A Phase III, Multicentre, Randomised Trial Comparing SARS-CoV-2 Re-Boost Vaccine Strategies in Immunocompromised Patients

Sample Handling Manual

Sponsor:	University of Birmingham
EudraCT Number:	2021-003632-87
Sponsor Number:	RG_21-112
CRCTU Protocol Number:	MX3010
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Approved by CI (or delegated individual):		
Name: Prof Carl Goodyear	Signature:	Date: 27 July 2021

Ensure all laboratory trial documentation references the identifiers and protocol version it relates to	
Full trial title	A Phase III, Multicentre, Randomised Trial Comparing SARS-CoV-2 Re-Boost Vaccine Strategies in Immunocompromised Patients
Short trial title	OCTAVE-DUO
IRAS ID	302634
R&D number	<to be confirmed>
EudraCT/Other trial Reg ID	2021-003632-87

Version History		
Version	**Date**	**Reason for change**
1.0	27 July 2021	***

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Section 1: Contacts

Role	Name & contact information
Sponsor	**University of Birmingham, Edgbaston, Birmingham. B15 2TT**
Trial Office **Email**	**OCTAVE-DUO Trial Office, Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham, Edgbaston, Birmingham, B15 2TT** ✉ **OCTAVE-DUO@trials.bham.ac.uk**
Local Laboratory Academic Lead	See separate document: "**OCTAVE DUO Study: Contacts for Sample Handling Manual"**
Participating site contact details	
Processing laboratory contact details	
Courier details (where required for site)	

Section 2: Purpose

The purpose of this Sample Handling Manual is to describe the standard operating procedures for collection of trial samples at the participating study site; and onward transportation of trial samples to the processing laboratory; for the clinical trial titled "A Phase III, Multicentre, Randomised Trial Comparing SARS-CoV-2 Re-Boost Vaccine Strategies in Immunocompromised Patients", abbreviated to OCTAVE-DUO.

This trial is sponsored by University of Birmingham, Edgbaston, Birmingham, B15 2TT.

This sample handling manual only includes standard operating procedures that apply to the participating site as described in the OCTAVE-DUO protocol.

The standard operating procedures for taking receipt of and processing of the trial samples at the coordinating processing laboratory are described in the current version of the "OCTAVE-DUO Laboratory Sample Processing Manual" and are not covered in this document.

The processes contained herein must be followed to ensure compliance with Good Clinical Practice (GCP) standards to assure the quality and integrity of the samples during collection and storage at the participating site for onward transportation to the coordinating processing laboratory.

Section 3: Roles and responsibilities

The collection, processing, storage and onward transportation of clinical study samples in accordance with this manual should be overseen by named individual(s) on the delegation log who assume responsibility for the conduct of this work at the participating site.

The Principal Investigator (or delegate) at the participating site must ensure that site personnel are appropriately trained and qualified to perform the roles and responsibilities assigned to them and is documented using the relevant documentation provided by the Sponsor via the OCTAVE-DUO Trial Office at Cancer Research UK Clinical Trials Unit (CRCTU), University of Birmingham; and that the site has the necessary resources to collect/process the samples. Participating site adherence to the Sample Handling Manual may be subject to audit by the Sponsor.

Section 4: Procedures

4.1 Study specific sample record logs and collection site documentation

The sample record log form will be completed by the participating site for the samples collected from each participant in this study and will record the Trial Number; participant initials; study visit; type and number of sample tubes collected; and date and time samples are collected.

The completed sample record form should be sent with the sample shipment and a copy retained at site in the investigator site file for audit purposes.

All relevant site documentation should be completed be stored on site in the investigator site file for audit purposes.

The most recent version of the study sample record log form and relevant site documentation will be provided to the site by the OCTAVE-DUO Trial Office.

4.2 Sample collection kits and site equipment required

4.2.1 Sample collection kit supplied/ required for sample processing

IMPORTANT: Collection of SST tubes; Lithium Heparin tubes and the Tempus RNA tube is MANDATORY for all sites. Collection of the 9ml EDTA tubes is optional and depends on feasibility of local laboratory to process this sample type.

Please check with your local site cohort lead/co-lead or other designated local study team individual for confirmation of the sample tube types to be collected.

Sample collection kits will be provided by the OCTAVE-DUO Trial Office and will contain the following:

Blood collection tubes
5ml serum separator tubes (SST) tube x 2
9ml EDTA vacutainer x 3 (for a minimum of 2 and maximum of 3 EDTA samples collected)
6ml Lithium Heparin tubes x 2
3ml Tempus Blood RNA tube x 1

Sundry items supplied in kit
Sample labels (some labels may not be used and depends on feasibility of local laboratory to process this sample tube type).
Sample record log form

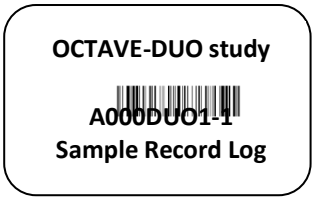
Sundry items supplied by site
Alcohol swab
Cotton swab
12-inch winged blood collection set x 1

4.2.2 Sample Collection site equipment required
None

4.3 Sample Labelling

The OCTAVE-DUO trial samples are individually labelled by the study nurse/study doctor collecting the samples at the participating site.

Example of label:



Sample labelling schema example

(Using alphanumeric sample identifier ”0001DUO”)

Alphanumeric sample identifier on label	**Label purpose/tube type**	
A0001DUO-1	Affixed to Sample Record Log form	
A0001DUO-2	Affixed to participating site paperwork	
B0001DUO-1	5ml SST Serum	Mandatory collection of these sample tubes
B0001DUO-2	5ml SST Serum	
C0001DUO-1	6ml Lithium Heparin	
C0001DUO-2	6ml Lithium Heparin	
D0001DUO-1	9ml EDTA	Collection of these tubes depends on feasibility of local laboratory to process this sample type
D0001DUO-2	9ml EDTA	
D0001DUO-3	9ml EDTA	
E0001DUO	Tempus RNA tube	Mandatory collection of this sample tube

Each label should be adhered to and wrapped around the tube in the orientation shown in figure 1.

Figure 1: sample label position and orientation using an SST tube as an example

4.4 Collection of Samples

All samples collected for experimental analysis must be taken by trained site staff using appropriate Personal Protective Equipment (PPE) compliant with local policies and procedures for the participating site, and in line with current government (regional/UK) guidelines and procedures relating to COVID-19.

4.4.1 Summary of Study Sample Collection

Table 1 outlines the schedule of events. Table 2 outlines the sample collection type and number per visit.

Table 1. Schedule of Events

	Screening	**Trial Entry**	**Baseline** *Prior to re-vaccination*	**Re-vaccination**[1]	**Post-re-vaccination**[2] *21 days post re-vaccination*	**3-month follow-up** *Seen in accordance with clinical practice*[3]
Eligibility assessment (including dip stick pregnancy test)	x					
Consent	x					
Randomisation		x				
Re-vaccination				x		
Data collection		x	x		x	x
Assessment of adverse events					x	
Research blood samples[4]			x[5]		x	
Participant Diary Booklet[6]			x		x	

Key

[1] At least 14 days after receipt of the second dose of vaccine

[2] Minimum 21 days + 14 days post re-boost vaccination

[3] Three months after re-vaccination, where possible data collected retrospectively from participants medical records, telephone follow-up permissible

[4] Research blood samples include: Whole blood, serum, plasma, and where possible peripheral blood mononuclear cells (PBMC)

[5] Research blood sample to be collected -14 to 0 days before re-boost vaccination

[6] Participant Diary Booklet handed out at baseline and collected at post re-vaccination appointment to aid in collection of Adverse Event (AE) data

Table 2: Participant visit schedule and sample collection

	Study Visit	
Sample collection tube type and number	**Baseline** Prior to re-vaccination	**Post-re-vaccination**[1] ≥21 days post re- vaccination
5ml SST serum vacutainer (yellow top) 2 x 5ml tubes Total volume = 10ml	X	X
6ml Lithium Heparin vacutainer (green top) 2 x 6ml tubes Total volume = 12ml	X	X
9ml EDTA vacutainer (purple top) Minimum of 2 (maximum of 3) x 9ml tubes Total volume = minimum 18ml; (maximum 27ml)	X	X
Tempus RNA blood tube (blue top) *1 x 3ml tube* Total volume = 3ml	X	X

KEY

[1] Minimum 21 days + 14 days post re-boost vaccination

IMPORTANT:

Blood samples will be stored at ambient temperature at the collection site until either transported by hand to the local on-site laboratory area for processing or pick up and transported by courier to the off-site processing laboratory. Samples are transported in UN3373 compliant packaging at ambient temperature.

4.4.2 Blood sample collection procedures and order of blood draw during phlebotomy procedure

Prior to carrying out this procedure individuals will have received appropriate training from their local health board for the blood collection procedure and infection prevention and control measures.
Perform hand hygiene using soap and water or alcohol-based hand rub.
Ensure appropriate personal protective equipment (PPE) is being worn for collection of samples.
Blood collection is performed using a 12-inch winged blood collection set (BD Vacutainer Safety-Lok Blood collection Set with pre-attached holder or equivalent).
Order of blood draw during phlebotomy procedure and number of inversions/other processing requirements after collection are as follows:

Order of Blood draw	Tube type and number	Tube inversions/other processing procedures after collection
1.	5ml SST vacutainers x 2	Gently invert*each tube 8 times
2.	6ml Lithium Heparin vacutainer x 2	Gently invert* each tube 8 times
3. (if collected)	9ml EDTA vacutainer x 2 (minimum) or 3 (maximum)	Gently invert*each tube 8 times
4.	3ml Tempus Blood RNA tube x 1	Shake vigorously for 10 seconds to ensure that the stabilizing additive makes uniform contact with the blood sample.
*An inversion is one complete rotation of wrist, 180 degrees and back.		

a) Tempus Blood RNA Tubes contain chemical additives. To prevent backflow from the tube into the individual's arm, observe the following precautions (see figure 2)
b) Place the blood donor's arm in a downward position.
c) Hold the tube vertically with the cap up.
d) Release the tourniquet as soon as the blood starts to flow into the tube.

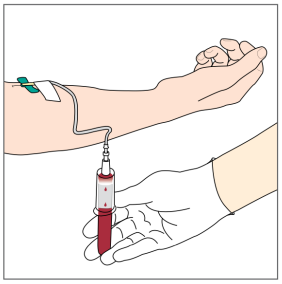


Figure 2. Tempus RNA Tube Position

e) Release the tourniquet as soon as the blood starts to flow into the tube.
f) Allow at least 10 seconds for a complete blood draw to ensure that the blood has stopped flowing into the tube before removing the tube from the holder.
g) It is important to ensure that blood flow has stopped to maintain the correct ratio of blood with the stabilizing agent.
h) Make sure the tube contents do not touch the cap or the end of the needle during venepuncture.
i) Remove the tube and shake vigorously for 10 seconds to ensure that RNA stabilizing reagent makes uniform contact with the sample.
j) Remove the winged needle blood collection set from the venepuncture site.
k) Apply cotton swab (or equivalent) to venepuncture site until bleeding has stopped and then apply small plaster or equivalent.
l) Discard used winged needle blood collection set into a sharps clinical waste bin.
m) Discard used PPE and any other clinical waste according to local site policy and perform hand hygiene procedure.
n) Don appropriate fresh personal protective equipment to package the blood samples blood samples into the provided UN3373 compliant packaging and arrange with the processing laboratory for pick up and transportation of the sample shipment to the processing laboratory.

IMPORTANT:

Blood samples will be stored at ambient temperature at the collection site until either transported by hand to the local on-site laboratory area for processing or pick up and transported by courier to the off-site processing laboratory. Samples are transported in UN3373 compliant packaging at ambient temperature.

4.5 Completion of study documentation and OCTAVE-DUO eCRF

4.5.1 Data Collection on eCRF

Data collected during each individual participant's study visit will be directly entered into the OCTAVE-DUO eCRF. This will include confirmation of collection of research blood samples.

4.5.2 Completion of Sample Record Log Form

a) The sample record log form will be completed by the participating site.
b) Attach a sample record log label in the upper right-hand corner of the sample record log form.
c) Complete each section of the sample record log form as described below:
    - Site Name
    - Trial Number
    - Participant initials
    - Sample time-point (baseline or day 21)
    - Date sample collected

- Time samples were collected
- Indicate type of samples collected (Yes/No or not applicable for collection site)
- Record the name of the person who packed and shipped samples

4.5.3 Completion of site-specific documentation

The person on site responsible for the collection of samples from each participant should adhere a copy of the sample record log label to any relevant site-specific documentation and file in the investigator site file.

4.6 Participating site sample processing

Depending on the local site arrangements samples may be processed at the local on-site laboratory area for processing or shipped to the off-site processing laboratory, for downstream processing and storage/onwards transportation to coordinating laboratories.

4.7 Sample packing procedures for research samples and onward transportation of samples to local on-site laboratory area/off-site processing laboratory

Contact details: See separate document - "OCTAVE-DUO Study: Contacts for Sample Handling Manual"

4.7.1 Sample packaging procedure

Each site should use their standard UN3373 compliant shipping boxes and other sundry items to pack and transport the samples from the participating site to the local on-site laboratory area/off-site processing laboratory .

Ensure that appropriate pre-printed external labels for intended recipient; shipping address and contact details; along UN 3373 hazard labels are attached to the shipment box.

IMPORTANT

Blood samples are shipped either by hand to local on-site laboratory area or by courier to off-site processing laboratory at ambient temperature.

4.7.2 Approved couriers for sample transfer to local on-site laboratory area/off-site laboratories for processing

All samples requiring off-site transportation by courier for this clinical trial will be transported using a courier firm that has been risk assessed and approved for transport of UN3373 Category B, Biological Substances.

4.7.3 Laboratory contacts to arrange transportation of sample packages

Once samples are ready for transport, the individual responsible for sample shipment on site should contact the designated individual at the local on-site/ off-site processing laboratory to arrange transport of the samples by hand or by courier to the local on-site/ off-site processing laboratory outlined in section 4.7 above.

4.7.4 Other considerations

If on shipping samples any errors with samples are noted, please contact the designated individual at the local on-site/off-site processing laboratory by telephone (if urgent) or by e-mail to describe the issues and decide on a plan for corrective action.
On reconciliation of sample record log form with the samples at the processing lab, if there are any errors then the staff will be in touch with staff at participating site.

Section 5: Participant Withdrawal

Please consult the relevant section in the OCTAVE-DUO protocol for procedures relating to the participant withdrawal from the study and contact the OCTAVE-DUO Trial Office at Cancer Research Clinical Trials Unit (CRCTU), University of Birmingham, for advice on procedures related to participant withdrawal.

Section 6: Non compliances and potential serious breaches in GCP

Procedures for handling non-compliance with GCP and /or the protocol for this clinical trial will be in accordance with the Sponsor's standard operating procedures, under the auspices of the OCTAVE-DUO Trial Office - Cancer Research Clinical Trials Unit (CRCTU), University of Birmingham, according to their local procedures.

Section 7: Protocol amendments

The processes to be followed when protocol amendments have been made and how the amendments will be distributed and implemented will be made in accordance with the Sponsor's standard operating procedures, under the auspices of the OCTAVE-DUO Trial Office - Cancer Research Clinical Trials Unit (CRCTU), University of Birmingham, according to their local procedures.