Chloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study

(COPCOV Study)

LABORATORY GUIDELINES & STANDARD OPERATING PROCEDURES

Version 6.0 dated 1 March 2021
Scope of this document

This document is intended to serve as a guideline for personnel performing laboratory and other related procedures for the research study entitled “Chloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study (COPCOV study)”. This document further contains Standard Operating Procedures to be followed by the study personnel. Unless otherwise agreed in advance, the guideline is applicable to all sites participating in the COPCOV study and to all personnel at these sites who will perform study related laboratory procedures.

This document must be viewed in conjunction with the most recent version of the COPCOV protocol. In case of discrepancies between the study protocol and lab guidelines, please implement procedures as described in the study protocol and immediately inform Ranitha Vongpromek (ranitha.vongpromek@wwarn.org) and Cholrawee Promnarate (cholrawee.promnarate@wwarn.org) of such discrepancies.
STANDARD OPERATING PROCEDURE

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

SOP Version: V6 SOP Date: 01 Mar 2021
[SOP template V2/22 July 2020]
1. Introduction to COPCOV Study Samples

COPCOV participants are followed up for up to 5 months; samples are collected following a defined scheme, as outlined below. Significant numbers of samples with varying destinations, volumes and associated procedures will be collected, it is therefore essential to maintain a clear sample labelling scheme.

1.1 Schedule of procedures for COPCOV study

<table>
<thead>
<tr>
<th>Procedures</th>
<th>Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
</tr>
<tr>
<td>Screening</td>
<td>1</td>
</tr>
<tr>
<td>Eligibility assessment</td>
<td>X</td>
</tr>
<tr>
<td>Informed consent</td>
<td>X</td>
</tr>
<tr>
<td>Demographics</td>
<td>X</td>
</tr>
<tr>
<td>Medical history</td>
<td>X</td>
</tr>
<tr>
<td>Randomisation</td>
<td>X</td>
</tr>
<tr>
<td>Set up mobile app</td>
<td>X</td>
</tr>
<tr>
<td>Given thermometer</td>
<td>X</td>
</tr>
<tr>
<td>Venous blood test</td>
<td>Y</td>
</tr>
<tr>
<td>Observed 1(^{st}) dose of study medication</td>
<td>X</td>
</tr>
<tr>
<td>Dispensation of study medication (unless)</td>
<td>X</td>
</tr>
</tbody>
</table>

\(^1\) ARI symptom onset: Day 0–Day 90

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<table>
<thead>
<tr>
<th>SOP TITLE: COPCOV Study Laboratory SOPs &amp; Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>diagnosed as COVID-19 before visit)</td>
</tr>
<tr>
<td>Compliance assessment</td>
</tr>
<tr>
<td>DBS</td>
</tr>
<tr>
<td>X*</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>Adverse event assessments</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>Questions about wellbeing, illness, COVID-19 diagnosis and clinical severity data</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>X</td>
</tr>
<tr>
<td>Nose and throat swab (+/- sputum)</td>
</tr>
<tr>
<td>X</td>
</tr>
</tbody>
</table>

1 Can be repeated on multiple occasions if illness worsens or new ARI during trial period.
2 If not already collected at Day 90.
3 If these timepoints are collected in vaccinated participants then no sample will be collected at Day 90.
Y 10mls of venous blood
Z 5mls of venous blood
* This sample is expected to be obtained from the venous blood sample drawn at the same visit. If necessary direct finger prick may be performed.
2. Guidelines & Standard Operating Procedures

2.1 Study Staff and Training

All study staff must undergo comprehensive training before the study is implemented. Refresher training sessions should also be planned and implemented. Various “Working Protocols” appended to this document should be used as supporting documents for these training sessions.

General Notes on Sample Collection, Labelling, Processing

- Always collect written informed consent from the participant prior to performing any study-related procedures that are not part of routine patient care.
- Collect samples before drug administration on all days.
- Do NOT freeze blood samples before processing.
- Keep at 2—8 °C for 6 hours if needed until processing. Process in a timely fashion.

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STANDARD OPERATING PROCEDURE

SOP TITLE: COPCOV STUDY LABORATORY SOPs & GUIDELINES

- Pre-label all cryovials and swabs before transferring specimen.
- Sample labelling on cryovials & Sample Log (see Section 2.2) must be done systematically AT THE SAME TIME.

2.2 SOP – Specimen labelling and tracking

Objective or Intended Use
To describe the procedures to be followed in the COPCOV study for specimen labelling, logging and tracking.

Principle
To ensure on study outcome, specimens collected during the course of a clinical study must be labelled using a robust system to ensure that data generated by the analyses of the specimens are linked back to the correct study subject.

A sample label consists of a unique barcode number along with space to be filled with the sample’s information. All samples which are stored or shipped to collaborating laboratories must have a barcode label with a unique Sample Number. This facilitates checking and tracking of specimens.

Specimens must be collected on the scheduled time-points as far as possible; in all cases, the actual date and time of collection must be noted. Further, information on the specimen such as the date and time of its collection and storage, approximate volume, etc. are noted on a Sample Log as basic indicators of specimen quality. All of the sample information is entered into a database along with the unique number thus creating a link between the study subject, the specimen and eventually the data generated from its analysis.

Sample labels will be used for the COPCOV study are resistant to ultra-low temperatures (down to -196°C) when used correctly. The labels must be stuck to dry surfaces only. These labels must only be used for cryovials and filter papers, they must NOT be used for Vacutainers/Microtainers.

Sample Logs are used to log relevant specimen information and to document the unique Sample Number assigned to each specimen which is tracked. The Sample Log will also be used as the “Packing List”. The original is to be sent along with the boxes containing the specimens when they are shipped from the site to the central laboratory and a copy should be kept on site. Each specimen is stored in the position already indicated on the Sample Log.

Materials and Equipment
For Labelling
- Sample labels (3.425” X 0.8” in Freezerbondz labels; to be used for all specimens stored or shipped to collaborating laboratories)
- Permanent/indelible marker

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[SOP template V2/22 July 2020]
**STANDARD OPERATING PROCEDURE**

**SOP TITLE:** COPCOV STUDY LABORATORY SOPs & GUIDELINES

**Method**

- Labelling

Sample labels (Cryolabels) will be used for all samples. These labels have been tested and selected for their ability to withstand ultra-low temperatures, including direct exposure to liquid nitrogen. The pre-printed sample labels ("Wraparoun Combo-barcode" labels) will be provided for study samples: All information on the label must be completed using permanent cryomarkers and stuck on all samples that will be collected for the study while the duplicate barcode number must be stuck on the sample logsample. This must be done systematically to avoid interchanging labels between samples. These labels are NOT be used for sample collection containers such as Vacutainers and Microtainers.

**Figure 1: "Sample Label"**

```
<table>
<thead>
<tr>
<th>Sub ID</th>
<th>Int.</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1844001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
```

```
Collection Date & Time
Sample Type
```

**"ALWAYS stick the label with clear-wraparound on the specimen and the label without wraparound on the Sample Log before labelling the next sample".**

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[SOP template V2/22 July 2020]
Duplicated barcode labelling of the sample and the Sample Log allows each sample and its associated information to be linked to a unique number which can then be used to track the sample. These wraparound labels must be stuck on all samples. Sample labels must NOT be used for sample collection containers such as Vacutainers and Microtainers.

Information entered on the Sample label:

I. Subject ID as noted on CRF.
II. Subject initials as noted on CRF.
III. Time point refers to the follow up day and is entered as
   a. Day 0-90 = D0 – D90 etc.
   b. In case of onset (Day with Symptom) of COVID-19 or ARI (acute respiratory infection), the time point is noted as prefix “DSYM” follow with the day of sample collected; i.e. on set of COVID day 55 is recorded as DSYM55.
   c. In case of an unscheduled visit, the time point is noted as prefix ‘UN’ follow with the day of sample collected; i.e. unscheduled visit day 55 is recorded as UND55.
   d. In case of vaccination
      i. Prior to vaccine (or within 3 days after first dose), the time point is noted as “DV”
      ii. Day 28 (+/-3 days) post first vaccine dose, the time point is noted as “DV 28”

IV. Actual Date & Time of Sample Collection
   a. Dates must be recorded in the following format: dd/mm/m/yy; i.e. 01/APR/20.

V. Time must be recorded in the 24-hr format; i.e. 1:30 a.m. is recorded as 01:30 and 1:30 p.m. is recorded as 13:30.

VI. Sample type shall be recorded as applicable.
   a. Plasma
   b. Serum
   c. Pellet
   d. TNS (Throat and Nose swab)
   e. DBS
   f. Sputum

• Sample Logs for samples

The Sample Log creates a physical link between a sample and the associated information. The label without the wraparound from the Combo label pair is stuck onto the Sample Log immediately after the label with clear-wraparound is stuck on the sample to ensure that the correct patient-sample-data link is created.
**STANDARD OPERATING PROCEDURE**

**SOP TITLE:** COPCOV STUDY LABORATORY SOPs & GUIDELINES

**Figure 2: Sample Log**

<table>
<thead>
<tr>
<th>COPCOV SAMPLE LOG: STUDY ROUTINE</th>
<th>Initial: SSS</th>
<th>D0 : 19-May-2020 10:00</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject No: A002-001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Planned Date/Time of Collection</th>
<th>Actual Date/Time of Storage</th>
<th>Sample Type</th>
<th>Vol. (mL)</th>
<th>Barcode</th>
<th>Lab.Tech (Initials)</th>
<th>Inventory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NA</td>
<td>Venous Blood</td>
<td>DBS (2 spots, 50μL/spot)</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D00</td>
<td>19-May-2020 10:00</td>
<td>EDTA 4 mL</td>
<td>Plasma (3 aliquots × 0.5 mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cell pellet (0.5 mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clotted Blood 6 mL</td>
<td>Serum (3 aliquots × 1 mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D30</td>
<td>18-Jun-2020 10:00</td>
<td>Finger prick</td>
<td>DBS (2 spots, 50μL/spot)</td>
<td>NA</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Not applicable, participant is vaccinated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D60</td>
<td>19-Jul-2020 10:00</td>
<td>Finger prick</td>
<td>DBS (2 spots, 50μL/spot)</td>
<td>NA</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Not applicable, participant is vaccinated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D90</td>
<td>17-Aug-2020 10:00</td>
<td>Venous Blood</td>
<td>DBS (2 spots, 50μL/spot)</td>
<td>NA</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Not applicable, participant is vaccinated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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SOP Version: V6 Date: 01 Mar 2021
[SOP template V2/22 July 2020]
## COPCOV SAMPLE LOG: STUDY-ONSET OF COVID OR ARI

<table>
<thead>
<tr>
<th>Subject No: A002-001</th>
<th>Initial: SSS</th>
<th>DO: 19-May-2020 10:00</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time Point</strong></td>
<td><strong>Actual Date/Time of Storage</strong></td>
<td><strong>Sample Type</strong></td>
</tr>
<tr>
<td>DSYM D</td>
<td></td>
<td>TNS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sputum</td>
</tr>
<tr>
<td>DSYM D</td>
<td></td>
<td>TNS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sputum</td>
</tr>
</tbody>
</table>

## COPCOV SAMPLE LOG: STUDY Vaccination

<table>
<thead>
<tr>
<th>Subject No: A002-001</th>
<th>Initial: SSS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time Point</strong></td>
<td><strong>Actual Date/Time of Storage</strong></td>
</tr>
<tr>
<td>DV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>DV28</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**STUDY:** Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting: a randomised, placebo-controlled prophylaxis study (COPCOV)
## COPCOV SAMPLE LOG: UNSCHEDULED VISIT

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Actual Date/Time of Storage</th>
<th>Sample Type (Mark &quot;X&quot; if collected)</th>
<th>Vol. (mL)</th>
<th>Barcode</th>
<th>Lab.Tech (Initials)</th>
<th>Inventory Box/Bag Post.</th>
</tr>
</thead>
<tbody>
<tr>
<td>USD</td>
<td></td>
<td>○ Clotted Blood</td>
<td>Serum (3 aliquots x 1 mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>○ Other (please specify)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>○ Other (please specify)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Information entered on the Sample Log:**

i. Subject ID as noted on CRF.

ii. Subject initials as noted on CRF.

iii. Actual Date & Time of Sample Collection and Storage
   - Dates must be recorded in the following format: dd/mmm/yy; i.e. 01/APR/20.
   - Time must be recorded in the 24-hr format; i.e. 1:30 a.m. is recorded as 01:30 and 1:30 p.m. is recorded as 13:30.

iv. Barcode label, a pair of duplicated barcode number must be stuck on sample log of an associated sample while the label with wrap-around stuck on sample tube swab or filter paper.

v. Laboratory technician's initials of who had processed sample.

vi. Box's name/number and position of sample storage.

Once completed, the Sample Log data must be entered to the database and data must be sent along with the samples/swabs to Bangkok.
Specimen labelling and storage

- Check sample log and/or COPCOCV Study Work Flow to determine which specimens are to be processed from the received blood sample.
- Prepare cryovials/swabs/filter paper if required:
  - Complete one sample label per cryovial/swab with the Subject ID, subject initials, follow-up time-point, date and time of collection and Sample type as indicated on section 2.2 “Labelling”.
  - On the sample log, enter the Date & Time of sample collection as indicated on section 2.2 “Sample log for samples”.
  - Attach the sample label with wrap-around to the cryovial/swab.
  - Attach the barcode label (sample label without wrap-around) to the Sample Log.
  - After processing the specimen, place it in sample box, enter Box No and position in the Sample Log, enter laboratory technician’s initials.

Pre-shipment specimen verification

- Verify the following for the specimens (cryoboxes should be placed in an insulated box with frozen ice-packs to prevent thawing while performing the verification):
  - All the cryovials/swab should be in the positions as indicated in the Sample Log.
  - All the barcodes must be associated with the correct specimen information.
  - Note any errors/rectifications on the Sample Log.
- Data from Sample Log will be used as packing list and data must be sent along with the specimens to MORU/WWARN-SML.

Additional notes

- A barcode scanner will be required in case data entry from the sample logs is performed at site. A scanner can be provided upon request or if it is locally procured, it must be capable of reading 2D barcodes (Data Matrix format; e.g. Zebra Symbol DS4308 or similar).
- Minimum requirements in case another labelling system is used at a site are:
  - Each aliquot of every sample must have a unique identifier and must be labelled with a waterproof label with indelible printing (e.g., thermal transfer printing) or writing.
  - Each aliquot/sample must be linked to a Subject ID and to a date, time, time-point of sample collection. This may done be by printing or by writing the Subject ID and other identifiers on the label along with the barcode or by electronic data capture.
  - All of the data recorded on the sample schedule or log as described above must be recorded and entered into databases and must be exportable in commonly used formats (.xlsx, .csv, etc.) The variables to record are: unique aliquot ID, Subject ID, date/time/time-point of specimen collection, date/time of specimen storage (for frozen specimens), volume of specimen (for plasma, serum, packed cells).

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2.3 SOP – Sample collection and processing to obtain plasma, serum and cell pellet

Purpose and scope:
This document describes the procedures for processing of blood samples to obtain plasma, cell pellet and serum for future analysis

- Serum at D0, D90, UN D≤150, DV and DV28
- Cell pellet at D0
- Plasma at D0

Whole blood collected in an EDTA tube (plasma and cell pellet samples) or in a serum tube (serum sample only) is to be processed to obtain plasma, cell pellet and serum as applicable. The tube should be at room temperature (18-25 °C) prior to use. Keep the sample at 2—8°C for 6 hours if it is not processed immediately after collection.

Centrifuge whole blood at 1500g for 10 minutes to ensure adequate separation/yields of plasma and removal of platelets from the plasma. Immediately obtain plasma, cell pellet and serum after centrifugation. Immediately freeze the plasma, cell pellet and serum samples at or below -80 °C in a laboratory freezer. Do not thaw sample after freezing. Record the clock time of sampling and storing and note any sign of haemolysis.

Equipment and materials

- Centrifuge
- Micropipette and tips
- 2 ml Cryovial
- Human readable label
- Indelible marker
- Sample label

Specimen

- EDTA anticoagulated blood
- Clotted blood

Procedures

- Complete sample label using an indelible marker and affix label on cryovials. Affix the duplicate barcode label on the corresponding line on the sample log.
- Centrifuge anticoagulated whole blood EDTA tube and/or clotted blood tube at 1500 xg, 10 minutes, 25 °C (4°C is acceptable) with no brake.
2.4 SOP – Preparation of Dried Blood Spots on Whatman 31 ET Chr paper for Chloroquine level determination

Purpose and scope
To collect whole blood on Whatman 31ET Chr Chromatography Papers for Chloroquine level determination.

Principle
Chloroquine/hydroxychloroquine can be extracted from dried capillary blood which has been blotted onto Whatman 31ET Chr Chromatography Paper. Whatman 31ET Chr Chromatography Paper is pure cellulose product from cotton linters with no additives. It is advisable to store the samples in individual sealable sachets with silica gel desiccant. 50 µL of blood should be applied to cards. A measured amount of blood is applied to ensure consistency and comparability of the results.

Specimen
- Venous blood from needle or capillary blood from finger-prick

Equipment and Consumables
- Whatman 31ET Chr Chromatography Paper
- Micropipette (20 – 200 µL)
- Micropipette tips (20 – 200 µL)
- Silica gel (desiccant) in a sachet
- Sealable plastic sachet
- Indelible marker
- Sample label

Method
- Label the plastic sachets (directly using an indelible marker) and the filter paper using pencil with the Subject No. Initials, Day of Follow-up, Date & Time of sample collection. Write the
date and time of the last drug intake (D30, D60 and D90 only) at the back of the filter paper, avoiding the sample areas.

- Collect venous blood sample or capillary blood sample from finger prick
  - DBS collection from Venous blood sample (For D0, D90 or DV only)
    - Use the leftover blood in the syringe after transferring to EDTA and/or Clotted blood tubes.
    - Directly drop blood from the needle onto the embossed circle areas on DBS paper until the embossed circle areas are completely filled. Make sure the blood soaks through to the other side of the filter paper - the blood spot should be roughly the same size on both sides of the paper.
  
  **NOTE:** If this method fails, collect DBS using the finger prick methods as described below.

  - DBS collection from capillary blood from finger prick
    - Wear a new pair of disposable gloves. Use an alcohol swab to clean the finger before puncturing. Allow the skin to dry.
    - Open the sterile lancet. Press the lancet toward the finger to puncture the finger, a little off the center of the finger pad. Discard the lancet after use. If done properly a single prick should be sufficient to collect all of the blood required.
    - Wipe away the first drop of blood with dry, clean cotton wool and apply gentle pressure to the finger. Discard cotton wool after use.
    - Apply moderate pressure, approximately 1 cm behind the site of the puncture, to obtain a drop of blood. Do not squeeze too tightly as it will cause tissue plasma to mix with and dilute the blood.
    - Release this pressure immediately to allow recirculation of the blood.
    - Apply 50 μL of blood onto the embossed circle areas on DBS paper using micropipette as figure 9, make two spots of 50 μL each. 50 μL spots are the requirement for this method.

      - Allow the blood to dry for 6 hours to overnight.
      - Protect the sample from dust, flies and direct sunlight
      - Samples should be dried in a way that they do not come into contact with other surfaces or samples while drying.
      - Refer to appendix 1 for the examples of good and bad quality DBS

- At the processing laboratory, stuff fill in the sample label using the information as written on the filter paper and place the sample label to the filter paper. Affix the duplicate barcode label on the corresponding line of the sample log.

- Storage
  - Place the paper card with DBS into its plastic sachet.
  - Add one sachet of desiccant and close bag well.
  - Store the filter paper card in a cool, dry place protected from dust and light.

Figure 9. Cards for collection of dried blood spots
2.5 SOP – Swab and Sputum Samples Collection

The procedure for obtaining a throat and nasal sample and sputum for the diagnosis of COVID-19 and other viruses will be followed to Micro SOPs v.2.0-2020-04-07 below.

2.5.1 Combined throat and nose swab done by the study staff

Purpose
This SOP describes the procedure for obtaining a throat and nasal sample for the diagnosis of COVID-19 and other viruses.

Samples in the COPCOV study will be taken at the research site or subject’s home, according to local practice.

If these guidelines differ slightly from the procedures in your hospital, do not worry.

Do what is your usual practice.

The aim is the same – obtain a good specimen ensuring maximum safety.

One swab will be used to take a combined throat and nasal sample. If subjects do not like this, opt for a nasal swab as recent but limited data suggest a higher yield of SARS-CoV-2 compared to a throat swab (Zou, Ruan et al. 2020).

Taking swabs requires respiratory precautions so full personal protective equipment (PPE) must be used by the person taking the swab:

- Long sleeved gown or plastic apron
- facial mask
- eye protection

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STANDARD OPERATING PROCEDURE

SOP TITLE: COPCOV STUDY LABORATORY SOPs & GUIDELINES
- gloves
- alcohol hand rub

Please refer to the donning-doffing SOP (based on practice in the UK) and the UK government website:

General points
To ensure a good quality specimen, it is important to collect epithelial cells from the nasal septum and the pharynx.

Do not rush the procedure and be smooth with your actions
For the throat swab avoid the sides of the mouth and tongue
For the nasal swab, ask the subject to clear their nose gently with a disposable tissue

Labelling the specimen tube

Label the specimen tube by filling in the following details. The information can be filled in a sticker label and place on the specimen tube or written directly on the specimen tube.

- Subject ID
- Initial
- Date and time of sample collection (record this when you arrive at the subject's home)
- Type of specimen
  - TNS = throat and nose swab
  - NS = nasal swab
  - TS = throat swab

Procedure
Tell the subject that you will take a throat and nose swab and what the mild ill effects might be e.g. sense of irritation, cough, sneeze, or gag

Obtain verbal consent from the subject before proceeding
Ask the subject to clear his/her nose gently with a disposable tissue and then wash his/her hands with soap and water.
Find a suitable surface to clean with alcohol and place your PPE, swabs, bottles and pen.
Wash your hands then don the PPE

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

Take the throat swab first:

- Open the sachet of swab, label the tube with the information of subject ID, subject initials, date & time of collection
- Remove the swab out of the tube, do not let the sterile swab touch your fingers or other objects
- ask the subject to open their mouth and say “aaaah”
- insert the dry viral swab into mouth
- swab the posterior pharynx then
- tonsillar areas
- rotate the swab so that all ‘sides’ of the swab sample cells

GOOD:
✓ Back of the throat
✓ Tonsils

UNSUITABLE:
× Sides of the mouth
× Tongue

The nasal swab

- insert viral swab straight and backwards through the nostril (not upwards) along the floor of the nasal passage for about 2 cm
- place sideways pressure on the swab to collect epithelial cells from the midline nasal septum and rotate the swab 2-3 times
- repeat this in the other nostril
- place swab directly into the tube, snapped at its break point and broken, and the cap screwed home to lock the swab with the cap
Doffing PPE

Remove the PPE, as per your hospital procedure, and place in a biohazard-labelled plastic bag.

Specimen management

The nurse will deliver the sample to the laboratory for processing (maximum 4 hours), or the sample can be stored in 2-8 °C for no longer than 3 days.

Swab sample will be recorded in the sample log using the sample label and affix a duplicated barcode label on the relevant sample type on sample log.

This SOP concerns one swab and in the sample log, the swab will be recorded as a "TNS", a throat and nose swab, even if only a throat or nasal swab was taken.

If it is your practice that two swabs are taken or that a nasopharyngeal (NP) swab is taken, then the sample log will be amended accordingly to e.g. TS, NS, or NPS.

References


2.5.2 Combined throat and nose swab by study participants

Purpose
This SOP describes the procedure for subjects to take their own throat and nasal swabs at home.
Contact with the study nurse is intended to be minimal.

Preparation before leaving for home visit
Before the nurse goes on the home visit, he/she should:
Tell the subject the approximate time of arrival
Remind the subject how to perform the throat and nose swab
Ask that any children be kept in a separate room when he/she arrives

Preparation of the specimen tube
Label the specimen tube by filling in the following details. The information can be filled in a sticker label and place on the specimen tube or written directly on the specimen tube

- Subject ID
- Initial
- Date and time of sample collection (record this when you arrive at the subject’s home)
- Type of specimen – TNS = throat nose swab.

Put the specimen tube and swab in a plastic zip-lock bag with absorbent material e.g. tissue paper and close the bag.

At subject's home
Just before the nurse arrives at the subject’s home, he/she should:

- wash his/her hands with alcohol
- wear an N95 mask
- put on gloves
- put on a plastic apron if going into the house

After the subject answers the door, the nurse must

- confirm the identity of the subject
- then either:
  - hand the subject the bag containing labelled swab, ask him/her to perform the swabbing and wait outside* or
  - hand the subject the bag containing labelled swab, ask him/her to perform the swabbing in a distant room while the study nurse waits near the front door

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

SOP Version: V6 Date: 01 Mar 2021
[SOP template V2/22 July 2020]
Once the subject has finished swabbing, he/she will drop the swab into a zip-lock bag and close the bag and hand the bag to the study nurse.

The zip lock bag is then placed in another zip lock bag which the study nurse holds open.

* Only if this does not attract on lookers or in an apartment block and there is sufficient privacy.

**Doffing PPE**
Remove the gloves & dispose in a disposable bag
Wash hands with alcohol
Remove apron & dispose in a disposable bag
Wash hands with alcohol
Remove mask & dispose in a disposable bag
Wash hands with alcohol

**General points**
To ensure a good quality specimen, it is important to collect epithelial cells from the pharynx/tonsils and nasal septum.
The throat swab will be taken first, followed by one nostril then the other
For the throat swab avoid the sides of the mouth and tongue
For the nasal swab, the subject should clear his/her nose gently with a disposable tissue

**Procedure**

**Throat swab**
Take the throat swab first:

- Open the sachet of swab, label the tube with the information of subject ID, subject initials, date & time of collection
- Remove the swab out of the tube, do not let the sterile swab touch your fingers or other objects
- the subject will open the mouth and say aaaaah then
- insert the dry viral swab into mouth and swab the posterior pharynx & tonsillar areas
- rotate the swab so that all 'sides' of the swab sample cells

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

UNSUITABLE:
- Sides of the mouth
- Tongue

The nasal swab
- then the swab is inserted into one nostril about 2 cm & rotated
- the same is done in the other nostril
- the swab is then replaced in its tube, snapped at its break point and broken, and the cap screwed home to lock the swab with the cap

Specimen management

The nurse will deliver the sample to the laboratory for processing (maximum 4 hours), or the sample can be stored in 2-8 °C for no longer than 3 days.

Swab sample will be recorded in the sample log using the sample label and affix a duplicated barcode label on the relevant sample type on sample log.

This SOP concerns one swab and in the sample log, the swab will be recorded as a “TNS”, a throat and nose swab, even if only a throat or nasal swab was taken.

If it is your practice that two swabs are taken or that a nasopharyngeal (NP) swab is taken, then the sample log will be amended accordingly to e.g. TS, NS, or NPS.

Reference

STUDY: Chloroquine/hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting: a randomised, placebo-controlled prophylaxis study (COPCOV)
2.5.3 Sputum sample collection at participant's home

Purpose
This SOP describes the procedure for obtaining a sputum specimen at home.

General points
To ensure a good quality specimen, it is important the subject has a productive cough.

This is a medium risk procedure.

Preparation before leaving for home visit
Before the nurse goes on the home visit, he/she should:

Tell the subject the approximate time of arrival

Ask that any children be kept in a separate room when he/she arrives

Labelling the specimen tube
Sputum sample will be collected in a 50mL conical tube. Label the specimen tube by filling in the following details. The information can be filled in a sticker label and place on the specimen tube or written directly on the specimen tube

- Subject ID
- Initial
- Date and time of sample collection (record this when you arrive at the subject’s home)
- Type of specimen – Sputum

Put the specimen tube and swab in a plastic zip-lock bag with absorbent material e.g. tissue paper and close the bag.

At subject’s home
Before the nurse arrives at the subject’s home, he/she should:

- wash his/her hands with alcohol
- wear an N95 mask
- put on gloves
- put on a plastic apron if going into the house

After the subject answers the door, the nurse must:

- confirm the identity of the subject
- then either:
Once the subject has finished with sputum collection, he/she will drop the swab into a zip-lock bag and close the bag and hand the bag to the study nurse.

The zip lock bag is then placed in another zip lock bag which the study nurse holds open.

* only if this does not attract on lookers or in an apartment block and there is sufficient privacy.

Doffing
Remove the gloves & dispose in a disposable bag
Wash hands with alcohol
Remove apron & dispose in a disposable bag
Wash hands with alcohol
Remove mask & dispose in a disposable bag
Wash hands with alcohol

Specimen management
The nurse will deliver the sample to the laboratory for processing (maximum 4 hours), or the sample can be stored in 2-8 °C for no longer than 2 days.

Sputum samples will be recorded in the sample log using the sample label and affix a duplicated barcode label on the relevant sample type on sample log.

Reference

2.6 SOP – Samples transportation from Clinic to The Processing Laboratory

Purpose and scope:
This document describes the procedures for sending whole blood, swab or sputum samples from clinic to processing laboratory.
The blood collection tubes or swabs should be at room temperature (18-25 °C) prior to use. Sample shall be kept at 2—8 °C if it is not processed immediately after collection.

**Equipment and materials**
- Absorbent material or gauze
- Secondary container or ziplock bag
- Outer container or styrofoam box
- Indelible marker

**Specimen**
- EDTA anticoagulated blood
- Clotted blood
- Swab
- Sputum

**Procedures**
- Prepare the Sample Log by printing out the ‘Sample Log’ tap from the ‘COPCOV Sample Log’ excel file. This is to be done at D0 only. The sample log will be kept with the staff responsible for sample processing & storage.
- Sample packing
  - Check if samples were collected as indicated on the sample schedule
  - Spray sample blood tubes with 70% alcohol
  - Put samples in the secondary container or rack or ziplock bag. Swab and sputum will be produced by the participants and will be provided to the study staff in a ziplock bag.
  - Spray the secondary container or ziplock bag with 70% alcohol. Samples of each participant shall be put in separated ziplock bag.
  - Put secondary container or zip lock bag in the outer container or styrofoam box. If gel packs are using to maintain temperature, avoid not to let sample tubes or cups touch with the gel packs.
  - Transfer samples to the processing laboratory, along with the sample log (D0 only).

2.7 SOP – Sample Shipment

**Purpose and scope**
To describe the procedures for shipment of samples or other biological, infectious, or otherwise hazardous substances.

**Principle**
All laboratories are required to transport samples and materials from time to time for various reasons which include external quality control, external proficiency testing programs, or for tests not performed in the lab. In biomedical laboratories, such exchanges of samples often involve the...
Transport of materials which are considered potentially infectious, and are thus classified as "Dangerous Goods". All materials classified as such must be packaged in ways which will protect all handlers and environments from potentially hazardous exposure to these materials.

Transport Conditions
Biological specimens or test materials can be very sensitive to the environment to which they are exposed. To obtain reliable results from biological materials, they must be protected from exposure to inappropriate temperature/light/humidity conditions at all times. This is of particular importance for the transport of such materials because it is during transport that samples are most susceptible to exposure to unsuitable conditions.

*Ambient transport:* Samples or materials which are not temperature-sensitive can be transported under ambient or room-temperature conditions. If the samples are correctly packed, there are no requirements for additional packaging components to maintain desired temperatures.

*Cold-chain transport:* Some materials such as reagent kits are required to be kept at 2 – 8 °C at all times, including during transport. Such temperatures can be achieved and maintained in thermally insulated boxes using partially melted ice-packs.

*Transport of frozen samples:* Depending on the temperatures required and the duration of transport, samples can be kept frozen during transport using ice-packs or dry ice. Frozen ice-packs can maintain samples below freezing temperatures for up to 5 hours if they are packed in well insulated cool-boxes with very little or no empty spaces. Only dry ice allows temperatures ≤ - 20 °C to be reached and maintained in cool-boxes. It is advisable to validate the use of ice-packs and/or dry ice as cooling agents before actual transport of the samples.

Transport Regulations
All transport of biological samples, whether national or international, is highly regulated. All shipments must be packaged & labelled correctly, and must be accompanied by prescribed information & documents. Failure to comply with the applicable regulations may render the samples liable to destruction by incineration.

Definitions
*Infectious Substance, Category A:* An infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease in otherwise healthy humans or animals. Relevant examples include samples taken from patients with suspected haemorrhagic fevers, cultures of *Mycobacterium tuberculosis*, *Shigella dysenteriae* type 1, HIV 1/2, etc. Category A infectious substances that can cause disease in humans or in humans and animals are assigned to United Nations number UN 2814, and its proper shipping name is "INFECTIONOUS SUBSTANCE, AFFECTING HUMANS". Category A infectious substances which cause disease only in animals are assigned to United Nations number UN 2900; their proper shipping name is "INFECTIONOUS SUBSTANCE, AFFECTING ANIMALS ONLY".
Infectious Substance, Category B: Any infectious substance which does not meet the criteria for inclusion in Category A. Category B infectious substances are assigned to the United Nations number UN 3373; their proper shipping name is “BIOLOGICAL SUBSTANCE, CATEGORY B”. Exemptions: Substances determined to present a low hazard are exempted from Dangerous Goods requirements and regulations. This determination must be based on professional judgment and must take into consideration known medical history, symptoms, and circumstances of the source (whether human or animal), and the endemic local conditions. Examples of exempted specimens include blood or urine intended to be tested for various routine biochemical, immunological, or endocrinological tests as well as samples to be tested for drugs (therapeutic or otherwise), alcohol, or cancer markers. Blood smear slides and dried blood spots on filter paper (DBS) can be considered exempt from Dangerous Goods requirements and regulations.

Sample containing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is considered as Infectious Substance, Category B.

Basic triple packaging system: This system of packaging is used for all infectious substances. It consists of three layers:
- A leak-proof primary receptacle(s), especially for liquid samples
- A leak-proof secondary packaging
- An outer packaging of adequate strength for its capacity, mass, and intended use, and with at least one surface having minimum dimensions of 100 mm x 100 mm

Note: For B substances, the primary and/or secondary packaging must be rigid, durable, and capable of withstanding a pressure differential of 95 kPa. For Category A substances, only packaging certified by the concerned authorities must be used.

Equipment

Packaging materials for category B substances
- Primary receptacle:
  - For solid samples: a silt-proof container, e.g., watertight plastic jar or sealed/resealable strong plastic bag
  - For liquid, frozen liquid, or semi-solid samples: a leak-proof, watertight, durable container, e.g., cryovial
- Secondary packaging: A second durable, watertight, leak-proof packaging to enclose and protect the primary receptacles, e.g., cryobox (sealed with Parafilm and/or adhesive tape) or a strong sealed/resealable plastic bag.
- Outer packaging: Any strong carton or box capable of protecting the materials packed inside from physical damage. Its smallest overall external dimension must be $\geq 10 \times 10$ cm (can be procured from the courier company being used for transport).

Packaging materials for DBS and other exempt substances

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STANDARD OPERATING PROCEDURE

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- Primary receptacle:
  - For DBS: Sealed or resealable plastic bag
  - For other exempt substances: Sealed or resealable strong plastic bag, watertight jar, or cryovial, as applicable

- Secondary packaging: Sealed or resealable strong plastic bag

- Outer packaging: Any strong carton or box capable of protecting the materials packed inside from physical damage. Its smallest overall external dimension must be \( \geq 10 \times 10 \) cm (can be procured from the courier company being used for transport).

Additional Equipment for Frozen Samples

- Dry ice
- Thermally insulated box (if dry ice is being used, the box must have appropriate markings on the outside, and must have a provision to let the carbon dioxide escape as the dry ice sublimes)

Method

Organisation of Samples for Transport

- Make a list of the samples to be sent. Use this list to pick out the samples and also as a check-list to mark the samples as they are put aside for shipment. 
  
  Note: If some samples are not found, note the reason on the check-list.

- Assemble and organise all the samples; prepare an itemised packing list which includes all samples that have been selected for shipment. Note: For samples being sent in more than one outer packaging, prepare a separate packing list for each separate outer packaging. For samples being shipped in more than one secondary packaging, prepare packing lists according to secondary packaging (box) numbers. If some samples are not shipped, note the reason on the packing list. If some samples are damaged or otherwise altered, make a note on the packing list.

Packing of Samples

- Ensure that each primary receptacle is tightly closed and that it has no obvious signs of damage, such as leaks or cracks.

- Place the primary container(s) into the secondary packaging; close and seal the secondary packaging using appropriate means (Parafilm, adhesive tape, heat-sealing, etc.)

- For liquid or frozen liquid samples, also pack absorbent materials into the secondary packaging to absorb all liquid in case of spillage.

- For samples being shipped under ambient conditions:
  - Place the samples within the primary & secondary packaging into the outer packaging.
  - Fill empty spaces within the outer packaging with cushioning materials in a way such that the samples are immobilised within the outer packaging.
  - Close the outer packaging securely and seal with adhesive tape.

- For samples being shipped in dry ice:
  - Fill the cool-box to about 1/4\(^{th}\) of its capacity with dry ice.
  - Place the samples within the primary and secondary packaging in the cool-box.
  - Completely fill up any remaining empty space with dry ice.
If a temperature monitoring device is being used, place it (or its probe) in the cool-box and close it; seal with adhesive tape.

Documentation

- Packing List/Proforma Invoice (Customs Invoice), which must include:
  - Shipper's address with the name and telephone number of a contact person
  - Receiver's (a.k.a Consignee) address with the name and telephone number of a contact person
  - Details of the samples, including number of packages, contents, weight, volume, and a list of the samples. A copy of the packing list must also be placed in the outer packaging.
  - Value of the contents ("No commercial value" if the materials are supplied free of charge)

Shipment Schedule

It is currently planned to request the sites to ship samples in 1 to 3 batches depends on study site laboratory facilities and number of sample storage and current situation/regulation/restriction at the site.

Once a batch of specimens is ready for shipment, please contact Mrs. Cholrawee Promnarate (cholrawee.promnarate@wwarn.org) along with scans of the sample logs/packing lists of the samples which will be shipped.

Documentation

All samples shipped out of a site must be accompanied by a Packing List which must include the barcode information of the samples. When shipping with a courier, please also include a Customs Invoice, Airway Bill and a Materials Transfer Agreement if applicable. Copies of these documents must be kept on site in the Investigator Site File and also sent to COPCOV Study Coordination Team by email.

2.8 Study Supplies

A list of major equipment and supplies being used at all sites as table below. Some items will be delivered from Bangkok to the sites.

2.8.1 List of equipment

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Components</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benchtop Centrifuge</td>
<td>• Centrifuge</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Swing-bucket rotor + round bucket</td>
<td></td>
</tr>
</tbody>
</table>

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2.8.2 List of consumables

<table>
<thead>
<tr>
<th>Lab Test/Procedure</th>
<th>Consumable Item</th>
<th>Note</th>
</tr>
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<tbody>
<tr>
<td>Labelling</td>
<td>Sample labels</td>
<td>Provided by MORU</td>
</tr>
<tr>
<td>Swab, Sputum and sample collection</td>
<td>Serum 6 mL tube</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EDTA 4 mL tube</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Needle 23G</td>
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<td></td>
<td>Syringes 10 mL</td>
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<td></td>
<td>Standard Virocult Swab</td>
<td>Provided by MORU</td>
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<tr>
<td></td>
<td>Cryovial 2 mL</td>
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</tr>
<tr>
<td></td>
<td>Cryobox for cryovial 2mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pipette tip 100 -1000 ul</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Conical tube 50 mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cryobox for conical tube 50 mL</td>
<td></td>
</tr>
<tr>
<td>Dried Blood Spot samples</td>
<td>Whatman 31 ET Chr paper</td>
<td>Provided by MORU</td>
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<tr>
<td></td>
<td>Silica gel</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ziplock bag 8x12cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pipette tip 20-200 μL</td>
<td></td>
</tr>
</tbody>
</table>

2.9 Safety

2.9.1 Personal Protection

Appropriate Personal Protective Equipment (PPE) must be used at all times when handling potentially infectious and/or dangerous substances. At a bare minimum, this includes the use of a lab coat and gloves. In addition, depending upon the procedure being performed, other PPE such as a face-shield or goggles, aprons, masks should be used as appropriate.

More details are provided in Appendix 2 and individual SOPs and this UK government web site:
2.9.2 Post-Exposure Prophylaxis

All sites should develop and implement a standard operating procedure to be followed in case of accidental exposure to blood and blood products, including spillage, and accidental needle stick injury.

2.10 Contingency Management

Power Failure

All sites should develop and implement a standard operating procedure to be followed in case of power-failure, including procedures to be followed in case of power outage during evening/night-time.

2.11 Communications

For specific issues, please contact the following person(s) and in all case, please cc William Schilling (William@tropmedres.ac)

<table>
<thead>
<tr>
<th>Topic of Communication</th>
<th>Contact Person</th>
<th>Email:</th>
<th>Based at:</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>William Schilling</td>
<td><a href="mailto:William@tropmedres.ac">William@tropmedres.ac</a></td>
<td>MORU, Bangkok</td>
</tr>
<tr>
<td>Sample preparation</td>
<td>Cholrawee Promnarate</td>
<td><a href="mailto:cholrawee.promnarate@wwarn.org">cholrawee.promnarate@wwarn.org</a></td>
<td>WWARN, Bangkok</td>
</tr>
<tr>
<td>Sample tracking &amp; labelling</td>
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<td>Sample shipment</td>
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## 3. Change Log

<table>
<thead>
<tr>
<th>Original Version</th>
<th>Dated</th>
<th>Changes made</th>
<th>Updated version</th>
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<tr>
<td>Version 1</td>
<td>31 MAR 2020</td>
<td>Document issued</td>
<td>N.A.</td>
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<td>Version 1</td>
<td>7 APR 2020</td>
<td>Section 2.2 SOP – Specimen labelling and tracking: Updated pictures of workflow, sample schedule, sample log and updated sample types. Section 2.3 SOP - Swab/Sputum and samples transportation from Clinic to The Processing Laboratory: Updated procedure. Section 2.5 SOP- Preparation of Dried Blood Spots on Whatman 31 ET Chr paper for Chloroquine level determination: Updated equipment/consumable and method Section 2.7 Study Supplies: Updated list of consumables Appendix 2: Updated table for safety recommendation</td>
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<tr>
<td>Version 2</td>
<td>23 APR 2020</td>
<td>Appendix 2: Updated WHO interim guidance for Laboratory testing for Corona disease (COVID-19) in suspected human cases</td>
<td>Version 3</td>
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<td>28 APR 2020</td>
<td>Section 1. Introduction to COPCOV Study Samples: Updated work-flow for unscheduled visit Section 2.2 SOP – Specimen labelling and tracking:  - Added time-point format for unscheduled visit  - Updated sample log’s picture  - Updated the information entered on the Sample Log Section 2.5 SOP-Swab and Sputum Samples Collection: Added SOP-Swab and Sputum Samples Collection Section 2.6 SOP- Samples transportation from Clinic to The Processing Laboratory: Move from section 2.4 to 2.6</td>
<td>Version 4</td>
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<td>Version 4</td>
<td>25 MAY 2020</td>
<td>Section 1.1 Schedule of procedures for COPCOV study: Changed schedule of procedure follow to protocol version 6 Section 1.2 Work-flow: Changed work-flow to version 4 Section 2.2 SOP – Specimen labelling and tracking:  - Added time-point format in case of vaccination  - Changed figure 2 Sample log to version 6 Section 2.3 Sample collection and processing to obtain plasma, serum and cell pellet: Added “DV”, “DV 28” and UN D≤150 to time point to collect serum Section 2.4 Preparation of Dried Blood Spots on Whatman 31 ET Chr paper for Chloroquine level determination: Added ‘DV’ to time point to collect DBS</td>
<td>Version 5</td>
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<tr>
<td>Version 5</td>
<td>1 MAR 2021</td>
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<td>Version 6</td>
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## 4. SOP signoff

<table>
<thead>
<tr>
<th>Authored by:</th>
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<tr>
<td>Chorrawee Promnarat and Ranitha Vongpromek</td>
<td>Chorrawee Promnarat&lt;br&gt;Ranitha Vongpromek</td>
<td>14 Mar 21&lt;br&gt;15 March 2021</td>
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<table>
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<tr>
<th>Approved by:</th>
<th>Signature:</th>
<th>Date:</th>
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</thead>
<tbody>
<tr>
<td>Mehul Dhorda</td>
<td></td>
<td>24 March 2021</td>
</tr>
</tbody>
</table>
Appendix 1: Examples for "good" and "bad" quality DBS.

- Good: No barcode
- Bad: Too Small, Not soaked through, Fungus

FRONT

BACK
### Appendix 2: Safety recommendation in handling samples with SARS-CoV-2

<table>
<thead>
<tr>
<th>Sample</th>
<th>Time-points</th>
<th>Recommended minimum PPE / safety measures</th>
<th>Justification</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBS</td>
<td>D0, 30, 60, 90</td>
<td>Collection &amp; processing: Standard PPE per local recommendations</td>
<td>Minimal risk of aerosol generation</td>
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<tr>
<td>Plasma</td>
<td>D0</td>
<td>Collection: Standard PPE per local recommendations</td>
<td>Minimal to low risk of aerosol generation; symptomatic patients will be excluded; viraemia is rare in asymptomatic individuals; transmission from blood or blood products not confirmed</td>
</tr>
<tr>
<td>Cell pellet</td>
<td>D0</td>
<td>Processing: Standard PPE per local recommendations</td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>D0, D90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNS</td>
<td>Onset of symptoms</td>
<td>Collection: Standard PPE per local recommendations</td>
<td>Risk of transmission by aerosols; reduced by maintaining adequate distance from the subject during sample collection and avoidance of direct contact with specimen containers; risk of transmission during processing reduced by using PPE, BSC</td>
</tr>
<tr>
<td>Sputum</td>
<td></td>
<td>Swabs, sputum containers must be labelled and then given to participants with a sealable plastic bag with instructions to put the specimen in the bag and to seal it before handing over to study staff. Adequate distance must be maintained from symptomatic participants while they are self-swabbing or producing sputum. Processing: Full PPE + BSC* per local recommendations</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Note: TNS or sputum processing is NOT recommended if no BSC is available on site, specimens MUST be frozen in primary specimen collection containers in such cases. Specimen containers must only be opened for aliquotting/processing in Biosafety Cabinets while using full PPE; any centrifugation must be in sealed cups which are loaded/emptied within the BSC.</td>
<td></td>
</tr>
</tbody>
</table>

Standard PPE: Lab coat/apron, gloves + eye protection per local recommendations

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**STUDY:** Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study (COPCDV)
**SOP TITLE:** COPCOV STUDY LABORATORY SOPs & GUIDELINES

Full PPE: Closed-front, cuffed lab coat, gloves worn over cuffs, mask (N95 or similar, fit tested), eye protection


Please follow the guidance provided in the following document regarding SARS-CoV-2 disinfection (see Section 3) and waste management (see Annex I: Section 5)

* Work in certified Class II BSC – Class A2 preferred – certified within the past 12 months
Laboratory testing for coronavirus disease (COVID-19) in suspected human cases

Interim guidance
19 March 2020

Background

This document provides interim guidance to laboratories and stakeholders involved in COVID-19 virus testing of patients.

It is based on the interim guidance on laboratory testing for Middle East Respiratory Syndrome (MERS) coronavirus. Information on human infection with the COVID-19 virus is evolving and WHO continues to monitor developments and revise recommendations as necessary. This document will be revised as new information becomes available. Feedback is welcome and can be sent to WHElab@who.int.

The virus has now been named SARS-CoV-2 by the International Committee of Taxonomy of Viruses (ICTV). This virus can cause the disease named coronavirus disease 2019 (COVID-19), WHO refers to the virus as COVID-19 virus in its current documentation.

Laboratory testing guiding principles for patients who meet the suspect case definition.

The decision to test should be based on clinical and epidemiological factors and linked to an assessment of the likelihood of infection. PCR testing of asymptomatic or mildly symptomatic contacts can be considered in the assessment of individuals who have had contact with a COVID-19 case. Screening protocols should be adapted to the local situation. The case definitions are being regularly reviewed and updated as new information becomes available. For the WHO suspected case definition see: Global Surveillance for human infection with coronavirus disease (COVID-19).

Rapid collection and testing of appropriate specimens from patients meeting the suspected case definition for COVID-19 is a priority for clinical management and outbreak control and should be guided by a laboratory expert. Speculated cases should be screened for the virus with nucleic acid amplification tests (NAAT), such as RT-PCR.

If testing for COVID-19 is not yet available nationally, specimens should be referred. A list of WHO reference laboratories providing confirmatory testing for COVID-19 and shipment instructions are available.

If case management requires, patients should be tested for other respiratory pathogens using routine laboratory procedures, as recommended in local management guidelines for community-acquired pneumonia. Additional testing should not delay testing for COVID-19. As co-infections may occur, all patients that meet the suspected case definition should be tested for COVID-19 virus regardless of whether another respiratory pathogen is found.

In an early study in Wuhan, the mean incubation period for COVID-19 was 5.2 days among 425 cases, though it varies widely between individuals. Virus shedding patterns are not yet well understood and further investigations are needed to better understand the timing, compartmentalization, and quantity of viral shedding to inform optimal specimen collection. Although respiratory samples have the greatest yield, the virus can be detected in other specimens, including stool and blood. Local guidelines on informed consent should be followed for specimen collection, testing, and potential future research.

Specimen collection and shipment

Safety procedures during specimen collection

Ensure that adequate standard operating procedures (SOPs) are in use and that staff are trained for appropriate specimen collection, storage, packaging, and transport. All specimens collected for laboratory investigations should be regarded as potentially infectious.

Ensure that health care workers who collect specimens adhere rigorously to infection prevention and control guidelines. Specific WHO interim guidance has been published.

Box 1. Biosafety practices in the laboratory

Testing on clinical specimens from patients meeting the suspected case definition should be performed in appropriately equipped laboratories by staff trained in the relevant technical and safety procedures. National guidelines on laboratory biosafety should be followed in all circumstances. There is still limited information on the risk posed by COVID-19, but all procedures should be undertaken based on a risk assessment. Specimen handling for molecular testing would require BSL-2 or equivalent facilities; attempts to culture the virus require BSL-3 facilities at minimum. For more information related to COVID-19 risk assessment, see: WHO interim guidance for laboratory biosafety related to 2019-nCoV. Samples that are potentially infectious materials (PIM) for polo need to be handled and stored as described in WHO document Guidance on minimum risks for facilities collecting handling or storing materials potentially infectious for polioviruses (PIM Guidance). For general laboratory biosafety guidelines, see the WHO Laboratory Biosafety Manual, 2nd edition before the 4th edition is released.

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

SOP Version: V6 Date: 01 Mar 2021
[SOP template V2/22 July 2020]