1. **PURPOSE**

This SOP provides supplemental information regarding procedures for screening the potential participants for inclusion in the study and the process for obtaining consent and enrolment and documentation related to these procedures.

Site staff should be familiar with the study protocol for all further requirements for study conduct.

2. **PROCEDURE**

2.1. **INCLUSION CRITERIA**

The Participant must meet ALL of the following:

1. Participant is willing and able to give informed consent for participation in the study and agrees with the study and its conduct

   *It will be important to ensure informed consent is obtained from the Participants and that they can stay in the study for up to 5 months.*

2. Agrees not to self-medicate with chloroquine, hydroxychloroquine or other potential antivirals

   *We will be using chloroquine/hydroxychloroquine as the active drug so if a Participant takes additional chloroquine or hydroxychloroquine, the participant may be at risk of increased toxicity or having an impacted effect on the virus.*

   *Antivirals should be avoided as they may have antiviral activity against the COVID-19 virus and/or may synergistically enhance the antiviral effect of chloroquine/hydroxychloroquine.*

3. Adults less than 70 years old at the time of consent

   *This is defined as the local legal age of an adult in a given country. We expect most participants will be less than 60 years old due to working status, but the maximum age allowed is 70, i.e., should not have reached their 70th birthday as of the time of consent.*
4. Not previously diagnosed with COVID-19

We must only enroll Participants who have not had a confirmed COVID-19 infection, in order to provide the best expected population who have not been previously exposed to COVID-19.

5. Not currently symptomatic with an ARI (acute respiratory illness)

Participants who have an active ARI cannot be enrolled, due to potential confounding of symptom assessment. This may also be an undiagnosed case of COVID-19.

6. Participant is a healthcare worker or is a person at risk of contracting COVID-19

Healthcare workers working in a facility where there are cases of either proven or suspected COVID-19 or anyone who is not a healthcare worker who is likely or determined to be at risk for contact with COVID-19 infection is eligible for inclusion.

Determination of risk and eligibility for this criterion is at the discretion of the site PI.

7. Possesses an internet-enabled smartphone (Android or iOS)

Note that an Android- or iOS-compatible tablet is also acceptable if the device has internet connection. Participants may not enter data through a laptop, as the ePRO system is app-based.

It is also recommended that where necessary, sites confirm participants are able and comfortable to use the app for the duration of study participation, e.g., if illiterate, prior to enrolment.

2.2. EXCLUSION CRITERIA

The Participant may not enter the study if ANY of the following apply:

1. Hypersensitivity reaction to chloroquine, hydroxychloroquine or 4-aminoquinolines

A known allergy (e.g. anaphylaxis, skin rash) to a drug is a contraindication to its use. This will be determined by history.

2. Contraindication to taking chloroquine as prophylaxis e.g. known epileptic, creatinine clearance < 10 ml/min

This will be determined by history. If a participant had a history of epilepsy in the past or is currently on treatment for epilepsy, he/she will be excluded from the trial.
A creatinine clearance of < 10 ml/min is defined as a suggested parameter for consideration of renal impairment; it is expected if this low level has been seen that a participant would be aware that he/she has renal impairment.

3. Already taking chloroquine, hydroxychloroquine or 4-aminoquinolines, or history of these medications within the previous 7 days

   This is self-explanatory.

4. Taking a concomitant medication described in Section 8.5

   Participants cannot be enrolled in the study if taking one of these drugs at the time of screening and it cannot be stopped. This includes the following:

   **Antiarrhythmic medications:** digoxin, amiodarone, sotalol, flecainide

   **Antiparasitic/malarial agents:** mefloquine, halofantrine, praziquantel

   **Antibiotics:** levofloxacin, moxifloxacin, ciprofloxacin, azithromycin, clarithromycin, erythromycin

   **Antifungal drugs:** fluconazole, ketoconazole, itraconazole, terfenadine

   **Psychoactive drugs:** lithium, quetiapine, chlorpromazine, thioridazine, ziprasidone, haloperidol, droperidol, methadone

   **Migraine treatment:** sumatriptan

   **Antihistamines:** astemizole

   **Antiemetics:** prochlorperazine, metoclopramide

   **Cancer treatments:** abiraterone, doxorubicin, dacarbazine, enzalutamide, idelalisib, mitotane

   **Other specific drugs:** ciclosporin, conivaptan, agalsidase alfa or beta, mifepristone, stiripentol

   Pls can also access crediblemeds.org to check other agents that may prolong the QT interval

5. Known retinal disease

   This exclusion criterion is included because long-term chloroquine use can cause irreversible retinal changes. Although we will only give chloroquine for three months, we do not want to increase the risk of exacerbating retinal disease.
6. Inability to be followed up for the trial period

*Follow-up is important in this study so if a participant thinks they cannot remain in the study for the required three months (five if they suffer an important drug reaction), they should be excluded from enrolment.*

7. Known prolonged QT syndrome (however ECG is not required at baseline)

*Chloroquine at the doses we plan to use may cause mild prolongation of the QT interval. If a participant knows he or she has QT prolongation, they should be excluded. If the site investigator has concerns they should address these further before confirming enrolment.*

8. Known pregnancy or women who are actively trying to become pregnant

*Pregnant women or participants who plan to be pregnant cannot be enrolled in the study. Although chloroquine has been safely used in pregnant women for the treatment of malaria, we do not know if there is any benefit in the context of prevention of COVID-19. As such, although this drug is considered safe, and the risks are low in pregnancy, we have opted to exclude women from the present study.*

9. Prior diagnosis of porphyria

*It is stated that porphyria may be exacerbated by this drug. Participants with porphyria are challenging because the disease is very rare and clinical experience is likely be limited to specialized units. Given this uncertainty as to whether there is a meaningful interaction between chloroquine/hydroxychloroquine and porphyria, we have opted to exclude participants with this condition from the study.*

*Other: Adults should have the body weight of ≥ 40 kg in order for proper dosing of study drug. In the unlikely scenario that a potential participant weighs less than 40 kg, the participant should not be included.*

*The investigator may consult the physician’s guidance documents for any further questions regarding eligibility of potential participants*

10. Previously received any dose of COVID-19 vaccine

*Participant who have received COCIV-19 vaccine before screening will not be eligible to enrol in the study. Note: if COVID-19 vaccination is received while in the study, the participant will be asked to discontinue study medication and remain in study follow up to the end.*
2.3. CONSENT

As this study enrolls healthcare workers and other staff working in a facility where there are cases of either proven or suspected COVID-19, it is important to explain to the participants that participation in the study is entirely voluntary and it will not have any negative impact to their current employment if they choose to decline to participate.

If the Participant agrees to participate, a research team member will go over the consent process and obtain consent from the Participant in writing. The Participant can refuse consent to participate even if all inclusion and exclusion criteria are fulfilled.

If the participant is illiterate, he or she can still be enrolled in the study so long as he or she can use the mobile application. The site PI or a team member will need to establish this. Screening and Enrolment Log

Re-consent:

Participants in the study will be asked to provide consent when new information becomes available or when there are changes in the study procedures which may affect the participant’s decision to continue participation in the study.
Protocol amendment v6 has included the implication of COVID-19 vaccination for the participants already in the study. The participants may receive vaccines while they are in the study follow-up and if this happens the study procedures will be altered. Hence, they need to provide additional consent (re-consent) to continue their participation and agree to the additional or change of study procedures.

Re-consent should be obtained from the participants soon after the amendment v6 and PIS/ICF have received the approval from the applicable ECs. Site staff should contact the participants by phone if the next monthly visit will not take place soon and record their decision in the phone contact log (or the consent document). The consent form for re-consent must be completed when the participants come to the clinic at the next visit.

If the participants do not agree to re-consent, they can still stay in the study and follow up as per protocol v5 (if not vaccinated). If vaccinated, they will be discontinued from the study.

2.4. SCREENING AND ENROLMENT LOG

Axiom Fusion captures the screening number, date of screening, reason for screening failure, date of randomization, and date of consent. These data can be generated via Fusion’s Screening and Enrolment Report.
2.5. Screening CRF

The Screening CRF must be completed for all Participants who were screened, regardless of whether they were enrolled or not enrolled in the study. In addition, all screened participants must be registered into Fusion including screen failed. Refer to the CRF completion guidelines for Screening CRF for further information and ePRO manual/instruction how to register participants into Fusion. The site investigator should sign the screening CRF to verify eligibility review prior to enrolment and randomisation.

2.6. Enrolment

Once the Participant is enrolled in the study, a study drug kit will be allocated by the relevant study staff in sequential order. Refer to COPCOVSOP IMP Management for details of drug allocation. The drug kit number is the unique Subject Number assigned to the individual and this number which will be used throughout the study period on all study documents (e.g. CRF, lab report, sample request forms). The participant’s name and other identifying information should not be written on the study documents except on the consent form and the Subject Identification log (DOB may be collected on the CRF when allowed per local standard).

2.7. Participant Identification Log

For every Participant enrolled in the study, please complete the Participant Identification Log which include the following: Participant ID number, initials, complete name, and contact details of current address and phone number. The Participant Identification Log is a confidential document and must be kept at the study site at all times, i.e. never send or share this document with other parties other than the site study team.

3. Related Documentation

- Attachment 1 - Screening CRF
- Attachment 2 - Axiom Fusion’s Screening and Enrolment log
- Attachment 3 - Participant Identification Log
### Screening Form

**Site Code:** [ ] [ ] [ ]  **Screening Number:** [ ] [ ] [ ]  **Date:**  [ ] [ ] [ ] [ ]

#### Inclusion Criteria (all should be "YES")
1. Adults (exact age is dependent on countries) less than 70 years old at the time of consent.  
   - [ ] YES  
   - [ ] NO
2. Not previously diagnosed with COVID-19  
   - [ ] YES  
   - [ ] NO
3. Not currently symptomatic with an Acute Respiratory Illness (ARI)  
   - [ ] YES  
   - [ ] NO
4. Participant is a healthcare worker or person at risk of contracting COVID-19  
   - [ ] YES  
   - [ ] NO
5. Possesses an internet-enabled smartphone (Android or iOS)  
   - [ ] YES  
   - [ ] NO
6. Agrees not to self-medicate with chloroquine, hydroxychloroquine or other potential antivirals  
   - [ ] YES  
   - [ ] NO
7. Participant is willing and able to give informed consent for participation in the study and agrees with the study and its conduct  
   - [ ] YES  
   - [ ] NO

#### Exclusion Criteria (all should be "NO")
1. Hypersensitivity reaction to chloroquine, hydroxychloroquine or 4-aminoquinolines  
   - [ ] YES  
   - [ ] NO
2. Contraindication to taking chloroquine as prophylaxis e.g. known epilepsy, known creatinine clearance < 10 ml/min  
   - [ ] YES  
   - [ ] NO
3. Already taking chloroquine, hydroxychloroquine or 4-aminoquinolines, or history of these medications within the previous 7 days  
   - [ ] YES  
   - [ ] NO
4. Taking a concomitant medication described in section 8.3 of the protocol  
   - [ ] YES  
   - [ ] NO
5. Known renal disease  
   - [ ] YES  
   - [ ] NO
6. Inability to be followed up for the trial period  
   - [ ] YES  
   - [ ] NO
7. Known prolonged QT syndrome (however ECG is not required at baseline)  
   - [ ] YES  
   - [ ] NO
8. Known pregnancy or women who are actively trying to become pregnant  
   - [ ] YES  
   - [ ] NO
9. Prior diagnosis of paroxysm  
   - [ ] YES  
   - [ ] NO
10. Previously received any dose of COVID-19 vaccine  
    - [ ] YES  
    - [ ] NO

Sites should refer to the physician's guidance document for any questions regarding eligibility.

**Is participant eligible:**  [ ] YES  [ ] NO  **Is participant enrolled:**  [ ] YES  [ ] NO

☐ I have reviewed the eligibility criteria and confirm that the participant is eligible.

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**Randomisation date:** [ ] [ ] [ ] [ ] [ ] [ ]  **Subject Number:**

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**STUDY:** Chloroquine/hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting: a randomised, placebo-controlled prophylaxis study (COPCOVID)

SOP Version: V3  
SOP Date: 3 Feb 2021  
[SOP template v2/22 July 2020]
Attachment 2 – Axiom Fusion’s Screening and Enrollment Log

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Attachment 3 – Participant Identification Log

Participant Identification Log

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**STUDY**: Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting: a randomised, placebo-controlled prophylaxis study (COPOCV)
4. **SOP VERSION HISTORY**

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<td>2 / 22 Jul 2020</td>
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                      2. Re-consent information is added  
                      3. All screened participants must be registered into Fusion including screen failed is added into screening CRF section. |

5. **SOP SIGNOFF**

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