifying information safe from anyone who should not see it. We will send the blood samples to a laboratory in the US for storage. We will keep them for as long as we have the funding and space to do so, which we hope will be many years. We will use the samples in the future for tests to help understand more about COVID-19 and how people respond to treatment for COVID-19. You and your regular doctor will not get any results from these tests. We will not test your DNA (your genes). We will not sell your samples and they will not be used for research aimed at making money (commercial research). The samples will not have any information connected to them that could identify you.

Why would you want to be in the study?

If you get the hIVIG, it may help you get better faster, although we do not know that for sure.

It is important to remember that half (50%) of the people in this study will not get the hIVIG.

By being in this study, you help study doctors learn more about how to treat COVID-19 in people in the hospital. Because so many people are getting hospitalized with COVID-19, this could be a big impact if a treatment proves to be effective.

Why would you NOT want to be in the study?

Only half (50%) of the people in this study will get the hIVIG. You may not get the hIVIG. If hIVIG turns out to be a good study treatment, you would not get that benefit. It's also possible that if you do get hIVIG, it may turn out not to be useful, or may cause side effects that are harmful to you.

You do not have to be in this study to receive treatment for COVID-19. You will continue to receive the usual supportive care for COVID-19 recommended by your hospital. Your other options include other experimental treatments. Your study doctor or regular healthcare provider can explain your options and their risks and benefits to you.

What are the side effects of the study hIVIG treatment?

hIVIG is usually very safe to give. Similar immunoglobulin preparations have been used in many different diseases over many years, but immunoglobulin prepared solely from individuals who have recovered from COVID-19 has not been studied before. In an earlier study of influenza hIVIG in people in the hospital with the flu, over 150 people got hIVIG. There were no serious problems that occurred in people because they got hIVIG.

All treatments cause side effects, and you may have some side effects from hIVIG. About 1% to 10% (1 in 100 people to 1 in 10 people) who get hIVIG get:

- A fever
- Chills
- Nausea
- Vomiting
- Dizziness
- Shortness of breath
- Rash
- Hives
- Headache

These side effects are usually not serious. These can happen during the infusion or afterwards and usually go away on their own or with short-term treatment. Although IVIG has been very safe for people with other diseases, less than 0.1% (less than 1 in

1,000) of people taking other types of IVIG for other illnesses have had very serious reactions to it, including a kind of lung injury called transfusion-related acute lung injury (TRALI).

People can have allergic reactions to drugs, including hives, trouble breathing, or other allergic responses. This is very rare but is also a possible effect of any drug. Allergic reactions may be severe or life-threatening.

In some laboratory studies, infusions of antibodies have made infections with viruses similar to the virus that causes COVID-19 worse. This is a very unlikely but possible side effect of the study treatment infusion in this study, and you will be closely monitored for any signs of this effect.

It is also possible that getting the study treatment infusions could cause problems with your health because of the amount of fluid given to you for the study treatment if you have some other health condition that affects how your body handles fluids. You will get up to about 400 mL of fluid for hIVIG or placebo, and about 100mL each day for remdesivir if you receive it.

Some people may have some side effects after the hIVIG infusions. Other people may have no side effects. You will be monitored closely during the infusions, and short-term medical care will be provided if there are side effects from the infusions that can be treated.

<u>What are the benefits and risks or side effects of remdesivir treatment?</u>

Remdesivir was recently shown to help people who are in the hospital with COVID-19 to get better faster than people who got a placebo. You may be given remdesivir to treat your COVID-19 even if you do not join this study if your regular doctor feels it is a good idea. If your study doctor considers that remdesivir is not a suitable study treatment for you, you can still join this study, and you will receive hIVIG or placebo without remdesivir. For example, remdesivir might be unsuitable for you if you have serious liver or kidney problems or an allergy to it.

The most common side effects of remdesivir include:

- Abnormal liver function test results
- Abnormal kidney function test results
- Fever
- Elevated blood sugar
- Constipation
- Nausea
- Vomiting
- Decreased appetite
- Headache

The abnormal liver and kidney function tests may last a few days or longer but came back to normal levels over time.

People can have allergic reactions to drugs, including hives, trouble breathing, or other allergic responses. This is very rare but is also a possible effect of any drug. Allergic reactions may be severe or life-threatening.

Some people may have some side effects after the infusion of remdesivir. Other people may have no side effects. You will be monitored closely during the infusions, and short-term medical care will be provided if there are side effects from the infusions that can be treated.

What are the side effects of the other study procedures?

As shown in the table of what will happen at each visit, you will have some extra blood drawn for laboratory testing and storage. You will also have an extra swab of your nose and throat that would not be done if you are not in the study. The risks and discomforts of these extra blood draws and swab are no different than what you would have if they were performed as part of your regular hospital care for COVID-19.

You may have pain or bruising at the site where the blood is drawn or the IV is inserted. You may feel faint. An infection at the site of the blood draw or IV insertion is possible.

The nose and throat swabs may cause discomfort, eyes watering, sneezing, or bleeding.

What if you are pregnant or breastfeeding?

If you are pregnant or breastfeeding, you can still join this study. However, we do not have any information about how the study drug may affect your baby. The risks to an unborn baby or a pregnant woman may possibly be serious. Please take this into account as you make your decision about whether to join this study.

Additional information:

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

Here is some additional information about the study that may help you make your choice about whether you want to be in the study.

The US National Institutes of Health (NIH), an agency of the US Federal Government, is paying for this study. Because public money is paying for the study, we are required to comply with all rules and regulations about research. We are doing this study according to internationally recognized standards of research as well as the laws of each country where the study is taking place.

This study is taking place in several countries. We expect to enroll about 500 people around the world.

You do not have to join this research study if you do not want to. If you choose to join the study, you can stop at any time by telling someone on the study team that you want to stop being in the study. If you choose not to join or to stop, your regular medical care will not change.

If we get any new information that might change whether you want to join or stay in the study, we will tell you right away.

Your study participation may be stopped without your consent if:

- The groups overseeing the study decide the study should be stopped;
- Your study team believes that being in the study is no longer in your best interests.

If your participation is stopped, you will still get the usual care given at your hospital for COVID-19.

If you do not want to be in this study, you will still get the usual care to treat COVID-19. However, you cannot get the hIVIG study treatment, because it is experimental.

What are the costs to you?

We will give you the study treatment (hIVIG or placebo) at no cost. We will also give you remdesivir at no cost. We will pay for all clinic visits, lab work, and other tests that are part of this study.

You, your insurance company, or some other third-party payer must pay for all other medicines and hospital costs, including other standard of care treatments for COVID-19.

Will you be paid to be in the study?

«Compensation»

We will compensate you for your time and inconvenience participating in the study. *[Specific details to be completed by site.]*

What if you are hurt as part of this study?

If you are hurt because of being in this study, the study site will treat your injury right away. You or your insurance will have to pay for this treatment. The study cannot pay you or pay for any care for study-related injuries or for your illness. By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

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 participating 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 Anti-Coronavirus Hyperimmune Intravenous Immunoglobulin (hIVIG) and Remdesivir used in this study. Participants using hIVIG and Remdesivir 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.

What happens to the blood samples and respiratory swabs?

We will send the blood and respiratory swab samples to a central laboratory in the United States of America. You and your study doctor will **not** get the results of any tests done on these samples.

The blood samples will measure how many COVID-19 antibodies are in your blood. This will tell us how your immune system responded to your COVID-19. The nasal swab will measure how much virus you have in your respiratory system.

Any blood samples that are left over after these tests will be stored at the central laboratory for as long as we are able to keep them. We hope to use these in the future to answer other questions about COVID-19. You and your study doctor will **not** get any results from these tests. Some of the blood will also be given to the company that made the hIVIG to help them learn more about its effects.

You can withdraw your consent for us to keep these specimens at any time. Let your study team know if you do not want the study to keep your specimens anymore, and every effort will be made to destroy all of your specimens that are still at the central laboratory.

How do we protect your privacy?

We will take every reasonable step to keep your health information private and to keep anyone from misusing it.

Your information (data) and samples will not be identified by name, or in any other way, in anything published about this study.

We will do everything we can to keep your personal information private, but we cannot guarantee that nobody will get it. We may have to release your personal information if required by law.

These people may see your medical and research information at your site:

- Advarra Institutional Review Board (Advarra IRB)
- The sponsor, other study research staff, and study monitors
- US and other participating countries' health regulatory agencies, including the US FDA
- The US National Institutes of Health (NIH) which is funding the study

They are committed to protecting your privacy.

As the research staff at the study site, we are required to make sure that people not involved with this study cannot see your research and medical information. We will keep your research files in a safe place and will handle your personal information very carefully.

Your study data are sent electronically to the UMN in the US through a secure application. By signing and dating this consent, you agree to have your data sent to UMN. No information that could directly identify you is sent to UMN. This is called "pseudonymized data." Access to the data at UMN is limited through security measures, and no data breach or unauthorized access has ever occurred in this system. After the study is over, the data will be stored securely for the period required by law.

Your study data will be shared with the US National Institutes of Health (which is paying for this study), and with the regulatory authorities that oversee the studies, including the US FDA, as required by law. Your study data will also be shared with the drug company that provides the hIVIG to help them develop the study drug.

UMN may share your data and specimens with other people who study COVID-19. UMN will remove any information that could possibly be used to identify you before sharing. This is called "anonymizing the data." We will not ask you for additional consent for this sharing. UMN will only share data and specimens for research projects that are approved by the group that is conducting this study.

This study has a Certificate of Confidentiality from the US Federal government. This means that UMN cannot share any data it has about you with national, state, or local civil, criminal, administrative, legislative, or other authorities unless you specifically allow us to share it, or it is being 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 participants.

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.

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 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.

Information on this study will also be posted in a similar format on a European Web site at www.clinicaltrialsregister.eu

To do this research, we will collect and use your personal data, as described above and in any HIPAA Authorization Form we have given you. Please tell us whether you agree to have us collect and use your personal data by placing your initials in front of your selection.

____**Yes**, I agree to the collection and processing of my personal data.

____**No**, I do not agree to the collection and processing of my personal data.

It is your choice whether you allow us to collect and use your data. However, you will not be able to be in this research and have a chance to get the experimental treatment if we cannot collect and use your data.

Whom to contact about this study

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 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: Pro00046242.

SIGNATURE PAGE FOR CONSENT TO PARTICIPATE IN THE RESEARCH STUDY

I have read the consent or have had it explained to me. I am satisfied that I understand the information. By signing and dating this consent, I am stating that I want to join this study. I understand that I do not waive any of my legal rights as a study participant by signing and dating this consent. I understand that I will receive a copy of the signed and dated consent.

If you agree to be in this study, please sign and date below.

_____ Date: _____

Signature of participant

_____

Printed name of participant

_____ Date: _____

Signature of study doctor/designee

_____

Printed name of study doctor/designee

FOR ADULTS NOT CAPABLE of GIVING CONSENT

_____ Date: _____

Signature of Legally Authorized Representative (LAR)

_____

Printed name of Legally Authorized Representative (LAR)

_____

Relationship of Legally Authorized Representative (LAR) to Participant

(Indicate why the LAR is authorized to act as a surrogate health care decision-maker under state or applicable local law)

Witness to Consent Interview

On the date given next to my signature, I witnessed the consent interview for the research study named above in this document. I attest that the information in this consent form was explained to the participant, and the participant indicated that his/her questions and concerns were adequately addressed.

_____ Date: _____

Signature of witness

_____

Printed name of witness

NOTE: This consent form, with the original signatures, MUST be retained on file by the Investigator of Record. A copy of the signed and dated consent must be given to the participant. A copy should be placed in the participant's medical record, if applicable.