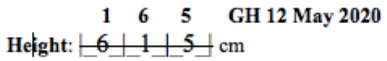
CRF COMPLETION GUIDELINES - UK

TABLE OF CONTENTS

Document version	Authors	Revision Notes
Version 2.0	F Croft	Updates to general section, follow-up form

GENERAL INSTRUCTIONS

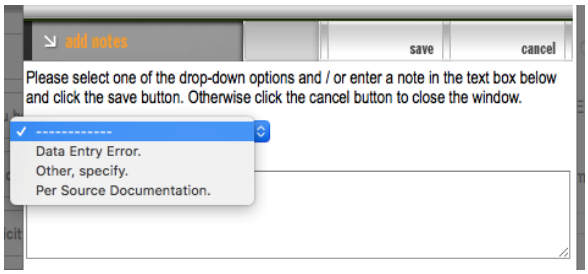
1. Answer every question, unless instructions state that a question should be answered conditionally
2. Free text entry (such as description of symptoms) should be brief and concise
3. Avoid the use of abbreviations unless commonly used medical terms
4. If using emergency paper CRFs:
    a. Circles (O) indicate single selection answers (choose one answer only). Square boxes (☐) indicate multiple selection answers (choose as many answers as are applicable).
    b. Mark an answer by marking a cross in the response box for example: ⊗**YES ; ☒ YES**
    c. Indicate **Subject Number** consistently in all CRF pages.
    d. Avoid writing outside of the provided spaces and do not include unsolicited text.
    e. Answer every question explicitly. **DO NOT** use ditto ("..") marks.
    f. Record data clearly in ink using CAPITAL LETTERS.
    g. Any update or correction to an entry in the CRF should be dated, initialed, and explained (if necessary). Strike through the original entry with a single line. **DO NOT** use correction fluid or completely obscure the original entry. e.g.



    h. Enter data from the paper CRFs into the study database within 24 hours of a participant's visit
5. **DO NOT** record person-identifying information such as names or phone numbers on CRF
6. Queries should be responded to within 5 working days
7. Once data entry is complete, mark the form as SDR. This will enable review and query generation by data managers and monitors. Select "Mark as SDR" from the Page Actions section.

You can revoke this action if data needs to be amended, or if it was marked SDR in error.

8. Further guidance e.g. Axiom Tips and Tools documents, is available within Fusion by selecting the "Study Info" tab

Date	- Record all dates in format DD/MMM/YYYY, i.e. **(**DAY/MONTH/YEAR**)** Example: [_**0**_][_**4**_]/[_M_] [_A_] [_Y_]/[_2_][_0_][_**2**_][_**0**_] - Provide actual dates by using the calendar or entering manually. - Partial dates are acceptable for concomitant medication. Select the appropriate icon to match the partial date known. If the date is completely unknown, enter your best estimate of the month and year, or year (without guessing). 
Time	- Record time in 24 hours format |_**0**_|_**0**_|:|_**0**_|_**4**_| (Four minutes past midnight) |_**0**_|_**8**_|:|_**2**_|_**4**_| (Twenty four minutes past 8 AM) |_**1**_|_**4**_|:|_**0**_|_**4**_| (Four minutes past 2 PM) - Provide actual time. If actual time is unknown, record NK (Not Known)
Initials	- Record initials of person completing the CRF; they must be listed as having CRF completion responsibility on the delegation log. - For sites using Electronic Data Capture, the username of the person performing the entry will be automatically recorded in the audit trail.
Date of CRF completion	- Actual date CRF is completed - For sites using Electronic Data Capture, the timestamp of data entry will be automatically recorded in the audit trail.
Data Corrections	- Amend the entry. A prompt box will appear for you to record the reason for the change  -
Participant facing CRF completion by site staff	- Enter the form then select the "submit form for subject" from the Page Actions section  -
Delete a blank addable form that has been created in error	e.g. Concomitant Medication. Select the form from the header bar  - Tick the box beside the form you wish to delete  - Select "delete item" from the Page Actions section

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SCREENING FORM

CRF QUESTION	COMPLETION INSTRUCTIONS
Site code	- A unique number identifying the Study Site. Automatically populated on eCRF. **Site Code: |_G_|_B_|_0_|_0_|_1_|**
Screening Number	- A sequential number assigned to ALL screened participants **Screening Number: |_0_|_0_|_0_|_1_|**
Inclusion criteria (Question 1 to 7) Exclusion criteria (Question 1 to 8)	- Mark **ONLY** one response YES or NO **Example ⊗YES ○NO**
Is participant eligible	- A participant is eligible if all Inclusion criteria are 'Yes' and all Exclusion Criteria are 'No' - Eligibility must be confirmed by an investigator sign-off prior to randomisation
Is participant enrolled	- If a participant is enrolled, they will be assigned a Subject Number. The rest of the CRF will be filled out.
Subject Number	- The Subject Number is the same as the Drug Kit number. Record the number appearing on the drug kit. If using paper CRF, attach a sticker from the drug kit onto the CRF. **Subject Number: |_E_|_0_|_0_|_1_|-|_0_|_0_|_1_|**
Randomisation date and time	- Refer to general instructions for format - Randomisation must not occur prior to investigator confirmation of eligibility

DEMOGRAPHICS

CRF QUESTION	COMPLETION INSTRUCTIONS
Date of birth Estimated age	- If date of birth in full, if known. If full date of birth is unknown, record estimated age in years. - Provide **ONLY** one response (either date of birth **OR** age)
Question No. 1, 3,4,5,7,9,10,11,12,13,14,15,16,17 and 18	- Provide a single response to the questions Example: Sex: ⊗ Male ○ Female ○Not specified
Question No. 6	- Multiple answers are allowed, check all applicable responses Example: 4. **Where do you work in the hospital?** ☑ Outpatients ☐ Intensive Care Unit ☑ Medical Ward ☐ Accident and Emergency ☐ Paediatrics ☐ Other:_____
Question No. 3,4, 6,7 and 11	- If **"OTHER"** checkbox is selected, please specify Example: 9. Drug allergy: ⊗Yes ○ No If yes which drug(s): _____**ASPIRIN**_____
Question 8, 9 and 10	- Record the actual Weight, Height and Temperature in Kg, cm and degrees Celsius respectively
Question 13	- If YES, add and complete the concomitant medication form

CO-MORBIDITIES

CRF QUESTION	- COMPLETION INSTRUCTIONS
19. Existing co-morbidities?	- If YES [⊗ Yes ○ No] , answer all questions (a) to (i) - If No [○Yes ⊗ No] , do not answer questions (a) to (i) - If a comorbidity not listed in (a) to (i) exists, record each additional comorbidity as a separate entry in (j) to (n)

SYMPTOMS

CRF QUESTION	COMPLETION INSTRUCTIONS
20. Current symptoms?	- If YES [⊗ Yes ○No], answer all question (a) to (v) - If other symptoms other than those covered in (a) to (v) exist, record each additional symptom as a separate entry in (w) and (x)

BASELINE VENOUS BLOOD

CRF QUESTION	COMPLETION INSTRUCTIONS
21. Baseline venous blood sample taken?	- If YES ⊗Yes ○No, record appropriate details in the Sample Log

STUDY DRUG ADMINISTRATION

CRF QUESTION	COMPLETION INSTRUCTIONS
22. Time of first dose of study drug	- Record actual time the first dose is given ,in 24 hour clock format

23. Number of tablets administered for first dose	- Record the total number of tablets prescribed as loading dose. e.g. an adult weighing 60Kg is prescribed a loading dose of 4 tablets.
23.Number of tablets taken (DOT)	- Record the number of tablets the participant is observed taking. e.g.If the participant is prescribed 4 tablets in total and takes 2 tablets at site and takes the rest of the tablets when at home, record 2.
24.Vomit	- If early vomiting occurs within 30 minutes of the first dose, the dose should be repeated. - Vomiting after this time does not require redosing. - The repeat dose should be taken when the participant feels better and when he/she takes his/her next meal. - If vomiting recurs, the participant will be withdrawn from the study because of drug induced vomiting.
25. Re-dose	- Indicate if participant was re-dosed.

FOLLOW-UP FORMS

CRF QUESTION	COMPLETION INSTRUCTIONS
Follow-up Forms: **Day 30** **Day 60** **Day 90** **Post Day 90**	- All participants will be routinely followed up on Days 30, 60 and 90. - Participants who develop an ARI will be followed up until resolution (28-60 days). - If follow-up extends beyond day 90 data will be recorded in the post Day 90 follow-up visit form. The maximum follow-up period is to day 150 for participants who develop an ARI at day 90. - If the post day 90 follow-up visit is not required, indicate as "Not Applicable"
Date of Visit	- Record actual date of the follow up visit - If a participant did not attend a scheduled visit, mark the visit as missed and leave the rest of the form blank.
1. Did you take study drug as prescribed?	- If participant did not take the drug 'Always' indicate the reason concisely
3. Number of tablets remaining	- Record the number of tablets the participants returns with to the follow-up visit
4. Date and time of last dose	- Refer to general instructions for format
Since the previous visit	- Question No. 5,6,7,8 and 9 select one response. If YES for: ○ **Question No. 5:** ▪ Answer "Yes" if the participant has had a positive antigen swab OR a positive blood antibody test ▪ record date of diagnosis ○ **Question No. 6:** ▪ select all applicable responses for other person(s) in the household diagnosed with COVID-19 ○ **Question No. 7:** ▪ Complete all questions, enter "0" if none ▪ specify "other" as appropriate ○ **Question No. 8 and 9:** ▪ "Admission duration" is the total number of days for all admissions ○ **Question No. 10:** ▪ Complete as appropriate
Question No. 11, 12,13,14, 15,16 and 17	- Select a single response

Follow-up post Day 90

CRF QUESTION	COMPLETION INSTRUCTIONS
Bio specimen collection date	- Record actual date of sample collection
Bio specimen type	- Indicate all that apply and specify if "other".

FINAL STATUS PAGE

CRF QUESTION	COMPLETION INSTRUCTIONS
Did the study participant receive a diagnosis of COVID-19 during the study?	- Provide response Yes or No - If YES, complete questions (a) to (d) - If NO, leave questions (a) to (d) blank
Subject has completed the study?	- Completion of study is defined as participant being seen until Day 90 (for participants negative for ARI/COVID-19) or until Day 90- 150 for participants diagnosed with ARI/COVID-19 during the study) - If YES, record date of completion: date the participant was last involved in a study-related procedure (i.e. date of last visit) - If NO, provide date of discontinuation: date the participant was involved in a study-related procedure (e.g. date of last visit) o Select the most appropriate reason for discontinuation (single-response) o If reason is death record date of death. Record NK if date of death is unknown o If Reason is 'Other', specify the reason
Investigator's statement	- A confirmation that the Investigator or designee per delegation log has reviewed the CRF as complete and accurate.

CONCOMITANT MEDICATION FORM

CRF QUESTION	COMPLETION INSTRUCTIONS
Concomitant Medication	- Complete this form with details of all drugs that the participant is taking during the study period, other than the study drug. o Select appropriate medication class from the code list. Specify if "other". o Record the generic name of the medication o Record drug indication for example Asthma, AE, Prophylaxis. o Record start date and end date; mark ongoing if participant is still taking drug at the last follow-up visit. o Indicate if drug is given to treat an SAE? Mark Yes or No o Record a number for dose o Indicate units, form, frequency and route by selecting from the code list. Specify if "other".

ADVERSE EVENTS FORM

CRF QUESTION	COMPLETION INSTRUCTIONS
Adverse events	- Complete the table if a participant reports being unwell with a symptom of grade 2 or above on the grading scale in CTCAE 5.0 (27Nov2017). Grade 1 (mild) AE may only be recorded if the event is an SAE. o Assign each AE with a unique and sequential number with the 1st AE being No. 1 o Indicate the event description by selecting from the code list. Specify if "other". o Complete AE start date, end date, if AE has not resolved on the last follow-up visit, leave end date as blank and indicate Outcome as Ongoing. o Indicate AE Relationship to drug, Severity, Action taken and Outcome by selecting from the code list. o If an AE meets the criteria for an SAE, please report an SAE. See protocol for definition of SAE

SERIOUS ADVERSE EVENT FORM

CRF QUESTION	COMPLETION INSTRUCTIONS
SAE No	- Assign a unique and sequential SAE number for each SAE. SAE numbers are sequential (1, 2, 3,) per patient. NOTE: All SAEs MUST be recorded as AEs
Linked AE number(s)	- Record all the AE numbers linked to this SAE - Refer to the AE form for the numbers
Type of report	- Indicate type of SAE report, 1st report is considered the initial report - Add subsequent forms for follow-up and final reports.
Onset date	- Record the date the SAE started
Date of awareness of SAE	- Record the date when the study team became aware of the SAE
End date Ongoing	- Record the date that the event stabilised, the condition returned to baseline or the condition resolved. - If event not resolved at time of writing the report, mark the 'Ongoing' checkbox
Final diagnosis/Syndrome	- Describe concisely, the final diagnosis, or main reason the SAE is being reported - If this is an initial report and the final diagnosis is not yet determined, the information recorded is provisional and may change in subsequent reports.
Participant Information	- Sex and height will be pre-populated.
Was this adverse event as a result of COVID-19? Was this an EXPECTED adverse event?	- Select one response
Has the participant had similar adverse events while in this study?	- If YES, specify how many times and describe briefly.
-Severity Grade -Relationship of SAE to Study Drug -Primary Reason SAE is Being Reported -Outcome of event	- Select one response. - If SAE outcome is death, record date of death. If an autopsy will be completed, send the autopsy report to the safety team, when available.
Alternative Aetiology	- Select one response to this question, if relationship to study drug is 'Not related' or 'Unlikely to be related' or 'Possibly related' or 'Probably related'
Study Drug Information	- Record total number of study drug tablets taken as at the time of making the report. Indicate date of last dose
Action taken with study drug	- Select one response
Relevant clinical data	- Indicate If the participant required hospitalisation. If YES, record the total number of days - Summarise this information from the COVID/ARI admissions worksheet. If any of the responses are YES, record the total number of each occurrence for the duration of hospitalisation.
-Relevant laboratory test, Other relevant tests	- Record results for relevant lab tests and investigations such as ECGs.

Events Summary	- Describe the SAE, including history of the event, associated signs and symptoms, alternative aetiologies, and clinical management.
SAE CRF sign off	- By the person completing the SAE and the Investigator.

COVID/ARI ADMISSIONS FORM

CRF question	Completion instructions
COVID/ARI Admissions form	- Complete daily ONLY for participants admitted with symptoms of an acute respiratory infection (ARI) or COVID-19 confirmed case. - Record actual date of observations o Oxygen saturation between 90% (inclusive) and 94% on room air o Oxygen saturation < 90% on room air Record Y(Yes) or N(No), as applicable for each of the questions. **Both** questions should be answered o Required* supplemental oxygen via face mask/ nasal prongs o Required* supplemental high-flow oxygen or non-invasive ventilation? o Required* intubation and mechanical ventilation o Required* ventilation and additional organ support or ECMO criteria met * Either the participant received the intervention or, in the opinion of the treating physician, the intervention was required but not delivered (*for example, due to resource constraints*) -Record Y (Yes) or N(No) for each of the questions. **All** questions should be answered

PREGNANCY REPORT FORM

CRF QUESTION	COMPLETION INSTRUCTIONS
Pregnancy No.	- Assign a unique and sequential number
Date of awareness of pregnancy	- Enter the date the site became aware of the pregnancy - This report should be completed, printed and forwarded to *COPCOV-Safety@tropmedres.ac* within 24 hours of the site becoming aware of the pregnancy
Date of Report	- Enter the date the report is being completed
Has the participant stopped their medication as a result of this pregnancy	- Answer YES or NO
Comments (if any)	- Record any relevant comments
Investigator sign-off	- Completed by Investigator