

ISARIC/WHO Clinical Characterisation Protocol UK (Scotland)

Recruitment Procedures for FRONTLINE CLINICAL RESEARCH STAFF

The most up to date versions of the **protocol** and **case report form** are available at isaric4c.net/protocols/

A **virtual site visit** is available at isaric4c.net/virtual_site_visit/

AIM: Please recruit the following patients **only**:

- Vaccine failure (positive COVID test - rather than displaying symptoms - >28d after having received a vaccine)
- Reinfection (proven after proven)
- Co-infection (flu/RSV)
- COVID associated hyper inflammation (MIS-A/MIS-C/PINS-TS) at any age
- Samples from patients with pathogens of public health interest including people identified as infected with SARS-CoV “variants of concern”
- All children

CONSENT: once the form is signed by a participant it is hazardous. To record consent, we suggest an independent witness observes the completed form then signs a fresh copy outside of the isolation area. Consent can also be obtained *by telephone* from participants or from relatives for proxy consent.

RECRUITMENT PACKS: Sample collection kits will be supplied to sites. Sample collections kits can be requested from: sarah.mcdonald@glasgow.ac.uk

Each kit will have a specific kit ID number, with each component within showing this kit ID and its own respective component ID for audit purposes.

Pods and bio-bags for shipping will also be supplied to sites. These can be requested from sarah.mcdonald@glasgow.ac.uk

OBTAIN SAMPLES according to the schedule. You can find out which tier you are operating at in the front page of the site file.

*If you have capacity to recruit at **TIER 2**:*

Day	1	2	3	4	5	6	7	8	9	28 days after discharge
Samples	R		S						S	C
Sample priority	1		2						3	4

R: recruitment sample; S: serial sample; C: convalescent sample.

If for any reason a sample cannot be collected on a given day, collect at the next opportunity.

If unable to collect all planned samples, ‘sample priority’ denotes the relative priority of each set of samples.

If patient is discharged before day 9, the day 9 sample set can be omitted.

*Or if your centre is recruiting at **TIER 1**:*

Day	1	2	3	4	5	6	7	8	9	28 days after discharge
Samples	R									
Sample priority	1									

CASE REPORT FORM DATA should be entered electronically at <https://ncov.medsci.ox.ac.uk/> using the REDCap platform. Please note the *clarified definitions of days* (admission, enrolment, day 1 etc) on front page 2 of the CRF (isaric4c.net/protocols/).

OBTAINING SAMPLES

All sample collection and aliquot tubes are supplied in the kit and are pre-labelled with the exception of Oracol, SAM and throat swab tubes. Labels for these are included within the kit. **Separate barcode labels are no longer required.**

To ensure samples are of optimum quality and suitable for analysis:

- * **RNA tubes:** collect *correct volume* of blood and *mix tube well* immediately after sample taken
- * Avoid over-filling **urine samples:** mark a line approximately half way down the container before giving to the patient and advise them to fill to that line and not above it.
- * Ensure all sample containers are *tightly closed, not overfilled* and *not externally contaminated* with any sample. Any samples that are leaking, contaminated or inappropriately closed have to be discarded upon receipt.

All samples should be double-bagged after collection and handled per local clinical and laboratory procedures. **Blood** and **pathogen** samples should be doubled bagged separately (with **urine** in separate bag within it in case of leakage). For convenience blood RNA tubes (Tempus/PAXgene) can be bagged with the pathogen samples. This is because **pathogen** samples will go straight to freezer storage without further handling to comply with PHE Guidance, while some **blood** samples will require processing before storage.

Completion of forms included in the kits and emailing to Sarah McDonald, as detailed below, is vital to link the Kit to a Patient and a timepoint - Please ensure you complete the forms

BIOLOGICAL SAMPLES TO COLLECT

Weight	Samples at recruitment (R)	Serial samples (S)	Convalescent samples (C)
>40kg	<ul style="list-style-type: none"> • 9ml EDTA blood • 3ml clotted blood • 3ml blood in RNA tube[#] • 3ml blood in sodium citrate tube • Oral Fluid (Oracol swab) • Research pathogen samples 	<ul style="list-style-type: none"> • 3ml EDTA blood • 3ml clotted blood • 3ml blood in RNA tube[#] • 3ml blood in sodium citrate tube • Oral Fluid (Oracol swab) • Research pathogen samples 	<ul style="list-style-type: none"> • 3ml EDTA blood • 3ml clotted blood • 3ml blood in RNA tube[#] • 3ml blood in sodium citrate tube • Oral Fluid (Oracol swab) • Research pathogen samples
20–40kg	<ul style="list-style-type: none"> • 6ml (3x2ml) EDTA blood • 3ml clotted blood • 3ml blood in RNA tube[#] • Oral Fluid (Oracol swab) • Research pathogen samples 	<ul style="list-style-type: none"> • 1ml EDTA blood • 2ml blood n RNA tube[#] • Oral Fluid (Oracol swab) • Research pathogen samples 	<ul style="list-style-type: none"> • 1ml EDTA blood • 3ml clotted blood • 2ml blood in RNA tube[#] • Oral Fluid (Oracol swab) • Research pathogen samples
<20kg	Refer to protocol. Table 3.		
Pathogen samples: <i>(double bag separately from blood samples)</i> <ol style="list-style-type: none"> 1. Throat swab <i>in viral transport medium (VTM)</i> 2. Nasal SAM strip* 3. Nasopharyngeal aspirate (NPA) in universal container OR (if NPA impossible) flocked throat swab <i>in VTM</i> 			

4. In all intubated patients with SARI or respiratory infection: endotracheal aspirate in universal container
5. Urine (~10ml in sterile universal container, if available; individually bagged). *Do not overfill.*
6. Rectal swab (*in VTM*) or stool (~10ml in sterile universal container/stool specimen container, if available)

*A video demonstrating correct use of nasal SAM strips can be found here: www.jove.com/video/56413

#Ensure RNA tube is filled with *correct volume and mixed well* immediately after blood sample is obtained.

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SAMPLE IDENTIFIERS: All data records entered on the REDCap system must be anonymised using a **five-digit site code** then **sequential four-digit patient number** e.g. 0001 and so on. The site codes for Scottish hospitals are listed in the Appendix. E.g. S116H-0001

LOCAL SAMPLE LOG: Please maintain an electronic log of samples obtained (patient study number, sample type, date obtained, timepoint)

SAMPLE TYPES



Clotted blood
(gold Vacutainer or brown Monovette)



EDTA blood
(purple Vacutainer or red Monovette)



Blood in RNA tube
(Tempus tube)

***mix well** immediately after blood sample taken



Blood in 3.2% sodium citrate tube



Nasal SAM strip



Saliva
(Oracol S14 Plus swab)



Nasopharyngeal, throat or rectal swabs
(swab in virus transport medium)



Respiratory secretions and urine
(universal container)



Stool
(universal container)

For practical or logistic questions please contact Clark Russell

The Roslin Institute, University of Edinburgh

clark.russell@ed.ac.uk

07891 053 625

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Information for LABORATORY STAFF

PROCESSING AND STORAGE OF SAMPLES AT SITE LABORATORY

Sample	Instructions for site laboratory
Pathogen samples ^a , Nasal SAM strips, Oracol swabs	No processing required. Do not open bags. Store upright at -80°C ^b
Clotted blood	Centrifuge 1500g for 10mins, ideally at +4°C. → serum (3x 1mL aliquots; store -80°C ^b) Discard remainder of clotted blood tube contents.
EDTA blood	Centrifuge 1500g for 10mins, ideally at +4°C. → EDTA plasma (3x 1mL aliquots; store -80°C ^b) → cell pellet (transfer to cryovial; store -80°C ^b) Discard remainder of EDTA blood tube contents.
3.2% sodium citrate blood tube	Centrifuge 2600g for 10mins with brake off (or slow stop). → citrated plasma (2x 1mL aliquots; store -80°C ^b) Discard remainder of citrate blood tube contents
Tempus RNA blood tube	Please freeze ASAP. No processing required. Freeze upright at -20°C; transfer to -80°C after 24h where possible. Do not defrost.

^aPathogen samples: throat swabs, other respiratory samples, urine or stool.

^bFreeze at -80°C where possible, or at least at -20°C.

Samples may be stored at +4°C out of hours and at weekends prior to processing and freezing.

Ensure paperwork is completed promptly in order to link a patient to a kit

SPECIMEN HANDLING

PHE have issued guidance on appropriate biosafety levels for handling specimens from patients with COVID-19: <https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens>

- **Section 5.1** Processing of respiratory tract specimens, faecal specimens, urine specimens, and tissue specimens in which virus has not been inactivated should be conducted at BSL3. No such processing is required for this protocol. **These samples should remain double bagged and frozen pending transport to the MRC-University of Glasgow Centre for Virus Research.**
- Section 5.2 **Accordingly, processing of whole blood, including aliquoting of serum and plasma can be conducted at BSL2**, as long as it is consistent with the terms of the local risk assessment.

- Section 6 **Manual centrifugation of specimens with infectious potential must be performed using sealed centrifuge rotors or sample cups. Rotors or cups should be loaded and unloaded in a Microbiology Safety Cabinet.**

Thus, blood from COVID-19 patients participating in the CCP-UK study may be spun and aliquoted in usual BSL2 laboratories.

PREPARATION OF SAMPLES FOR ONWARD TRANSPORT TO GLASGOW

Double bagged samples should be placed together into the sealable UN3373 compliant plastic pod and kept frozen. We suggest for convenience all samples are stored and frozen in this pod prior to collection. **Label the pod with the kit ID and patient ID using an alcohol resistant marker.**

Contact Sarah McDonald (sarah.mcdonald@glasgow.ac.uk) to arrange transport to Glasgow. This will be booked with CryoPDP at a mutually agreed date & time. The courier will provide outer transport boxes half-filled with dry ice. When packing the secondary safety containers please decontaminate the outside of each container with 70% ethanol or IMS, place the container inside a biobag along with some absorbent material (eg tissue), and seal the bag. Following this please spray the outside of the biobag with 70% ETOH/IMS before placing in the dry ice boxes.

The courier should provide all labels required, but if needed the delivery address is as follows:

Dr Sarah McDonald
MRC-University of Glasgow Centre for Virus Research
Sir Michael Stoker Building
Garscube Campus
464 Bearsden Road
Glasgow
G61 1QH
Tel: 0141 330 2989

Please make sure that copies of all Sample Information and Sample Notification Sheets have been emailed to sarah.mcdonald@glasgow.ac.uk prior to shipping.

Each shipment must include the Sample Information Sheets, a description of known pathogens contained and contact information, place these sheets between the secondary container and outer packing. This is a legal requirement under the Carriage of Dangerous Goods and Use of Transportable Pressure Equipment Regulations 2009.

APPENDIX: SITE CODES

Location	Location Name
A101H	Arran War Memorial Hospital
A103H	Ayrshire Central Hospital
A105H	Kirklandside Hospital
A110H	Lady Margaret Hospital
A111H	University Hospital Crosshouse
A112H	Brooksby Day Hospital
A114H	Warrix Avenue Mental Health Community Rehabilitation Unit
A201H	Ailsa Hospital
A202E	Maybole Day Hospital
A208H	Biggart Hospital
A210H	University Hospital Ayr
A211H	Arrol Park Resource Centre
A214H	Three Towns Resource Centre
A215H	East Ayrshire Community Hospital
A216H	Girvan Community Hospital
A217H	Woodland View
B103H	The Knoll Hospital
B104H	Galavale House
B105H	Hawick Community Hospital
B108H	Andrew Lang Unit
B114H	Kelso Hospital
B118H	Hay Lodge Hospital
B120H	Borders General Hospital
B121H	Hawick Psychiatric Day Hospital
B122H	Hawick Psychogeriatric Day Hospital
B123H	Peebles Psychogeriatric Day Hospital
B124H	Galashiels Psychogeriatric Day Hospital
B127H	Eyemouth Day Hospital
B128H	Crumhaugh House
B129H	Melburn Lodge
B130H	Huntlyburn House
Y101H	Castle Douglas Community Hospital
Y103H	Crichton Royal Hospital
Y105H	Nithbank Hospital
Y106H	Kirkcudbright Cottage Hospital
Y107H	Thomas Hope Hospital

Y108H	Lochmaben Hospital
Y109H	Moffat Community Hospital
Y110H	Newton Stewart Hospital
Y114H	Thornhill Hospital
Y120H	Annan Hospital
Y124H	Cromarty
Y126H	Acorn House
Y129H	Wellgreen Cottages
Y130H	Innistaigh
Y132H	Cardoness
Y134H	Treastaigh
Y135H	Nithview Day Hospital
Y136H	Laurel Bank (CETU)
Y138H	Heather Lodge (CETU)
Y142H	Lismore
Y144H	Galloway Community Hospital
Y145H	Midpark Hospital
Y146H	Dumfries & Galloway Royal Infirmary
F701H	Cameron Hospital
F704H	Victoria Hospital
F705H	Victoria Maternity Unit
F708H	Adamson Hospital
F709H	St Andrews Community Hospital
F710H	Randolph Wemyss Memorial Hospital
F711H	Whytemans Brae Hospital
F712H	Stratheden Hospital
F714H	Weston Day Hospital
F716H	Glenrothes Hospital
F805H	Queen Margaret Hospital
F810H	Lynebank Hospital
V102H	Falkirk Community Hospital
V105H	Bo'ness Hospital
V106H	Bellsdyke Hospital
V201H	Stirling Community Hospital
V214H	Lochview Hospital
V215H	Bungalows/Red Lodge
V216H	Clackmannanshire Community Healthcare Centre
V217H	Forth Valley Royal Hospital

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N101H	Aberdeen Royal Infirmary
N102H	Woodend General Hospital
N103H	City Hospital
N104H	Woolmanhill Hospital
N106H	The Baird Family Hospital
N111H	Hyperbaric Centre
N121H	Royal Aberdeen Children's Hospital
N151H	Aboyne Hospital
N161H	Aberdeen Maternity Hospital
N181H	Glen O'Dee Hospital
N183H	Roxburghe House
N184H	Maidencraig House
N198H	Royal Cornhill Hospital
N331H	Inverurie Hospital
N332H	Insch & District War Memorial Hosp.
N333H	Peterhead Community Hospital
N334H	Fraserburgh Hospital
N335H	Jubilee Hospital
N336H	Turriff Cottage Hospital
N337H	Chalmers Hospital
N352H	Ugie Hospital
N401E	Buckie Day Hospital
N411H	Dr Gray's Hospital
N431H	Seafeld Hospital
N432H	Stephen Cottage Hospital
N433H	Turner Memorial Hospital
N434H	Leancoil Hospital
N451H	Fleming Cottage Hospital
N492H	Rehabilitation Hospital
N494H	Kincardine Community Hospital
N495H	Pluscarden Clinic
N496H	375 Great Western Lodge
N499H	Elmwood
N500H	Aberdeen Community Health and Care Village
C204H	Dumbarton Joint Hospital/Riverview Resource Centre
C206H	Vale of Leven General Hospital
C310H	Ravenscraig Hospital
C313H	Inverclyde Royal Hospital

C403H	Dykebar Hospital
C418H	Royal Alexandra Hospital
C419H	Larkfield Unit
C420H	Blythswood House
G106H	Glasgow Dental Hospital and School
G107H	Glasgow Royal Infirmary
G108H	The Princess Royal Maternity Unit
G109H	Lightburn Hospital
G110H	Acorn Street Day Hospital
G112H	Parkview Resource Centre
G113H	Auchinlea Resource Centre
G207H	Stobhill Hospital
G212H	Shawpark Resource Centre
G214H	Springpark Resource Centre/Day Hosp
G302H	Leverndale Hospital
G303H	Mearnskirk House
G306H	New Victoria Hospital
G405H	Queen Elizabeth University Hospital
G408H	Florence Street Mental Health Resource Centre
G410H	Shawmill Resource Centre
G504H	Gartnavel General Hospital (Admin Purposes)
G505H	Gartnavel Royal Hospital
G507H	Centre for Integrative Care
G513H	Royal Hospital for Children
G516H	West Glasgow
G517H	Beatson West of Scotland Cancer Centre
G596H	Anvil Resource Centre
G598H	Arran Resource Centre
G599H	Riverside Resource Centre
G600H	Festival Business Park
G602H	Eastwood Resource Centre
G603H	Arndale Resource Centre
G605H	Bridgeview Resource Centre
G607H	Woodlands Resource Centre
G608H	2-4 Waterloo Close
G609H	The Orchards
G610H	Pineview
G611H	Netherton

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G612H	Rowanbank Clinic
G613H	Skye House
G614H	Orchard View
G615H	The Mary Aitkenhead Centre
C101H	Argyll and Bute Hospital
C106H	Cowal Community Hospital
C108H	Islay Hospital
C113H	Victoria Hospital
C114H	Victoria Hospital Annexe
C121H	Lorn & Islands Hospital
C122H	Campbeltown Hospital
H101H	Dunbar Hospital
H103H	Caithness General Hospital
H104H	Wick Town and County Hospital
H106H	Lawson Memorial Hospital
H201H	RNI Community Hospital
H202H	Raigmore Hospital
H208H	Nairn Town and County Hospital
H210H	Ian Charles Community Hospital
H211H	St Vincent's Hospital
H212H	Belford Hospital
H213H	Glencoe Hospital
H214H	Mackinnon Memorial Hospital
H215H	Portree Hospital
H217H	Ross Memorial Hospital
H219H	County Community Hospital Invergordon
H221H	Osprey House
H223H	New Craigs Hospital
H224H	Mid-Argyll Community Hospital and Integrated Care Centre
H225H	Dunaros Community Hospital
H226H	Migdale Hospital
H227H	Mull and Iona Community Hospital
H228H	Aviemore Hospital (Land)
L103H	Coathill Hospital
L104H	Victoria Memorial Cottage Hospital
L105H	Wester Moffat Hospital
L106H	University Hospital Monklands
L203H	Cleland Hospital

L204H	Hartwoodhill Hospital
L206H	Kello Hospital
L207H	Lady Home Cottage Hospital
L209H	Lockhart Hospital
L211H	Roadmeetings Hospital
L213H	Strathclyde Hospital
L216H	Kirklands Hospital
L218H	Airbles Road Centre
L302H	University Hospital Hairmyres
L304H	Stonehouse Hospital
L305H	Udston Hospital
L306H	Coathill House
L307H	Beckford Lodge
L308H	University Hospital Wishaw
L395E	Red Deer Centre/Day Hospital
S102H	Belhaven Hospital
S103H	Corstorphine Hospital
S107H	Edenhall Hospital
S108H	Edington Cottage Hospital
S109H	Herdmanflat Hospital
S113H	Roodlands General Hospital
S114H	Royal Victoria Hospital
S116H	Western General Hospital, Edinburgh
S201H	Astley Ainslie Hospital
S203H	Chalmers Hospital
S206H	Edinburgh Dental Institute
S209H	Liberton Hospital
S217H	Royal Edinburgh Hospital
S225H	Royal Hospital for Sick Children (Edinburgh)
S232H	Cambridge Street Day Centre
S234H	William Fraser Centre
S235H	The Islay Centre
S240H	Glencorse Day Centre
S241H	Bonnyrigg Day Centre
S243H	Ballenden House
S305H	St Michael's Hospital
S306H	Tippethill Hospital
S307H	Whitburn Day Hospital
S308H	St John's Hospital

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S309H	Inchkeith House
S310H	Ferryfield House
S311H	Bathgate House Day Hospital
S312H	Learning Disabilities Service Healthcare Houses
S313H	Ellen's Glen House
S314H	Royal Infirmary of Edinburgh at Little France
S315H	Findlay House
S316H	Princess Alexandra Eye Pavilion
S317H	Whitburn House
S318H	Midlothian Community Hospital
S319H	Royal Hospital for Children and Young People
S320H	East Lothian Community Hospital
D101H	State Hospital
D102H	Golden Jubilee National Hospital
R101H	Balfour Hospital
R103H	The Balfour
Z102H	Gilbert Bain Hospital
T101H	Ninewells Hospital
T104H	Kings Cross Hospital
T107H	Royal Victoria Hospital
T113H	Dundee Dental Hospital
T115H	Strathmartine Hospital
T116H	Armitstead Child Development Centre
T120H	Hawkhill Day Hospital
T121H	Dundonald Centre
T122H	Dudhope House (Young Persons Unit)
T123H	Royal Victoria Day Hospital
T202H	Perth Royal Infirmary
T205H	St Margaret's Hospital
T207H	Aberfeldy Cottage Hospital
T209H	Blairgowrie & Rattray Cottage Hospital
T215H	Murray Royal Hospital
T221H	Scone Day Hospital
T304H	Arbroath Infirmary
T305H	Brechin Infirmary
T309H	Little Cairnie Hospital
T310H	Montrose Royal Infirmary
T312H	Stracathro Hospital

T313H	Whitehills Hospital
T314H	Gowanlea
T316H	Crieff Community Hospital
T317H	Carseview Centre
T319H	Whitehills Health and Community Care Centre
T320H	Pitlochry Community Hospital
T321H	Perth Dental Hospital
T322H	Kingsway Care Centre
T323H	Bluebell Intermediate Care Unit
T324H	Dudhope Young Peoples Inpatient Unit
T325H	CAMHS Hospital Unit
W106H	St Brendans Cot Hospital
W107H	Western Isles Hospital
W108H	Uist & Barra Hospital