	INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY (HFH IRB form rev: 6/6/2019)	DATE: MRN: NAME:
APPROVAL PERIOD Apr 07, 2020 – Apr 05, 2021 INSTITUTIONAL REVIEW BOARD	**PROJECT TITLE:** **WHIP Covid-19 Study: Will Hydroxychloroquine Impede or Prevent COVID-19**	

Principal Investigator (PI): **Dr. William O'Neill, MD**
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Sponsor: **Henry Ford Health System**

1. INTRODUCTION

You are being asked to participate in a research study. The box below highlights key information about this research for you to consider when making a decision whether or not to participate. More detailed information is provided after the box. No research activity is to be conducted until you have had an opportunity to review this consent form, ask any questions you may have, and sign this document.

Key Information for You to Consider
Voluntary Consent. You are being asked to participate in a research study. Participation is voluntary. There will be no penalty or loss of benefits if you choose not to participate or discontinue participation. **Purpose**. The Purpose of this research study is to determine whether or not the medication hydroxychloroquine has a preventive effect against infection from COVID-19 virus in healthcare workers, first responders and public transportation workers who may have been exposed to COVID-19**.** **Duration**. It is expected that your participation will last up to 8 weeks. **Procedures and Activities**. You will be asked to come to a study visit in person 3 times, once to start, at 4 weeks, and at 8 weeks. At the first (baseline) and 4 week visits, you will receive study medication, have a blood draw, and fill out surveys. At week 8 (final

visit), you will only have a blood draw and fill out surveys. At weeks 1, 2, 3, 5, 6, and 7 you will be contacted by phone to see how you have been feeling.

Risks. Some of the foreseeable likely risks or discomforts of your participation include slight pain, discomfort, and possibility of bleeding or bruising at the needle insertion site during blood draw, dizziness, fatigue, ringing in the ears, headaches, or irritability. More detailed information can be found in the "*What Are The Risks, Discomforts, And Inconveniences Of The Study?*" section in the Consent Form.

Benefits. You may not directly benefit from this research. However, the information learned from your participation may help others in future.

Alternatives. Participation is voluntary and the only alternative is to not take part in this research study.

2. DISCLOSURE OF POTENTIAL CONFLICT OF INTEREST

The Henry Ford Health System (HFHS) investigator(s) on this study are also healthcare providers. They are interested in the knowledge to be gained from this study and are interested in your well-being. The investigators have no financial conflicts of interest to disclose.

3. WHY IS THIS RESEARCH BEING DONE?

You have been asked to take part in a research study because you are a healthcare worker, first responder or public transportation worker, who may be at increased risk of becoming infected with COVID-19.

The purpose of this research study is to demonstrate whether the use of hydroxychloroquine can prevent SARS-CoV-2 infection causing COVID-19 disease.

A total of approximately 3,000 people will be enrolled with Henry Ford Health System (HFHS).

As part of this study, you will receive hydroxychloroquine medication or placebo (a pill that looks like the medication but does not contain any medication or other active ingredients). This drug is not approved by the FDA (U.S. Food and Drug Administration) for this purpose. However, this medication is approved by the FDA for treatment of malaria, lupus, and rheumatoid arthritis and has been used for these purposes in millions of people.

The purpose of this Phase IV study is to determine if there is another purpose for this marketed medication.

4. WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

If you agree to take part in this study, your participation will last a total of 8 weeks. As part of this study, you will have 3 study visits in person at one of the Henry Ford Health System hospitals, and 6 follow up phone calls.

Before you begin the study, you will have the study reviewed with you by study staff, you will read through this consent form, and you will have the opportunity to ask any questions about the study. If you wish to continue in the study you will sign this consent form. Then you will complete 3 surveys about your demographics (items like your age, sex, race, etc.), health, and symptoms. It is important that you inform the study personal about all medications you are currently taking. These includes over the counter medications such as Tylenol or herbal supplements. This will assure that it is safe for you to take part in this research project. Your body temperature will be taken with a thermometer and recorded. A temperature higher than 100.4 degrees Fahrenheit will exclude your participation. These will be reviewed by a study doctor. Your survey responses should be accurate to the best of your knowledge. Based on your answers you will be told if you are eligible to continue the study. If yes, you will then have a blood draw (total amount of blood from all study visits combined will be about 150 milliliters (mL), or 30 teaspoons), be randomized (what this is and how it happens is explained below) and then receive the study medication and be told how to take the medication for the next 4 weeks.

A study staff person will call you weekly at weeks 1, 2, 3, 5, 6 and 7. You will come to the study clinic during week 4 for a blood draw, symptom assessment and to receive your next 4 week medication supply. You must bring back any unused medication at this visit. You must not save any of the pills or give any of the pills to another person to take. At week 8 you will repeat the week 4 clinic visit. Below is a summary of the procedures of this study.

During the study, at first visit (baseline), you will have the following procedures:
• Review and Sign Informed Consent Form. Complete a Medical History Survey, Demographic Survey, Symptom Survey. Have a Blood Draw (about 50 mL or 10 teaspoons) and receive a 4 week supply of Study medication (30-45 min)
During the study, at visit weeks 1, 2, 3, 5, 6, 7, you will have the following procedures:
• Receive a phone call to see how you have been feeling and report how much study medication you have left (pill count) (10 min)
During the study, at visit week 4, you will have the following procedures:
• Status update and symptom survey, blood draw (about 50 mL or 10 teaspoons), return any unused study medication and receive 4 week supply of study medication (15-20 min)
During the study, at visit week 8, you will have the following procedures:
• Status update and symptom survey, blood draw (about 50 mL or 10 teaspoons), return any unused study medication (15-20 min)

For some research studies, including the one you are being asked to join, you will be given the results of certain tests. The blood samples collected may not be able to provide results immediately. The study investigators will provide these results to you once they are available. At this time we are not sure how long this will take. The COVID-19 study testing results are non-diagnostic of active infection. Rather, study testing will only determine positive past exposure to the COVID-19 virus (a carrier of the virus). If you have a positive COVID-19 test during the study (positive past exposure), **OR** have symptoms of COVID-19 infection (cough, fever, tiredness, difficulty breathing), you will be referred to your healthcare provider or employee health department for additional testing and treatment as recommended by your employer guidelines. If you have a positive COVID-19 test during the study **AND** have symptoms of COVID-19 infection, then you will stop taking study drug and be referred to your healthcare provider or employee health department for additional testing and treatment as recommended by your employer guidelines. If you test positive for COVID-19 disease through your local employer guidelines, then you will stop taking study medication because it will no longer be necessary to try to prevent COVID-19 and your healthcare provider will guide treatment for COVID-19. You will have a final follow up phone call and visit for blood draw if able (when recovered and no longer quarantined). You will also return any unused study medication at that final visit.

Your study blood samples and data will be collected and stored within the Henry Ford Translational and Clinical Research Centers bank.

THIS IS A RANDOMIZED AND BLINDED STUDY: There will be 3 randomized groups to this study and one non-randomized comparative group. You will be randomized into one of the study groups described below. Randomization means that the group you are assigned to will be chosen by chance (like a roll of a dice). A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have a one in three chance of being placed in any group, and a 2 in 3 chance of receiving the study drug.

> If you are in group 1, you will take 400 mg of hydroxychloroquine by mouth once weekly, and placebo pills that look like hydroxychloroquine, but has no hydroxychloroquine in it, on the other 6 days for 8 weeks.

If you are in group 2, you will take 400mg of hydroxychloroquine by mouth on the first day (baseline visit), and then take 200mg of hydroxychloroquine once daily for 8 weeks.

If you are in group 3, you will only take placebo pills that look like hydroxychloroquine, but has no hydroxychloroquine in it.

Because all of the pills will look the same you will not know which of the groups you are in. The study staff you see will not know this either. This is an important part of this study design to truly see if the study drug will prevent COVID-19 infection. You may not split the pills to try to make them last longer or give them to anyone else. If you stop taking study drug for any reason you will need to return unused pills. After the study is completed you will be told which study group you were in.

If you are already taking hydroxychloroquine prior to study enrollment for an indicated medical condition, you will be in the non-randomized comparator group. You will not receive study medication and should continue to follow prescribed regimen by your doctor. All procedures including the study visits at 4 and 8 weeks (surveys, blood draws) along with the phone calls will be performed similar to the randomized groups

You must inform the study staff immediately if you will start any new medications while participating in the study to ensure no drug interactions occur with the study drug. These includes over the counter medications such as Tylenol or herbal supplements. This will help to ensure assure that it is safe for you to take part in this research project.

5. WHAT ARE THE RISKS, DISCOMFORTS, OR INCONVENIENCES OF THE STUDY?

While you are in the study, you are at risk for the following side effects:

Likely– may happen in up to 10% or more of those taking the drug
• Vertigo (dizziness),

- Tinnitus (ringing in the ears),
- fatigue,
- headaches,
- irritability

Less Likely

- nausea,
- vomiting (throwing up),
- decreased appetite,
- fainting during blood draw

Rare but Serious -only likely to happen in fewer than 1% of those who take the study drug

- drug allergic reactions such as, rapid swelling beneath the skin, difficulty breathing, skin rash, skin itching, skin discoloration, hair color changes, hair loss, skin eruptions with blood, lymphatic, and internal organ involvement, sensitivity to light, and redness and peeling of the skin. Skin rash with blisters, whole body skin and mucous membrane rash, and severe whole body skin and mucous membrane rash have also been reported,
- cardiac arrythmias with risk of death (heart-beat abnormalities and palpitations that could lead to death),
- hypoglycemia with concomitant hypoglycemic medications (low blood sugar, especially when taking medications to control your blood sugar),
- visual changes (effects on your eyesight),
- retinal disease (effects on part of the eye that changes the light it receives to nerve signals)
- white blood cell count reduction (lower counts of blood cells that help fight infections)

The researchers will try to minimize these risks by carefully screening participants for reasons that it may not be safe to take the study drug. Study participants will be monitored by research staff for any

bad reactions to the study medication during the weekly calls. If you believe you are having a reaction to the study drug you may call the study staff at 313-574-2651 to discuss. If you are having a serious drug reaction or if you believe you may be COVID-19 infected, you should immediately seek medical attention.

If you begin taking any new drugs during this study, it is very important that you should immediately inform the study staff. Some drugs should not be taken with the study drug.

You may not split the pills to try to make them last longer or give them to anyone else. Splitting pills may leave a powder residue and could be inadvertently ingested by children and other people for whom it is not safe, or pets.

There may be additional risks or discomforts that are not known at this time. Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study. If you are currently in another study, took part in one recently, or if you consider another study in the future, please inform the research staff right away.

There could be risks to you or your unborn child that the investigators cannot predict. Because of this, you cannot be in this study if you are pregnant, breast feeding a child, or trying to become pregnant. You must use at least 2 forms of effective birth control measures, such as birth control pill or medications, condoms, vasectomy of partner or hysterectomy. If you become pregnant while enrolled in the study the study drug may have a risk to the pregnancy and unborn child. If you become pregnant while taking the study medication and within 28 days following the last dose of the study medication you must inform the research team.

BREACH OF CONFIDENTIALITY RISK: Additional risks include a potential breach of confidentiality of your personal information. The measures taken to protect your personal information and any possible disclosure are described in the section below titled "*How will my personal information be protected*?"

BLOOD DRAW RISK: Blood samples will be obtained from your veins. Possible side effects of obtaining blood samples are pain, bruising, bleeding, or infection at the blood draw site. Occasionally nausea, lightheadedness or fainting may occur. This study will follow all standard blood draw techniques to minimize these risks.

6. WHAT ARE THE BENEFITS TO TAKING PART IN THE STUDY?

You may not directly benefit from this research; however, we hope that others are helped in the future by what is learned.

The purpose of this research study is to demonstrate whether the use of hydroxychloroquine can prevent SARS-CoV-2 infection which causes COVID-19 disease.

Research using your data and biospecimens (including de-identified samples) can lead to new discoveries, such as new tests, drugs, or devices. Your biospecimens may be used for commercial profit, however, you will not have rights to these discoveries or any proceeds from them. Your study blood samples and data will be collected and stored within the Henry Ford Translational and Clinical Research Centers bank.

7. WHAT OTHER OPTIONS ARE THERE AND WHAT ARE MY ALTERNATIVES?

Participation is voluntary. The only alternative is to not take part in this research study.

8. HOW WILL MY PERSONAL INFORMATION BE PROTECTED?

Research records will not include names, registration numbers, or other information that is likely to allow someone other than the researchers to link the information to you. The researchers will label research records with a unique code and keep any master key that links your name and data and/or specimens in a separate location. The researchers will maintain all study records (including any codes) in a locked, secure location. Your research information will not be made a part of your regular

medical record. If the researcher orders any tests, the order and results may become part of your regular medical record. All electronic files containing identifiable information will be password protected and only the members of the research staff will have access to the passwords. If researchers share your data and/or specimens with others, the information will be coded as described above to help protect your identity. At the conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and you will not be identified in any publications or presentations. The researchers will maintain any data described in this paragraph in accordance with the security provisions of this paragraph until destroyed by the researchers. Records will be kept up to 5 years on site.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without your additional informed consent.

You should also know that the HFHS Institutional Review Board (IRB) and IRB Administration Office may inspect study records as part of its auditing program, but these reviews only focus on the researchers. The IRB is a group of people who review research studies to protect the rights and welfare of research participants.

To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be submitted to the FDA. It may be submitted to governmental agencies in other countries where the study drug may be considered for approval. Medical records, which identify you and the consent form signed by you, will be looked at by the FDA and other regulatory agencies.

9. WHAT IF I GET SICK OR I AM INJURED?

There is no federal, state, or other program that will compensate you or pay for your medical care if you are injured as a result of participating in this study. You and/or your medical insurance may have to pay for your medical care if you are injured as a result of participating in this study.

By signing this consent form, you do not give up any of your legal rights in the event of an injury.

10. WHO DO I CONTACT WITH QUESTIONS ABOUT THE STUDY OR TO REPORT AN INJURY?

Dr. William W. O'Neill, MD or his staff member has explained this research study and has offered to answer any questions. If you have any additional questions about the study procedures, or to report an injury you may contact Dr. O'Neill, MD by phone at 313-574-2651 or by email at WHIPCOVID19@hfhs.org. Medical treatment is available to you in case of an injury.

If you would like to discuss your rights as a research participant, discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research, you may contact the Henry Ford Health System IRB Administration Office by phone at (313) 874-4464 or by email at research_admin@hfhs.org. The IRB is a group of people who review the research to protect your rights.

A description of this clinical trial will be available on 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.

11. DO I HAVE TO PARTICIPATE IN THIS STUDY?

You do not have to be in this study if you do not want to. If you agree to be in the study, but later change your mind, you may drop out at any time. Inform the research staff/study doctor if you are thinking about stopping or decide to stop. There are no penalties or loss of benefits to which you are otherwise entitled if you decide that you do not want to participate. Your decision to participate, withdraw your participation, or decline to participate will have no impact on any aspect of your employment at Henry Ford Hospital.

If this happens, you may be asked to return for a visit for safety reasons. You will get the same medical care from HFHS whether or not you participate in this study. You will be told about any significant information that is discovered that could reasonably affect your willingness to continue

being in the study. You will be notified of all significant new findings during the course of the study that may affect your willingness to continue.

12. WHO ELSE CAN STOP MY PARTICIPATION?

The principal investigator, sponsor, or your doctor can end your participation in the research study at any time. If this happens, you will be asked to return for a visit for safety reasons.

13. WILL IT COST ANYTHING TO PARTICIPATE?

Taking part in this study may lead to added costs to you or your insurance company. Items related to your routine medical care will not be covered. If your insurance company is billed, you may be responsible for payment of any deductibles, coinsurances and co-payments required by your insurer. Additional costs may include: Transportation costs, and parking. You have the right to ask what it will cost you to take part in this study. If you have any questions about the costs of this study, please ask the study doctor, a member of the study staff, and/or your health care provider.

14. WILL I BE PAID TO PARTICIPATE?

There is no compensation available to you for your participation in this study.

DOCUMENTATION OF CONSENT

By signing this form, I agree that I have read and understand this form and that I agree to participate in the research project described above. I have been given enough time and opportunity to ask about

the details of the research study and to decide whether or not to participate. Its general purposes, the particulars of my involvement and possible risks and inconveniences have been explained to my satisfaction. I understand that I can withdraw at any time without giving any reason without my medical care or legal rights being affected. My signature also indicates that I have received a copy of this consent form.

The researchers in this study might want to ask you to participate in additional studies. In some cases, you might be a good candidate for a particular study because of your health history information.

I am willing to be contacted for future research studies. Please initial below.

_____ I agree

_____ I refuse

_____	_____	_____
Signature of Subject	Date	Time

_____

Printed Name of Subject

_____	_____	_____
Signature of Person Obtaining Consent	Date	Time

_____

Printed Name of Person Obtaining Consent