Outcomes Related to COVID-19 Treated with Hydroxychloroquine among In-patients with Symptomatic Disease

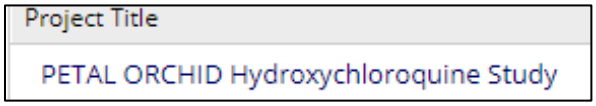
Standardized Operating Procedures

Contents

Screening

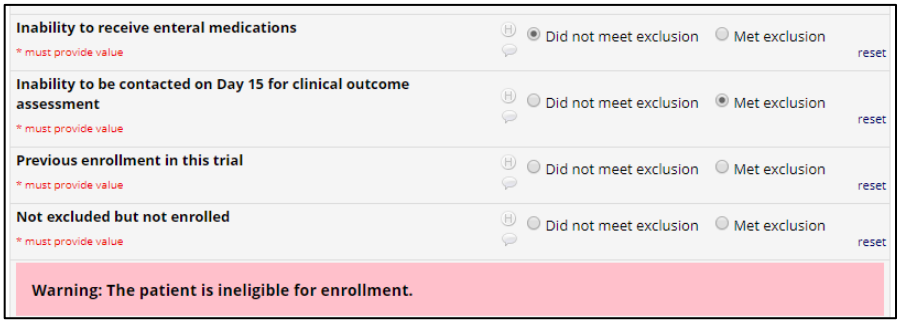
1. Identify a patient with known or suspected COVID-19

2. INCLUSION CRITERIA - Determine whether the patient meets inclusion criteria
    a. If patient does not meet inclusion criteria, do not record as a "screen fail"
    b. If patient meets inclusion criteria, retrieve previously assigned PETAL ID or generate new PETAL ID
    c. Open "PETAL ORCHID Hydroxychloroquine Study" database in REDCap



    d. Select "Add new record"
        i. select "Eligibility Criteria" CRF
            1. Enter PETAL ID, month of screening, year of screening
            2. Select that patient "Met inclusion"

3. EXCLUSION CRITIERA - Determine whether patient meets exclusion criteria
    a. If patient meets an exclusion criterion, select "Met exclusion", which records patient as a "Screen Fail" → Complete form, save, and exit



    b. If patient does not meet any exclusion criteria, select "Did not meet exclusion" for all exclusion criteria

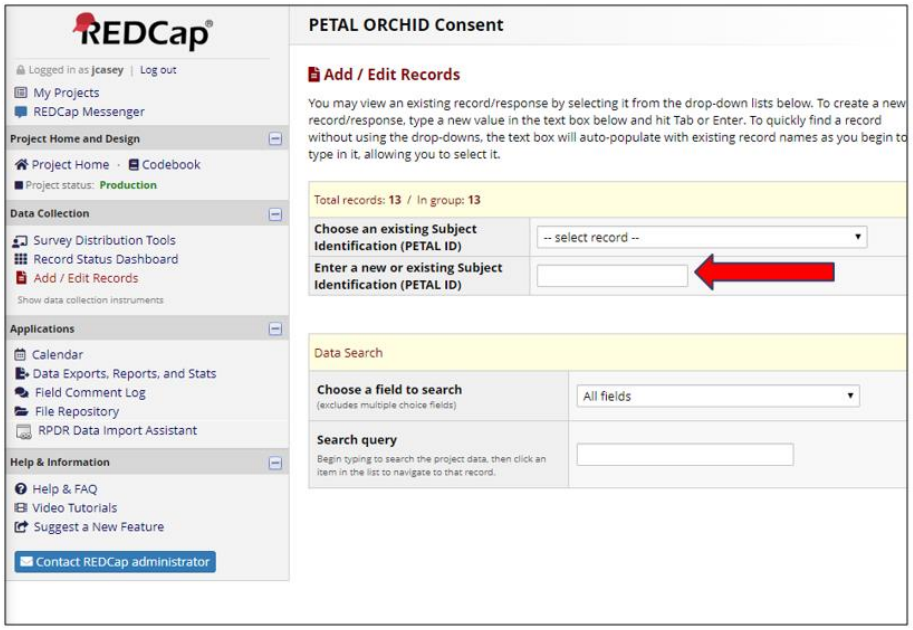
4. COMMUNICATION - For a patient who meets all inclusion criteria and no exclusion criteria, consult with the treating clinicians to provide permission to approach the patient or LAR for informed consent discussion
    a. If treating clinicians decline → record as "No"
    b. If treating clinicians provide permission → record as "Yes"

Informed Consent

1. CREATING RECORD IN CONSENT DATABASE
    a. Open the "PETAL ORCHID Consent" REDCap database

    PETAL ORCHID Consent

    b. Select "Add/Edit Records" to create a new record using the patient's **PETAL ID**



2. ENTER "PARTICIPANT INFORMATION"
    a. Select "Participant Information" and enter PETAL site, date, patient's name and date of birth, and medical record number (plus LAR information, if applicable)
        **Step required to connect to correct consent form in E-Consent*

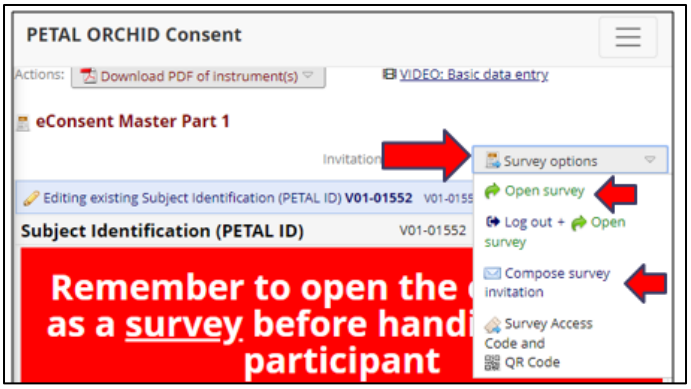
3. OBTAIN CONSENT USING **ONE OF TWO APPROVED OPTIONS**:
    a. Electronic approach (**"E-Consent"**) **REDCap version developed by coordinating center but not required*
        i. Electronic version of consent opened on study device or sent as link to subject / LAR
        ii. Consent discussion (in-person or by (video)phone), electronic signature
        iii. Patient/LAR receives electronic copy of consent
    b. Paper approach (**"Scanned Consent"**)
        i. Paper consent delivered to bedside or sent by email (if sent by email, LAR must have access to printer)
        ii. Consent discussion, patient/LAR signs paper consent
        iii. Photo of consent signature page uploaded to REDCAP or emailed with encryption
        iv. Paper consent remains with patient

****Both E-Consent and Scanned Consent can be completed in-person or remotely, and both processes can be used on either a study device or a participant device***

Option #1 for Consent: **"E-CONSENT"**

c. For English Consent, Open **"eConsent Master Part 1"**; for non-English consents open appropriate "Short Form (if available)"

d. Select "**Survey Options**"

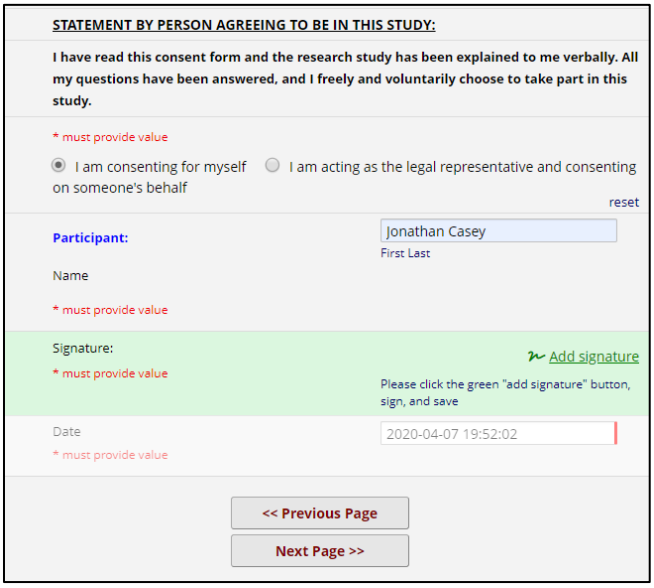


i. If consenting using a study device, click ""**Open Survey**."

ii. If consenting using a patient/LAR device, Click "**Compose Survey Invitation**" which allows the survey to be sent as an email to the participant/LAR

e. Review consent with patient/LAR

f. Patient/LAR electronically signs consent



g. Consent is locked and stored as a PDF in REDCap

h. A local copy of signature page ("eConsent Part 2" for English Consent) should be printed for local records or archived in an electronic database outside of REDCap ***prior to randomization*** (instructions below)

i. Patient/LAR must receive copy of consent (this does not occur automatically, even if survey was sent by email to patient/LAR)

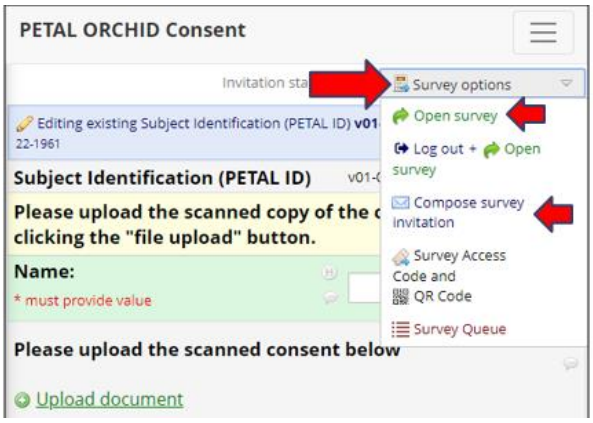
i. If using own, device, patient/LAR may download when completing survey

ii. Or, signed copy can be delivered by encrypted email to patient/LAR

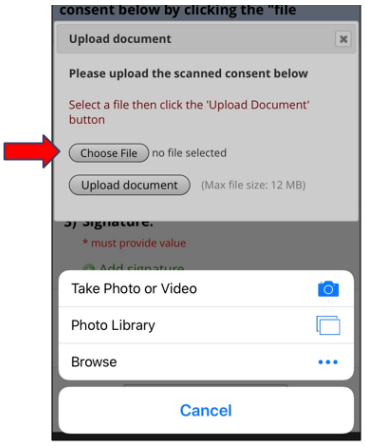
iii. Or, if consenting a patient on a hospital device, it is acceptable to leave an unsigned paper copy of consent

Option #2 for Consent: **"SCANNED CONSENT"**

j. Paper consent is brought to the bedside or delivered to the LAR by email/fax
k. Consent is reviewed and patient/LAR signs paper consent
l. A photograph of the signature page is taken using either the patient/LAR device or a study device approved to store PHI (photo may be taken directly or through the window or glass door leading into the patient's room)
m. The signature page is uploaded to REDCap using a survey in "Signed Consent" form, which contains an upload link. To start, open the "Scanned Consent" form
    i. Select "**Survey Options**"



    ii. If photo is being uploaded using a study device, click ""**Open Survey**."
    iii. If photo is being uploaded using patient/LAR device, this survey can be sent by email by clicking "**Compose Survey Invitation.**" Patient/LAR will receive link to a survey that allows photo upload
n. Photo is uploaded using survey tool by selecting "Upload Document," followed by "Choose file," and then selecting the signature page

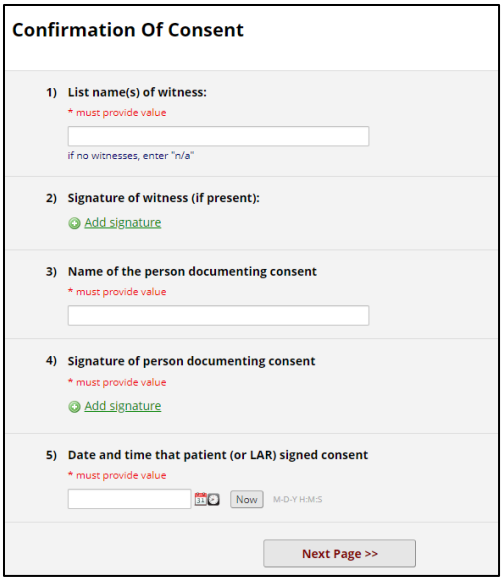


o. The person uploading the consent picture (study staff/patient/LAR) provides name, electronically signs form, and submits
p. PDF including picture of signature page is locked and stored in REDCap
q. A local copy of signature page ("eConsent Part 2" for English Consent) should be printed for local records or archived in an electronic database outside of REDCap ***prior to randomization*** (instructions below)
r. Patient/LAR retains signed paper copy of consent
s. If photo, was taken on study device, it should be deleted after upload to REDCap

Confirmation of Consent

**Regardless of type of consent pursued, investigator and witness must also provide signatures to affirm that informed consent was provided. These signatures must be in a different form than the consent which may be completed remotely*

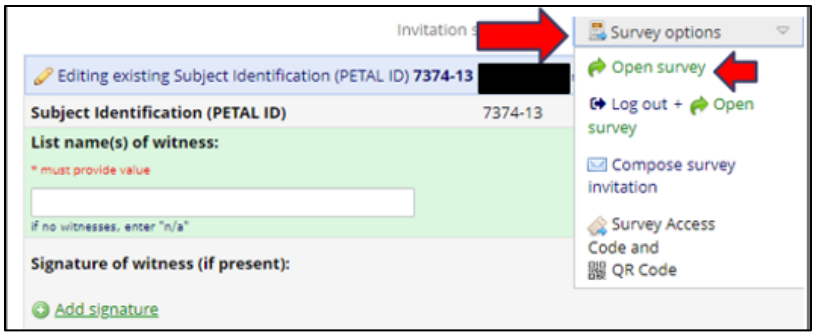
t. Open "Confirmation of Consent"



u. Research staff provide names, electronic signature, and date/time. Research staff also documents whether a translator was used and, if so, records translator identity (name or ID number).

v. Research staff **"Saves"** form (information saved prior to opening form as a survey will be retained when form is later opened/sent as a survey; locked PDF is not generated into form is completed as a survey)

w. Select "**Survey Options"** and "Open Survey"



i. If witness is present in same location as study staff, click **"Open Survey"**

ii. If witness is located in remote location, click "Compose Survey" and send survey to witness by email

x. Witness provides names and signatures and submits form.

y. PDF of research staff and witness signatures is locked and stored in REDCap and can be accessed in REDCap for printing

z. A local copy of signature page ("eConsent Part 2" for English Consent) should be printed for local records or archived in an electronic database outside of REDCap ***prior to randomization*** (instructions below)

Documentation of Written Consent if E-Consent and Scanned Consent Not Possible

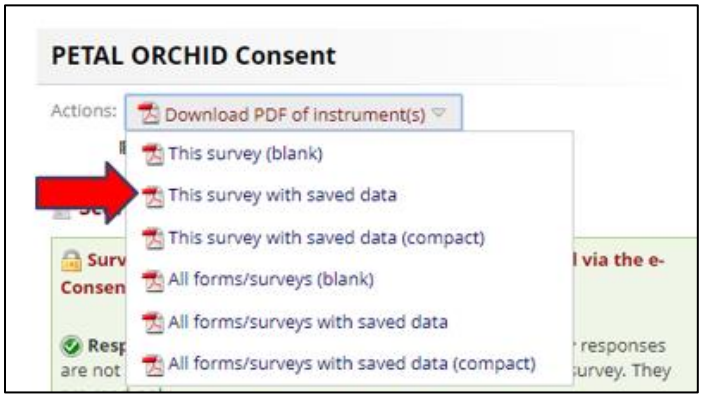
a. The electronic "no touch" methods of documenting written consent, described above, are the preferred methods of consent for ORCHID. In cases where these methods are unavailable, FDA recommends documenting the completion of written informed consent through attestations from both a study member involved in the consent process and an impartial witness using the following steps:
    i. An unsigned paper consent form is provided to the patient by a heath care worker or study member who has entered the room
    ii. The study member obtaining consent arranges an in-person meeting or three-way call or video conference with himself/herself, the patient, and an **impartial witness** (e.g. bedside nurse, patient advocate; impartial witness may not be member of the research team)**.** If desired and feasible, additional participants requested by the patient (e.g., next of kin).
    iii. Investigator reviews consent and answers questions. Witness confirms that patient's questions have been answered
    iv. Patient signs the paper informed consent document while witness is listening on the phone or directly observing.
    v. Patient provides verbal confirmation that he/she would like to participate in the trial and he/she has signed and dated the informed consent document that is in their possession
    vi. Study member and witness document that the patient has provided written informed consent in REDCap by completing the following steps:
        1. Open and complete the "Participant Information form"
        2. Open the form "Alternative Documentation Of Informed Consent (Study Staff)," select "Survey Options" and "Open Survey"
        3. Study member who obtained consent confirms that retention of written consent or electronic consent was not possible, documents method of consent conversation (phone/video), lists names of those present, confirms written consent was obtained, signs, and submits
        4. Study member opens "Alternative Documentation Of Informed Consent (Witness)," selects "Survey Options," "Compose Survey" and sends survey to witness by email
        5. Witness opens survey link, provides names and electronic signatures and submits form (creating locked PDF).
        6. Finally, Study member signs a paper copy of the informed consent (save for files) and uploads signature page to REDCap.
    vii. Source documents for this process, which should be printed for local records or archived in an electronic database outside of REDCap, prior to randomization include:
        1. Paper informed consent (signed by study staff)
        2. "Alternative Documentation Of Informed Consent (Study Staff)" "Alternative Documentation Of Informed Consent (Witness)"
b. **This process can only be used for a participant who is providing his/her own consent and not from an LAR.**

Non-English Language Consents

a. Informed consent can be obtained from non-English speaking patients using a qualified interpreter and a short-form consent or a translated version of the consent form
    i. If the appropriate language short-form is not available, the patient is ineligible
b. Either process of "no-touch" consent ("E-Consent" or "Scanned Consent") can be used
    i. Only some languages have forms available for "E-Consent" (e.g. Spanish)
    ii. More options are available with the standard PETAL paper short forms which can used with the "Scanned Consent" process. Available languages include:
        1. Arabic, Dutch, French, German, Greek, Haitian-Creole, Hebrew, Italian, Portuguese, Russian, Somali, Spanish, Traditional Chinese, and Vietnamese
c. When this method is used, **there must be a witness to the oral presentation**.
d. The subject/LAR only signs the short form.
e. Research staff signs the signature page of the full English consent (using either the "E-Consent" or "Signed Consent" processes described above)
f. Witness and research staff sign the "Confirmation of Consent" (described above)
g. Patient/LAR must receive a copy of the consent and short form
h. Identity of translator must be documented in "Confirmation of Consent" form. Translator signature may be required at some centers based on local context

Downloading/Printing Copies of Consent Documents

i. Open form to be printed
    i. "eConsent Part 2" for patient/LAR signature from E-Consent
    ii. "Scanned Consent" for patient/LAR signature from paper consent process
    iii. "Short Form" for non-English consents
    iv. "Confirmation of Consent" for witness/research staff signatures
    v. "Alternative Documentation of Written Consent"
j. Click "Download PDF of Instrument(s)" and "This survey with saved data" to open PDF for printing.



Consent for Continued Participation

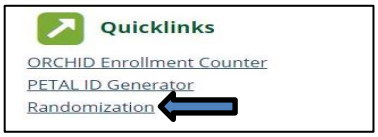
**In cases where consent is obtained from LAR, but patient regains decision capacity during hospitalization, consent for continued participation should be obtained*

a. Patient is provided with copy of consent and consent for continued participation is discussed
b. If patient agrees, consent is documented using the E-Consent process and "Consent for Continued Research Participation" form in REDCap
    i. If consenting using a study device, click ""**Open Survey**."
    ii. If consenting using a patient/LAR device, Click "**Compose Survey Invitation**" which allows the survey to be sent as an email to the participant/LAR
c. Patient provides electronic signature to affirm consent for continued participation and submits
d. Consent is locked and stored as a PDF in REDCap and can be accessed in REDCap for printing (if needed) for local use/storage.

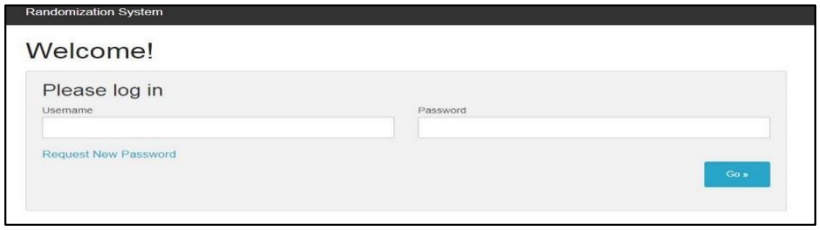
Enrollment and Randomization

1. RANDOMIZATION – For an eligible patient for whom informed consent to participate has been obtained, perform randomization
    a. Log into http://petalnet.org/
    b. Select "ORCHID" under the Studies section on the main page

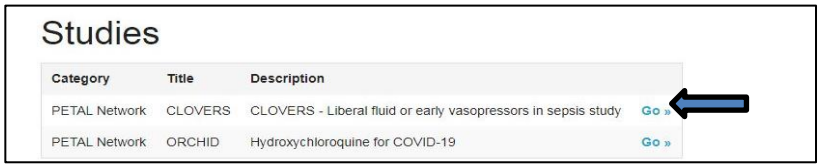
    c. Select "Randomization" to enter the randomization website



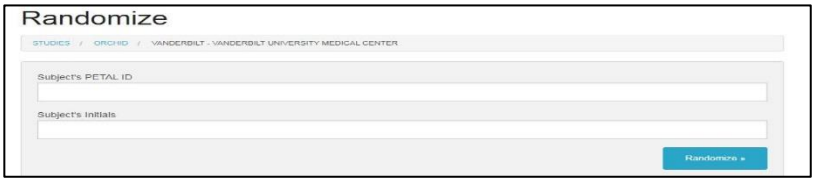
    d. Log in to the website (https://rs2.partners.org/rs/login)



    e. Select 'Go' next to the ORCHID study



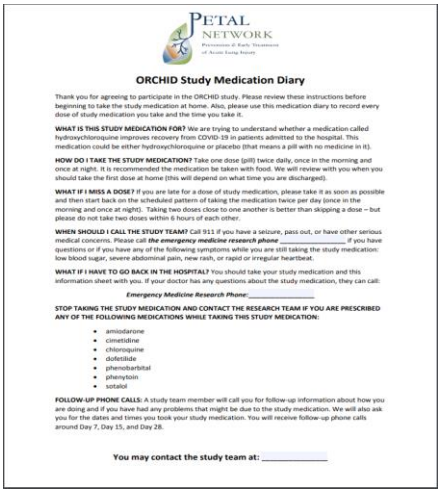
    f. Select site
    g. Enter Petal ID and patient initials



    h. Click randomize → an email with the ORCHID ID and randomization date and time will be sent to study personnel and the investigational pharmacy

2. PHARMACY – For a patient who has been randomized:
    a. Order the study medication in the electronic order entry system

b. Adjust the date and time of first dose to be given "NOW" instead of at a future scheduled time
c. Provide pharmacy with appropriate documentation to receive study drug
d. Deliver bottle of medication containing all 10 doses of study drug to bedside nurse
e. Educate bedside nurse on study procedures and study drug administration
f. Provide the bedside nurse with the Medication Diary – which will be used by patient to record remaining doses of study drug if discharged from the hospital before all 10 doses are completed



PETAL NETWORK
Prevention & Early Treatment of Acute Lung Injury

ORCHID Study Medication Diary

Thank you for agreeing to participate in the ORCHID study. Please review these instructions before beginning to take the study medication at home. Also, please use this medication diary to record every dose of study medication you take and the time you take it.

WHAT IS THIS STUDY MEDICATION FOR? We are trying to understand whether a medication called hydroxychloroquine improves recovery from COVID-19 in patients admitted to the hospital. This medication could be either hydroxychloroquine or placebo (that means a pill with no medicine in it).

HOW DO I TAKE THE STUDY MEDICATION? Take one dose (pill) twice daily, once in the morning and once at night. It is recommended the medication be taken with food. We will review with you when you should take the first dose at home (this will depend on what time you are discharged).

WHAT IF I MISS A DOSE? If you are late for a dose of study medication, please take it as soon as possible and then start back on the scheduled pattern of taking the medication twice per day (once in the morning and once at night). Taking two doses close to one another is better than skipping a dose – but please do not take two doses within 6 hours of each other.

WHEN SHOULD I CALL THE STUDY TEAM? Call 911 if you have a seizure, pass out, or have other serious medical concerns. Please call ***the emergency medicine research phone*** ___ if you have questions or if you have any of the following symptoms while you are still taking the study medication: low blood sugar, severe abdominal pain, new rash, or rapid or irregular heartbeat.

WHAT IF I HAVE TO GO BACK IN THE HOSPITAL? You should take your study medication and this information sheet with you. If your doctor has any questions about the study medication, they can call:

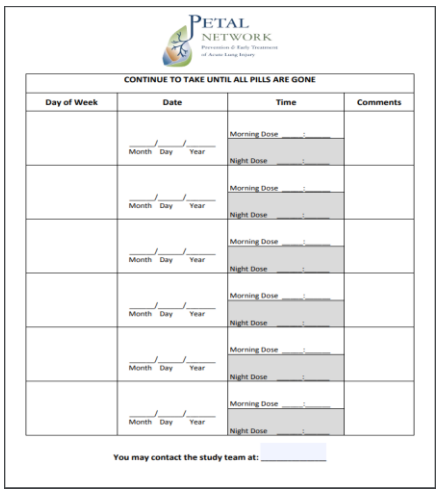
Emergency Medicine Research Phone:_____

STOP TAKING THE STUDY MEDICATION AND CONTACT THE RESEARCH TEAM IF YOU ARE PRESCRIBED ANY OF THE FOLLOWING MEDICATIONS WHILE TAKING THIS STUDY MEDICATION:

- amiodarone
- cimetidine
- chloroquine
- dofetilide
- phenobarbital
- phenytoin
- sotalol

FOLLOW-UP PHONE CALLS: A study team member will call you for follow-up information about how you are doing and if you have had any problems that might be due to the study medication. We will also ask you for the dates and times you took your study medication. You will receive follow-up phone calls around Day 7, Day 15, and Day 28.

You may contact the study team at: _____



PETAL NETWORK
Prevention & Early Treatment of Acute Lung Injury

CONTINUE TO TAKE UNTIL ALL PILLS ARE GONE

Day of Week	Date	Time	Comments
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	

You may contact the study team at: _____

3. Documentation – For a patient who has been enrolled:
   a. Document patient to be "on study" in the electronic health record (e.g., a "research note").
   b. Update patient information in enrollment log or PETAL ID tracker (if applicable to your site)

4. Data Collection – For a patient who has been enrolled and randomized:
   a. In the PETAL ORCHID Hydroxychloroquine Study REDCap database, ensure the following CRFs are complete:
      i. Eligibility criteria
      ii. Randomization
      iii. Contact information
      iv. Dose 1 of study drug

PROCEED TO DRUG ADMINISTRATION AND ON-STUDY MONITORING SOPs

Administering Study Drug by Mouth

1. Pharmacy should dispense a bottled labeled study drug containing 12 total doses of study drug, which should be stored by the bedside nurse on the patient's ward in the same location as "home medications"
2. Study drug should be given by mouth with a small amount of liquid and should not be given within 1 hour of receipt of antacids
3. For the first two doses of study drug, the bedside nurse should administer two tabs by mouth (400 mg of hydroxychloroquine or placebo)
4. For the subsequent eight doses of study drug, the bedside nurse should administer one tab by mouth (200 mg of hydroxychloroquine or placebo)
5. If the patient is unable to swallow, please use SOP for medication by tube

Administering Study Drug by Tube

For sites using study drug tablets provided by the coordinating center, the beside clinical nurse should complete the following steps:

1. Crush the tablet in a pill crusher
2. Place the crushed tablet in a specimen cup
3. Add 30 ml of water to the specimen cup
4. Mix the solution
5. Pull solution up into a syringe
6. Inject the solution into the tube
7. Flush the tube with 30 ml of water

For sites using study drug capsules compounded by the local pharmacy, the beside clinical nurse should complete the following steps without study personnel or treating clinicians present:

1. Open the capsule
2. Dump the contents of the capsule into a specimen cup
3. Add 30 ml of water to the specimen cup
4. Mix the solution
5. Pull solution up into a syringe
6. Inject the solution into the tube
7. Flush the tube with 30 ml of water

Dose Adjustments if Hydroxychloroquine Received before Randomization

Patients may receive up to 1 dose of hydroxychloroquine in the 10 days prior to randomization and still be eligible for enrollment in the ORCHID study. If a patient received hydroxychloroquine within the 24 hours prior to randomization, the dose of study drug may need to be adjusted:

1. If the patient received a **400 mg dose** of hydroxychloroquine **less than 24 hours prior to randomization**, the loading dose will be reduced by administering only 1 pill (200 mg of hydroxychloroquine or placebo) at the time of the second dose of study drug. The patient will still receive 10 total doses of study drug with the updated schedule:
    a. 400 mg dose (2 pills) following randomization for **1 dose**
    b. 200 mg dose (1 pill) twice daily for **9 doses**
    c. If a standard pill supply (12 pills) has been provided, 1 pill should be disposed of by study staff.
    d. Timing and documentation of study drug administration in REDCap will not be affected by this dose change.
2. If the patient received a **200 mg dose** of hydroxychloroquine **less than 24 hours prior to randomization, OR** receives a dose of any size **more than 24 hours prior to randomization**, the patient will receive the standard dosing regimen including a full loading dose:
    a. 400 mg dose (2 pills) following randomization for **2 doses**
    b. 200 mg dose (1 pill) twice daily for **8 doses**

Late, Delayed, Missed, and Held Doses of Study Drug

The planned dosing of the study drug is BID (e.g., 10:00 and 18:00).

"LATE" - Any dose given after the scheduled administration time but before the next scheduled dose is due is defined as "late". "Late" doses of study drug are to be given as soon as possible and prior to the next dose. Subsequent doses are continued as scheduled until all 10 doses are completed. The date and time of each of the 10 doses is recorded in the CRFs.

Example: A dose scheduled at 18:00 that at 23:30 has not yet been given is defined as "late". This dose should be given as soon as possible and the next scheduled 10:00am dose and all subsequent doses should be given as scheduled and recorded in the CRFs.

"**DELAYED**" – The first two (2) doses of a study drug that are NOT given before the next scheduled dose is due are defined as "delayed". When "delayed" doses occur, those doses are not taken immediately but instead the regular BID doses are continued until all 10 doses of the study drug have been taken. For a patient with one delayed dose, this would mean taking the final dose of study drug 12 hours later than initially scheduled. For a patient with two delayed doses, this would mean taking the final dose of the study drug 24 hours later than initially scheduled. Even if two "delayed" doses occur, under no circumstances should study drug should be taken after 11:00 on Study Day 7. When two or fewer "delayed" doses occur, the date and time at which each subsequent dose was actually received should be recorded in the CRF for doses 1-10. The date and time of the dose will make clear in the data collection where in the scheduled sequence the delayed dose occurred.

Example: A dose scheduled at 10:00 that at 22:00 has not yet been given is defined as "delayed". This dose should not be given immediately. Instead, the patient should continue to take the regularly scheduled 10:00 and 18:00 doses until all 10 doses are gone (which will mean taking the "delayed" dose 12 hours after the previously scheduled final dose. The date and time each dose was actually received should be recorded in the CRFs.

"**MISSED**" – Any doses of study drug beyond two (2) that are NOT given before the next scheduled dose is due are defined as "missed". When "missed" doses occur, those doses are not taken. The regular BID doses are continued until all 10 doses of the study drug have been taken or 11:00 on Study Day 7, whichever occurs first. All doses not taken by the morning of Study Day 7 are discarded. For a patient with two delayed doses followed by a third dose not administered before the next scheduled dose is due, the patient would only receive a total of 9 doses of the study drug. For any dose which is "missed" rather than "late" or "delayed", record in the CRF for that dose "No" for the question "Was dose X of study medication given?" and provide the reason "Missed - unable to be logistically administered during the scheduled window".

Example: A patient goes to surgery for 14 hours and then loses enteral access such that on Study Day 3 the 10:00 and 18:00 doses are not administered and on Study Day 4, the 10:00 dose is not administered. The first two doses are "delayed" and will be taken 12 and 24 hours after the scheduled end of therapy, but not later than 11:00 on Study Day 7. The third dose is "missed" and will be recorded as "missed" in the CRF such that the patient will only receive 9 total doses of study drug.

"**HELD**" – Any dose(s) intentionally not given because on-study monitoring identified a safety concern (e.g. QTc >500 or patient was receiving a medication that was considered to be contraindicated with hydroxychloroquine). When "held" doses occur, those doses are not taken. For any dose which is "held," record in the CRF for that dose "No" for the question "Was dose X of study medication given?" and provide the reason (e.g. "On-study monitoring with QTc>500ms"). If study drug can be resumed, remaining doses are administered as scheduled. Total number of administered doses will be 10 minus the number of "held" doses.

Example: On-study monitoring at 8:00 on Study Day 3 finds most recent EKG with QTc=550ms. Study drug is "held" for 24 hours. Doses scheduled for this 24-hr period (e.g. dose 5 and 6) are recorded as not administered for the reason of "On-study monitoring with QTc>500ms." If repeat EKG on Study Day 4, shows QTc < 500 ms, study drug may resume with Dose 7.

Stopping Study Drug

Per Section 4.6 of Trial Protocol, study drug may be stopped temporarily or permanently for:

2. Adverse events
    a. If the patient experiences an Adverse Event that the patient (or legally authorized representative), treating clinicians, or investigators feel merits temporarily or permanently stopping the study drug, the study drug should be stopped immediately and the study PIs and CCC should be notified to assist with recording and reporting the Adverse Event.
3. Safety Outcomes
    a. If the patient experiences a Safety Outcome that the patient (or legally authorized representative), treating clinicians, or investigators feel merits temporarily or permanently stopping the study drug, the study drug should be stopped immediately and the study PIs and CCC should be notified to assist with recording and reporting the Adverse Event (*all Safety Outcomes that lead to permanent discontinuation of the study drug are also reported as Adverse Events*).
        - Whether a Safety Outcome merits temporarily or permanently stopping the study drug may be determined with input from the patient (or legally authorized representative), treating clinicians, site investigators, and CCC or trial PIs.
        - Safety Outcomes definitely or probably related to the study drug and Safety Outcomes that are potentially serious (e.g., seizure, ventricular arrhythmia, cardiac arrest, rash) should result in stopping of the study drug.
        - Safety Outcomes determined to be definitely or probably NOT related to the study drug that are not determined to be serious (e.g., atrial arrhythmia, elevation in AST or ALT, acute kidney injury, receipt of renal replacement therapy, hypoglycemia, lymphopenia, anemia, or thrombocytopenia) will not necessarily result in stopping of the study drug

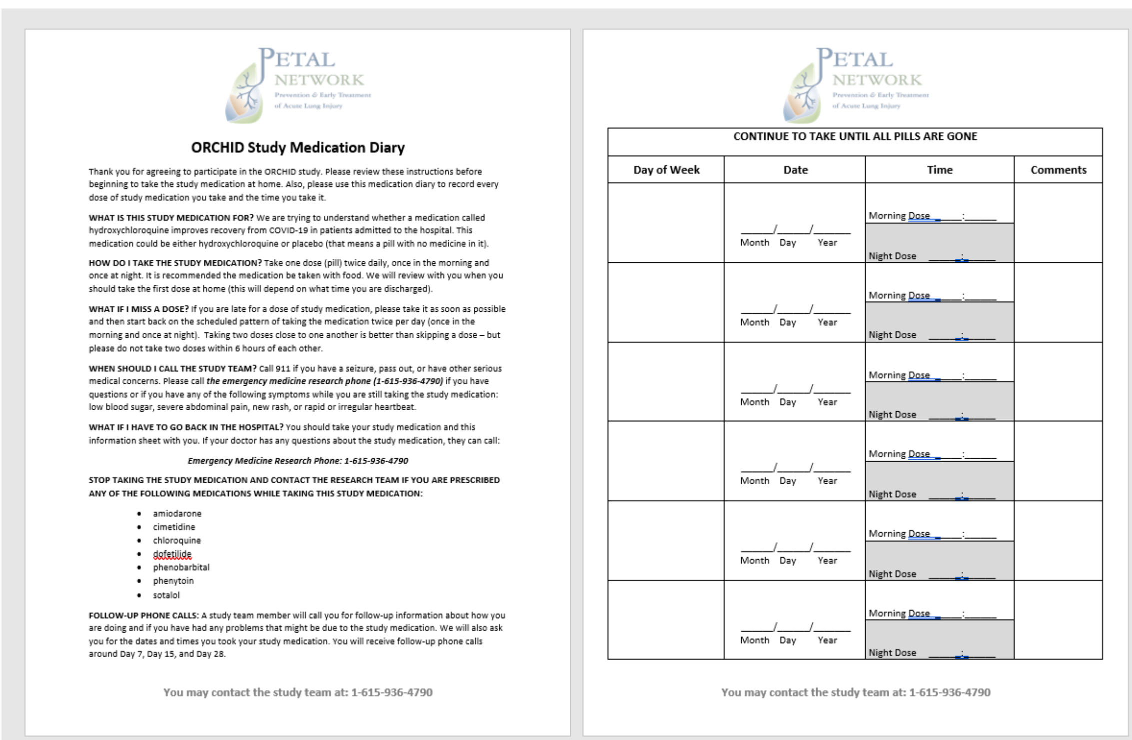
4. Results of on-study monitoring – If a QTc between randomization and end of study drug receipt is > 500 ms, the study drug will be stopped for 24 hours and a repeat EKG will be performed daily until either the QTc is < 500 ms or 5 days after randomization is reached.

If the daily on-study monitoring for medication interactions indicates a potential interaction with a medication that treating clinicians feel is required and with which treating clinicians and the investigator feel it would be unsafe to administer hydroxychloroquine, the study drug will be stopped.

5. Clinical Deterioration – For patients who experience a decrease of 1 point or more on the COVID scale (e.g., moving from standard nasal cannula to high flow nasal cannula) for which treating clinicians wish to stop the drug in order to unblind group assignment and administer open-label hydroxychloroquine to patients in the placebo group, trial protocol allows them to do so. All further management is deferred to treating clinicians. These crossovers must be recorded and reported to DSMB.

Discharge Procedures and Study Drug at Home

1. On the day treating clinicians determine the patient is to be discharged from the study hospital, study personnel should:
    a. Ensure the bedside nurse provides the patient with the bottle of study drug assigned to the patient containing any remaining doses (if applicable)
    b. Ensure the patient leaves the hospital with the "Study Medication Diary" indicating when each remaining dose of study drug should be taken (if applicable)
    c. Ensure that any "missed" doses of study drug have been removed from the bottle and destroyed so that the patient does not take any dose of study drug after 11:00 on Study Day 7 (if applicable)
    d. Confirm contact information for patient and secondary contact and remind the patient that study personnel will contact the patient for telephone follow up on Study Days 8, 15, 29 (if applicable)



PETAL NETWORK
Prevention & Early Treatment of Acute Lung Injury

ORCHID Study Medication Diary

Thank you for agreeing to participate in the ORCHID study. Please review these instructions before beginning to take the study medication at home. Also, please use this medication diary to record every dose of study medication you take and the time you take it.

WHAT IS THIS STUDY MEDICATION FOR? We are trying to understand whether a medication called hydroxychloroquine improves recovery from COVID-19 in patients admitted to the hospital. This medication could be either hydroxychloroquine or placebo (that means a pill with no medicine in it).

HOW DO I TAKE THE STUDY MEDICATION? Take one dose (pill) twice daily, once in the morning and once at night. It is recommended the medication be taken with food. We will review with you when you should take the first dose at home (this will depend on what time you are discharged).

WHAT IF I MISS A DOSE? If you are late for a dose of study medication, please take it as soon as possible and then start back on the scheduled pattern of taking the medication twice per day (once in the morning and once at night). Taking two doses close to one another is better than skipping a dose – but please do not take two doses within 6 hours of each other.

WHEN SHOULD I CALL THE STUDY TEAM? Call 911 if you have a seizure, pass out, or have other serious medical concerns. Please call ***the emergency medicine research phone (1-615-936-4790)*** if you have questions or if you have any of the following symptoms while you are still taking the study medication: low blood sugar, severe abdominal pain, new rash, or rapid or irregular heartbeat.

WHAT IF I HAVE TO GO BACK IN THE HOSPITAL? You should take your study medication and this information sheet with you. If your doctor has any questions about the study medication, they can call:

Emergency Medicine Research Phone: 1-615-936-4790

STOP TAKING THE STUDY MEDICATION AND CONTACT THE RESEARCH TEAM IF YOU ARE PRESCRIBED ANY OF THE FOLLOWING MEDICATIONS WHILE TAKING THIS STUDY MEDICATION:

- amiodarone
- cimetidine
- chloroquine
- dofetilide
- phenobarbital
- phenytoin
- sotalol

FOLLOW-UP PHONE CALLS: A study team member will call you for follow-up information about how you are doing and if you have had any problems that might be due to the study medication. We will also ask you for the dates and times you took your study medication. You will receive follow-up phone calls around Day 7, Day 15, and Day 28.

You may contact the study team at: 1-615-936-4790

PETAL NETWORK
Prevention & Early Treatment of Acute Lung Injury

CONTINUE TO TAKE UNTIL ALL PILLS ARE GONE

Day of Week	Date	Time	Comments
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	
	___/___/___ Month Day Year	Morning Dose ___:___ Night Dose ___:___	

You may contact the study team at: 1-615-936-4790

Daily On-Study Screening

- **Doses**: On each Study Day 1-5 for which the patient is an inpatient, evaluate medication administration and record in the CRF the date and time of each dose of study drug.
- **Day 2-5 Assessments**:
    - *Daily assessments when patient is an inpatient*
    - *Day 2: From time of randomization to 8am on Study Day 2*
    - *Days 3-5: From 8am-8am*
    - Assessments include:
        - ***COVID Ordinal Outcomes Scale***: Worse value on that calendar day.
        - ***Contraindicated medications***: If identified on that calendar day, contact treating clinicians to determine which drug is to be discontinued (i.e. study drug or contraindicated drug – one MUST be discontinued).
        - ***Medication Interactions***: If medication with potential interaction is identified on that calendar day, alert clinical treating team and document on CRF.
        - ***Adverse Events:*** Assessed for that calendar day and recorded in AE CRF
        - ***Safety Outcomes:*** Assessed for that calendar day and recorded in Safety Outcomes CRF
            - Follow AE recording and reporting rubric, including recording and reporting a Safety Outcome that is "Probably or Definitely related" to study procedures or results in discontinuation of study drug as an AE.
        - ***Daily Laboratory Assessment :*** In the 24 hours prior to 0:800 (i.e., not for that calendar day).
        - ***Clinical EKG***: If clinical EKG and telemetry rhythm strip both available, use clinical EKG. EKGs are assessed in the 24 hours prior to 0:800 (i.e., not for that calendar day).

QTc Assessment

QTc Assessment at 24-48 hours after first study drug

1. Participants will receive an assessment of the QTc between 24-48 hours after the first administration of study drug, unless:
    a. The participant has been discharged from the hospital
    b. Study drug has been discontinued
2. The QTc may be assessed with:
    a. electrocardiogram (EKG), or
    b. rhythm strip (e.g., telemetry)
3. If an EKG or rhythm strip (e.g., telemetry) has been performed as part of clinical care between 24-48 hours after the first administration of study drug, study personnel will:
    a. Record the QTc value and date and time of assessment from the clinical EKG or rhythm strip in REDCap under the "QTc assessment at 24-48 hours" CRF
    b. Determine if the QTc is ≥ 500 ms and, if so, stop the study drug and monitor QTc daily until QTc is < 500 and study drug can be restarted
4. If an EKG or rhythm strip has not been performed as a part of clinical care between 24-48 hours after the first administration of study drug, study personnel will:
    a. Order an EKG or rhythm strip as a part of study procedures
    b. Record the QTc value and date and time of assessment from the research EKG or rhythm strip in REDCap under the "QTc assessment at 24-48 hours" CRF
    c. Determine if the QTc is ≥ 500 ms and, if so, stop the study drug and monitor QTc daily until QTc is < 500 and study drug can be restarted
5. If an EKG or rhythm strip cannot be performed between 24-48 hours for an inpatient, the study drug will be stopped until a QTc is assessed and demonstrated to be <500 ms, at which point the study drug will be resumed with any doses missed due to the absence of QTc assessment recorded in the Dose CRF

Clinical EKGs on Study Days 2-5

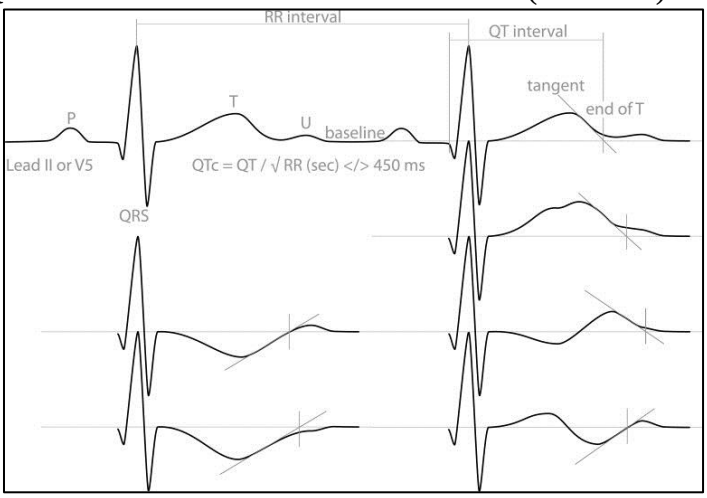
1. On Days 2-5, study personnel will review the electronic health record to determine whether the participant has received an EKG as part of clinical care in the 24 hours prior to 08:00 on that study day, unless:

a. The participant has been discharged from the hospital
b. Study drug has been discontinued

2. If no EKG has been performed as a part of clinical care in the 24 hours prior to 0800 on this study day, study personnel select "No" to the question "Was a clinical EKG performed on this study day?"
3. If an EKG was performed as a part of clinical care in the 24 hours prior to 0800 on this study day, study personnel select "Yes" to the question "Was a clinical EKG performed on this study day?" and:
    a. Record the date and time and value for QTc
    b. Determine if the QTc is ≥ 500 ms and, if so, stop the study drug and monitor QTc daily until QTc is < 500 and study drug can be restarted

Measuring the QTc

1. For EKGs, the official QTc value read by the clinical expert interpreting the EKG should be used. When more than one QTc value is provided, the "QTc F" or "Fridericia" rate correction value should be used.
2. For EKGs without an official read by a clinical expert or for rhythm strips, a study physician at the study site should measure the QTc using the following procedure:
    a. Examine lead II if available (if not available, use lead V5, V6 or I, if available)
    b. Begin QT measurement at the start of the Q wave if present (otherwise at the start of the R wave)
    c. End QT measurement at the end of the T wave (as shown):



    d. Correct for heart rate using Fridericia correction ($QTc = QT / RR^{1/3}$ [sec])

Management of a Participant with a QTc ≥ 500 ms

1. For a participant who is receiving study drug on Days 1-5 of the study for whom a clinical or research QTc assessment demonstrates at QTc ≥ 500 ms, study personnel should:
    a. discontinued study drug for 24 hours
    b. repeat EKG daily until
        i. QTc is less than 500 ms, at which time study drug is resumed until 5 days after enrollment, or
        ii. 5 days after enrollment is reached without resumption of study drug
    c. value for the QTc should be recorded in the Daily Assessment CRF and the holding or administering the study drug should be recorded in the Dose CRF

Protocol Deviations

This page is only to be completed when a protocol deviation occurs.

Protocol Deviation ID – Utilize sequential numbering (1, 2, 3) for each randomized patient.

Please note that each patient will utilize “1” as the initial protocol deviation ID.

Phone Calls

Use Follow Up Phone Call Script and Data Collection Tool to guide interview questions.

For patients discharged from the study hospital prior to the Day 8, Day 15 or Day 29 assessment, perform these assessments via telephone follow-up.

- The Day 8 call window will be Day 8 through 14.
- The Day 15 call window will be Day 15 through 22.
- The Day 29 call window will be Day 29 through 36.

During the follow up telephone calls, interview the patient, LAR, or facility staff to assess:

- Date and time of each dose of study drug taken or missed since hospital discharge (*this assessment only required for those discharged before completing study drug and whose completion of study drug has not been assessed at a prior follow up phone call*)
    - If the dose of the drug is known to have been taken, answer "Was dose X of study medication given?" in REDCap as "Yes", even if date and time is unknown
    - If date of dose is known but time of dose is unknown, record the date and complete time as "00:00"
- COVID Ordinal Outcome scale
    - Date of death (if applicable)
- Non-laboratory safety outcomes after hospital discharge (e.g., seizure)
- ED visit, hospital readmission, and oxygen receipt after hospital discharge
- Adverse Events

<u>Phone Call Special Considerations:</u>

- *Day 8*: If patient discharged on study drug, collect dates and times of doses taken and document on corresponding Dose CRFs.
- *Day 29*: Collect final vital status.
    - Additional CRF pages completed in conjunction with Day 29 Phone Call include:
        - Safety Outcomes, AEs, Post Discharge Outcomes, Vital Status
- Safety Outcomes are assessed and indicated on phone call script if the patient has had no readmission to study hospital. If patient has been readmitted and EMR information is available, complete entire Safety Outcomes CRF (i.e. lab values, specific cardiac arrhythmias)

In-hospital Medications, Microbiology, and Outcomes

To be completed at hospital discharge. All information in this CRF is limited to the initial (index) hospitalization and censored at hospital discharge. Do not use information from the follow up telephone calls or readmissions to complete this CRF.

- **Microbiology**
  - Indicate date and time SARS-CoV-2 test was collected (required)
  - Indicate date and time SARS-CoV-2 test *resulted* IF available.

- **In-hospital Outcomes**
  - First and final receipt during index hospitalization of:
    - Oxygen
    - High flow nasal cannula
    - Noninvasive ventilation
    - Invasive ventilation
    - ECMO
    - Vasopressors
    - ICU admission

End-of-study Outcomes

To be completed at Day 29.

- **Safety Outcomes**: Complete any remaining unanswered questions utilizing information from Day 8, 15, and 29 phone calls as well as any additional information in EMR.
- **Post Discharge Outcomes**: Complete any remaining unanswered questions utilizing information from Day 8, 15, and 29 phone calls as well as any additional information in EMR.
- **Vital Status**
- **Patient withdrawal**

Review of Chest Imaging

NOTES:

- For the ORCHID study, radiology reports are sufficient for the collection of bilateral infiltrates. Manual review by study physicians is not required
- Patients are assessed for bilateral infiltrates at baseline (within the 48 hours prior to randomization) and in the 8 days after randomization. Once a patient is documented as having bilateral infiltrates, there is no need to review subsequent studies
- The "In-Hospital Imaging" case report form in REDCap will serve as the source document for all documentation of ARDS
- It is not required that the radiology report specifically address the presence of effusions, lobar/lung collapse, nodules, cardiac failure or fluid overload. If these findings are not mentioned, they are assumed to be absent.

INSTRUCTIONS

1. Open the "In-Hospital Imaging" case report form in the REDCap
2. If the patient had available chest imaging in the 48 hours prior to randomization, select "Yes," and document what type of imaging was reviewed
3. Document whether radiology reports from imaging in the 48 hours prior to randomization, noted **"bilateral opacities"** or **"bilateral consolidation"** without suggesting that these opacities/consolidations could be fully explained by effusions, lobar/lung collapse, nodules, cardiac failure or fluid overload.
4. *If patient did not have bilateral opacities prior to randomization*, review available chest imaging (x-ray, CT scan, etc.) obtained between randomization and day 8 for the development of bilateral opacities and document what type of imaging was used for review.
5. *If patient did not have bilateral opacities prior to randomization*, document whether radiology reports from imaging between randomization and study day 8, noted **"bilateral opacities"** or **"bilateral consolidation"** without suggesting that these opacities/consolidations could be fully explained by effusions, lobar/lung collapse, nodules, cardiac failure or fluid overload.

ORCHID Study Product Dispensing SOP

Date: 9 APR 2020
Version: *1*
Author(s): Matt Semler, MD; Donna Torr, PharmD, Nancy Ringwood, RN

Title: ORCHID: **O**utcomes **R**elated to **C**OVID-19 treated with **H**ydroxychloroquine among **I**n-patients with symptomatic **D**isease

Purpose: To ensure accurate dispensing and documentation of Hydroxychloroquine and placebo for the ORCHID RCT.

Dosage & Dosing Frequency:

Participants confirmed to meet all eligibility criteria who have provided informed consent will be randomized 1:1 to oral hydroxychloroquine versus placebo.

ACTIVE: Hydroxychloroquine: 200 mg oral tablets of hydroxychloroquine sulfate

- **Dose 1:** 400 mg (2 tablets)
- **Dose 2:** 400mg (2 tablets)
- **Doses 3-10**: 200 mg (one tablet) twice daily
- **Dosing Regimen**: A total of 10 doses over 5 days

PLACEBO:

- Participants randomized to the control group will receive matching placebo enterally twice daily matching the dosing regimen described above for hydroxychloroquine.

Preparation and Administration

Preparation:

1. **HOSPITAL STOCK:** Hydroxychloroquine 200 mg oral tablets. A placebo should be compounded as described in the **PLACEBO ORCHID Compounding SOP**. Hospital stock Hydroxychloroquine should be compounded as per the **ACTIVE ORCHID Compounding SOP** so that it matches the placebo.
2. **DRUG COMPANY PROVIDED SUPPLY:** Hydroxychloroquine 200 mg oral tablets and matching placebo will be provided (this supply will not require compounding).

Administration (Active and Placebo):

1. Dispense all 10 doses (12 tablets) at randomization
2. Dispense in a tight, light-resistant container as defined in the USP/NF
3. **BLINDING:** Study subjects, nurses, research staff, and the clinical team will be **blinded** to the study treatment assignment.

First dose of study drug must be administered **within 4 hours of randomization.**

Study Dosing Plan:

DOSE 1: 400 mg (or placebo)	**DOSE 2 (2 tablets): 400mg (or placebo)**
DOSE 3 : 200 mg (or placebo)	DOSE 4: 200mg (or placebo)
DOSE 5: 200 mg (or placebo)	DOSE 6: 200mg (or placebo)
DOSE 7: 200 mg (or placebo)	DOSE 8: 200mg (or placebo)
DOSE 9: 200 mg (or placebo)	DOSE 10: 200mg (or placebo)

Dispense all 10 doses (12 tablets) upon randomization to the unit (ED, floor, or ICU)

Labeling guidelines: Medication Dose Packs

Labels for doses dispensed to subjects should follow FDA and ICH guidelines for investigational new drugs and your institutional requirements.

Storage Requirements

Store at room temperature [20° to 25°C (68° to 77°F), allows excursions between 15° and 30°C (59° and 86°F)].

- Daily temperature logs of the drug storage area should be maintained
- Study medication should be stored in a locked area only accessible to pharmacy staff

Documentation and inventory control requirements

Please include the following information when documenting drug accountability for ORCHID. A template is available, or your current drug inventory log/system can be used.

1. Date of dispensing
2. Identification of product administered
3. Dosage
4. Subject's identification code (PETAL ID Number)
5. Dispensing pharmacy personnel initials
6. Manufacturer's lot number
7. Balance on hand
8. Documentation of lost or damaged doses.

Final Disposition of Drug Company Provided Study Product

Ensure the following documentation for drug disposition:

- Shipping records showing receipt of the study product
- Dispensing/administration records showing usage of the product
- Reconciliation records for unaccounted-for product
- Final disposition records

Applicable Regulations and Policies:

- FDA CRF 21; Subpart D: 312:61: Control of Investigational Drug
- FDA CRF 21; Subpart D: 312:62a,c: Disposition and Record Retention
- Guideline for Good Clinical Practice (ICH E6); 4.6: Investigational Products
- **PLAQUENIL® HYDROXYCHLOROQUINE SULFATE TABLETS, USP** Package Insert
- ORCHID Process Document: Randomization-Pharmacy
- ORCHID Compounding SOP-ACTIVE
- ORCHID Compounding SOP-PLACEBO

ORCHID Study Documents

1. ORCHID Enrollment Tool
2. ORCHID Study Medication Diary Template
3. ORCHID HCO Follow Up Phone Call V1.0

ORCHID Step by Step

Petal ID _____ ORCHID ID_____ MRN_____

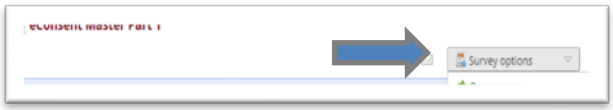
☐ 1. **VERIFY** Screen patient for eligibility. If all inclusion criteria are met, generate a Petal ID and enter into the Project Title: PETAL ORCHID Hydroxychloroquine Study database (not Consent database). If an exclusion is met, enter patient as screen fail. If no exclusions are met, notify research MD.

☐
- ➲ Check the Petal ID Tracker to make sure subject does not already have a Petal ID
- ➲ Get Petal ID from ORCHID study web page on PETAL website (petalnet.org)

☐ 2. **COMMUNICATE** Ask admitting physician's permission to approach patient for study.

☐ 3. **CONSENT** Open PETAL ORCHID Consent database.

1. **Push** the "Create " button to create a new record and enter participant information along with Petal ID.
2. **Provide patient** with paper copy of consent.
3. **Open** up eConsent Master Part 1 **as a survey.**
4. Click ***"Next Page"*** to move to eConsent Part 2.
5. Patient **signs** "Part 2" of eConsent
6. Research team **opens** the form entitled ***"Confirmation of Consent page"*** and both the witness and person obtaining consent sign the eConsent



Note: Obtain date of symptom onset and 1-2 alternative contacts and enter into Redcap at bedside

☐ 4. **RANDOMIZE** Go to website https://rs2.partners.org/rs/login **Save** link to your computer. (Backup: can get from PETAL website and **save** to your computer)

☐ 5. **PHARMACY** 1) Place order in EHR, 2) Ensure first dose is given "NOW" and not at the default time, 3) Obtain the medication and educate clinical team on administration, 4) Provide clinical team with medication administration schedule for patient to take home if discharged before study day 5.

☐ 6. **DOCUMENT** Add patient to:

- *EHR –* place patient "On Study" and complete consent note
- *ORCHID Enrollment Log*
- *Petal ID Tracker* or ask someone else to do it until you get access

☐ 7. **REDCAP** Enter data into the 'PETAL ORCHID Hydroxychloroquine' database.

ORCHID Study Medication Diary

Thank you for agreeing to participate in the ORCHID study. Please review these instructions before beginning to take the study medication at home. Also, please use this medication diary to record every dose of study medication you take and the time you take it.

WHAT IS THIS STUDY MEDICATION FOR? We are trying to understand whether a medication called hydroxychloroquine improves recovery from COVID-19 in patients admitted to the hospital. This medication could be either hydroxychloroquine or placebo (that means a pill with no medicine in it).

HOW DO I TAKE THE STUDY MEDICATION? Take one dose (pill) twice daily, once in the morning and once at night. It is recommended the medication be taken with food. We will review with you when you should take the first dose at home (this will depend on what time you are discharged).

WHAT IF I MISS A DOSE? If you are late for a dose of study medication, please take it as soon as possible and then start back on the scheduled pattern of taking the medication twice per day (once in the morning and once at night). Taking two doses close to one another is better than skipping a dose – but please do not take two doses within 6 hours of each other.

WHEN SHOULD I CALL THE STUDY TEAM? Call 911 if you have a seizure, pass out, or have other serious medical concerns. Please call ***the emergency medicine research phone*** **_____** if you have questions or if you have any of the following symptoms while you are still taking the study medication: low blood sugar, severe abdominal pain, new rash, or rapid or irregular heartbeat.

WHAT IF I HAVE TO GO BACK IN THE HOSPITAL? You should take your study medication and this information sheet with you. If your doctor has any questions about the study medication, they can call:

Emergency Medicine Research Phone:**_____**

STOP TAKING THE STUDY MEDICATION AND CONTACT THE RESEARCH TEAM IF YOU ARE PRESCRIBED ANY OF THE FOLLOWING MEDICATIONS WHILE TAKING THIS STUDY MEDICATION:

- amiodarone
- cimetidine
- chloroquine
- dofetilide
- phenobarbital
- phenytoin
- sotalol

FOLLOW-UP PHONE CALLS: A study team member will call you for follow-up information about how you are doing and if you have had any problems that might be due to the study medication. We will also ask you for the dates and times you took your study medication. You will receive follow-up phone calls around Day 7, Day 15, and Day 28.

CONTINUE TO TAKE UNTIL ALL PILLS ARE GONE			
Day of Week	**Date**	**Time**	**Comments**
	_____/_____/_____ Month Day Year	Morning Dose _____:_____ Night Dose _____:_____	
	_____/_____/_____ Month Day Year	Morning Dose _____:_____ Night Dose _____:_____	
	_____/_____/_____ Month Day Year	Morning Dose _____:_____ Night Dose _____:_____	
	_____/_____/_____ Month Day Year	Morning Dose _____:_____ Night Dose _____:_____	
	_____/_____/_____ Month Day Year	Morning Dose _____:_____ Night Dose _____:_____	
	_____/_____/_____ Month Day Year	Morning Dose _____:_____ Night Dose _____:_____	

Instructions: For participants discharged from the study hospital, we will perform follow up assessments by telephone on Day 8 (window 8-14), Day 15 (window 15-22), and Day 29 (window 29-36). During these telephone calls, we will interview the patient, LAR, or facility staff to assess:

- COVID Ordinal Outcome Scale
- Safety Outcomes
- Adverse Events
- Study Day-specific data
  - Day 8 (or 15 or 29 if not done on Day 8) – Collect doses of study drug after discharge
  - Day 29 – Collect final vital Status

PETAL Subject ID _____ **Randomization Number** _____

Study Day for which assessment is being performed (circle one): Day 8 Day 15 Day 29

Date associated with Study Day: _____/_____/_____

Date call performed: _____/_____/_____ Time call performed: _____:_____

Research team member making call: _____

Hello, my name is _____ and I am calling from _____ hospital. I am calling you because you (or your loved one) were part of a research study about taking Hydroxychloroquine (the ORCHID study) when you (or your loved one) were in the hospital recently. An important part of this study is to find out how participants are doing after they leave the hospital. We also would like to know if participants needed other care after leaving the hospital.

I would like to ask you a few questions about how you (or your loved one) are doing. This should take about 5-10 minutes. Is this a good time to talk? If not, may we call back at another time?

Response received from Participant/Surrogate

- ☐ **Yes** → Continue conversation
- ☐ **No**, please call back → Arrange date and time for call back
- ☐ **No**, declined to participate in follow up call → Obtain and document:
  - Vital Status, data/time of death, safety outcomes and AEs
  - Document in a Note to File if unable to determine vital status and safety

COVID Ordinal Outcomes Scale

Which of the following best describes you on _____?
(Date associated with Study Day)

- ☐ Not hospitalized without limitation in activity
  - o "*I have no problems doing my usual activities*"
- ☐ Not hospitalized with limitation in activity
  - o "*I have slight, moderate, or severe problems doing my usual activities*"
- ☐ Hospitalized not on supplemental oxygen
- ☐ Hospitalized on supplemental oxygen
- ☐ Hospitalized on non-invasive ventilation or high flow nasal cannula
- ☐ Hospitalized on invasive mechanical ventilation or ECMO
- ☐ Dead
  - o If died, date of death: _____/_____/_____

Symptoms

Which of the following symptoms were you experiencing on _____?
(Date associated with Study Day)

- ☐ Cough
- ☐ Fever (temperature > 99.5ºF with a thermometer)
- ☐ Feeling feverish (even if temperature was not taken)
- ☐ Shortness of breath
- ☐ Chest tightness
- ☐ Sore throat
- ☐ Weakness or fatigue
- ☐ Other: _____

Saftety Outcomes

Have you experienced any of the following?

- ☐ Seizure: Date of first occurrence _____/_____/_____
- ☐ Low blood sugar with symptoms: Date of first occurrence _____/_____/_____
- ☐ Skin rash or mouth sores: Date of first occurrence _____/_____/_____
- ☐ Started dialysis: Date of first occurrence _____/_____/_____

Post-discharge Outcomes

Have you visited the Emergency Department since you were discharged from the hospital?

- ☐ Yes: Date _____/_____/_____ → record in post-discharge outcomes CRF
- ☐ No

Have you been readmitted to the hospital since you were discharged from the hospital?

- ☐ Yes: Date _____/_____/_____ → record in post-discharge outcomes CRF
- ☐ No

Have you received supplemental oxygen since you were discharged from the hospital?

- ☐ Yes: Date of final O2 use _____/_____/_____ → post-discharge outcomes CRF
- ☐ No

New Health Issues

Have you experienced any other health problems since discharge from the hospital or any worsening of health problems that began in the hospital?

- ☐ No
- ☐ Yes, if yes
  - o Date of onset: _____/_____/_____
  - o Category of problem:
    - ▪ Nervous system (e.g., hearing changes)
    - ▪ Circulatory system (e.g., low blood pressure)
    - ▪ Respiratory system (e.g., coughing up blood)
    - ▪ Digestive system (e.g., vomiting)
    - ▪ Renal system (e.g., blood in the urine)
    - ▪ Endocrine system (e.g., high blood glucose)
    - ▪ Integumentary system (e.g., rash or skin changes)
    - ▪ Hematological system (e.g., bleeding or bruising)
    - ▪ Muscular system (e.g, muscle weakness)
    - ▪ Skeletal system (e.g., broken bone)
    - ▪ Reproductive system (e.g.,
    - ▪ Other
  - o Description of problem: _____

_____

_____

***Refer to AE or Reaction flowchart to determine if issue should be reported as AE**

If dose CRFs are not complete in REDCap,

collect date/time of any doses after hospital discharge:

	Dose 2	Dose 3	Dose 4	Dose 5	Dose 6	Dose 7	Dose 8	Dose 9	Dose 10
Date									
Time									