

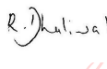

# SepTiC

Sepsis Trials in Critical Care

## SAMPLE HANDLING AND REPORTING MANUAL

Protocol No: 22SM8039

**Effective Date: 10 November 2023**

<b>Prepared by: Name:</b>	<b>Title:</b>	<b>Signature:</b>	<b>Date:</b>
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## 1. Introduction

The purpose of this document is to describe the procedures for biological sample collection, handling and shipping in the SepTiC study.

## 2. Scope

This procedure is applicable to participating investigator sites.

## 3. Abbreviations

ICTU	Imperial Clinical Trials Unit
GM-CSF	Granulocyte-macrophage colony-stimulating factor
SSPM	Study Specific Procedure Manual
SST	Serum-separating tube

## 4. Responsibilities

Site staff (e.g.: Research Nurse, Investigators)	<ul style="list-style-type: none"><li>• Collect samples in accordance with protocol and sample collection manual</li><li>• Ship collected samples to central lab (via PO box)</li><li>• Maintain oversight of kit levels at site and inform Trial Manager/Monitor when sample kits need to be replenished</li></ul>
Trial Manager/Monitor	<ul style="list-style-type: none"><li>• Maintain oversight of samples stored at central lab and master sample log</li><li>• Create and ship sample kits to participating sites</li></ul>

## 5. References

- Good Clinical Practice (ICH- GCP) Guidelines
- Data Protection Act (2018)

## 6. Procedures for participating sites

### 6.1. Sample Timepoints

For **all** participants, up to 20ml of blood will be collected on inclusion and sent to the central lab, via a PO box, for storage (Imperial College London). of DNA, RNA and serum for future research.

- Baseline serum sample collected in a 5ml SST tube, yellow top
- Baseline DNA sample collected in a 4ml EDTA tube, purple top
- Baseline RNA sample collected in a 2.5ml PAX gene tube

For participants in the **Diagnostic arm** of the trial randomised to treatment (PCR test):

- An additional 10ml blood sample will be taken after randomisation for rapid PCR-based pathogen testing and sent to the central lab.
- Results will be sent to the site and the SepTiC study team.
- If participants are randomised to standard of care then **no** sample is taken

For participants in the **GM-CSF** arm of the trial an additional 3 x 2.5ml blood samples collected via PAX gene tubes for RNA storage will be collected at the following timepoints:

- At randomisation into the GM-CSF arm, before the first dose of the drug is administered.
- Day 3 after randomisation.
- Day 5 after randomisation.

### 6.2. Sample Kits and Collection

The SepTiC study team will provide sites with all required consumables. Each site will receive the following consumables:

- 10ml EDTA tubes
- 4ml EDTA tubes
- 5ml SST serum tubes
- Paxgene tubes
- Blood tube labels
- RoyalMail Safebox
- Sample collection and shipping form
- Sample ID labels for sample shipping form

#### **6.2.1 Order of draw:**

*If collecting blood from an indwelling line (arterial or central line) draw 5ml of blood and discard prior to collecting research samples.*

Collect the baseline blood samples in the following order (a-d):

- a. **ALL PATIENTS: 4ml EDTA tube for the baseline DNA sample**



Collect 4ml of whole blood in the EDTA tube and gently invert 10 times. Post immediately following the instructions in section 6.8. If it is not possible to post on the same day as collection then refrigerate (4-8°C) and post the next day.

- b. **ALL PATIENTS: SST tube for the baseline serum sample**



Collect 5ml of whole blood in the SST tube (yellow top) and gently invert 10 times. Post immediately following the instructions in section 6.8. If it is not possible to post on the same day as collection refrigerate (4-8°C) and post the next day.

- c. **ALL PATIENTS: PAX gene tube for baseline RNA sample**



Collect 2.5ml of whole blood into each PAX gene tube.

**Note:** The fluid in the PAXgene RNA tube is toxic, as shown in the label. The manufacturer advises that the tube should always be held in the vertical position during blood collection, with the bung at the top and the fluid at the bottom. It is important to make sure the spike in the vacutainer does not sit in the fluid during blood collection and that the tube is not positioned above the patient. In theory, if there was negative pressure in the vessel then the tube fluid could flow backwards towards the patient, if the tube was upside down.

After collection gently invert the tube 10 times to ensure mixing of the blood with the fluid in the tube. Post immediately following the instructions in section

6.8. If it is not possible to post on the same day as collection refrigerate (4-8°C) and post the next day.

**The following sample is only for patients who have been randomised to 'Treatment' in the Diagnostic arm of the study.**

**Do not collect for patients randomised to standard of care in the Diagnostic trial.**

d. 10ml EDTA tube for the PCR diagnostic test



Collect 10ml of whole blood in the EDTA tube and gently invert 10 times.  
**Please note: 10ml of blood is required for the PCR diagnostic test. Please ensure the bottle is filled when collecting blood for this test.** Post immediately following the instructions in section 6.8. If it is not possible to post on the same day as collection, refrigerate (4-8°C) and post the next day.

### **6.2.2 GM-CSF samples:**

The following samples are only for patients who have been randomised to the GM-CSF arm of the study.

Additional PAX gene tubes should be taken, following the instructions in 6.2.1:

- At randomisation into the GM-CSF arm, before the first dose of the drug is administered.
- Day 3 after randomisation.
- Day 5 after randomisation.

Samples should be taken and sent on the same day they are collected. These samples will be sent separately to the samples in section 6.2.1.

### **6.3. Sample ID**

Each sample kit will have a unique sample ID. Please ensure that only one kit is used per patient. The sample IDs will follow the following format:-

Study (**ST**) Site Number (e.g.: **123**) Sample ID\* (e.g.:**1234**) . Sample type

*\* this will be different to the patient's trial ID.*

The sample types are:

- S – Serum Tube
- D – DNA (4ml EDTA) Tube
- T – Test (Diagnostic) Tube
- R – RNA (PAX gene) Tube
  - R1/ R2/ R3 – RNA (Pax gene) Tube – **GM-GSF patients only**

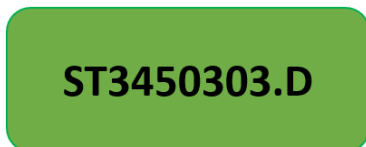
#### 6.4. Labels

Labels will be provided per patient to the site with the consumables listed above.

- Each sample pack will contain white blood tube labels **with a barcode** and sample ID as the image.



- Once the sample is collected, the label will need to be attached to the associated tube **before** shipping.
- Each site will receive 7 white blood tube labels per patient, for example:
  - ST1231234.S
  - ST1231234.D
  - ST1231234.T
  - ST1231234.R
  - ST1231234.R1
  - ST1231234.R2
  - ST1231234.R3
- Each site will also receive 7 corresponding-coloured labels which will have a sample ID **only**. These are to be attached to the sample shipping form to avoid any errors of handwriting sample ID's.



- example label.

#### 6.5. Sample Collection

Once the samples are collected, and correct labels attached, complete the sample collection and shipping form (see Attachment A).

## 6.6. Processing

Sites will not process any samples. All processing will take place at the Imperial College MDU Lab/ SepTiC Study Team Lab.

## 6.7. Storage/ Out of hours collection

Samples can be stored at room temperature until posting, please **post as soon as possible**. If the samples cannot be posted on the same day, samples can be stored in the fridge (4-8°C) and posted the next day.

## 6.8. Sample shipping to central lab

6.8.1 Samples will be posted directly to a PO Box at the following Post Office Collection Point: Westbourne Grove Customer Service Point 16a Westbourne Grove, London, W2 5RH. The PO box can receive samples from Monday until Saturday (apart from bank holidays). If the sample is collected late on a Saturday, please store in a 4-8°C refrigerator and post on Monday. The Royal Mail First Class Safe Boxes provided will aim to deliver samples to the Central Lab (via a PO box) for the next day.

6.8.2 Samples will need to be sent to the central lab (via a PO box) using the Royal Mail First Class Delivery Safebox which will be provided by the study team (see image below)



6.8.3 The RoyalMail Safebox includes:

- Royal Mail Safebox Outer Box
- A5 PathoSeal 95
- 50ml Absorbent Material Gripseal Bag
- Prepaid Postage Label (incorporating UN3373 Label)

**Please note:** The total sample volume/mass in the box must not exceed 50ml



6.8.4 Follow the instructions included on how to package the samples and assemble the box:

- 1) Wrap sample tube(s) in absorbent sheet and place into the grip seal bag and close.
- 2) Place the filled grip seal bag into the PathoSeal bag.
- 3) Close the PathoSeal bag following the instructions printed on the bag.
- 4) Place the completed PathoSeal bag and sample shipping form into the Safebox
- 5) CHECK all samples have been included before closing and ensure total sample volume **does not exceed** 50ml.
- 6) Close the Safebox ensuring the security tab is tucked in.
- 7) The return address and postcode (for the PO box) will be completed on the Safebox ready for posting.
- 8) Apply prepaid postage label over the instructions printed on the box, ensuring it wraps round and over the tuck in security tab.
- 9) You can post First Class Safebox™ in the majority of Royal Mail Post Boxes subject to aperture size.

**Note:** the completed sample shipping form must be completed and sent with every Safebox – see attachment A.

### 6.9. Lab receipt hours

The lab is open to receive and process PCR samples Monday – Saturday, apart from during the college closure dates below.

The SepTiC team will inform sites of the final date that samples can be sent prior to closure dates. Any samples sent late on a Friday may not arrive until Monday.

	<b>Imperial College Closure Days</b> <b>(Do not send samples on these days)</b>
Christmas 2023/2024	Friday 22 <sup>nd</sup> December 2023 – Monday 1 <sup>st</sup> January 2024
Easter 2024	Wednesday 27 <sup>th</sup> March 2024 – Tuesday 2 <sup>nd</sup> April 2024

### 6.10. Diagnostic PCR sample reporting

A copy of the results of the diagnostic PCR test will be sent to the site (details included on the sample shipping form) and the SepTiC study team ([septic@imperial.ac.uk](mailto:septic@imperial.ac.uk)).

Ensure that the results are filed with the patient's electronic/paper notes.

The SepTiC Trial Manager/Monitor will enter the PCR test results onto the eCRF.

## 7. Revision History

<b>SSPM Ref.</b>	<b>Date Effective</b>	<b>Reason for update (page and section of change)</b>
V1.0	10 Nov 2023	First version

# ATTACHMENT A: SAMPLE SHIPPING FORM



Date Shipped: \_\_\_\_ / \_\_\_\_ / \_\_\_\_\_

## SAMPLE SHIPPING FORM

*Please fill in this form prior to sending out the sample.*

<b>Site name</b>		<b>Site number</b>	
<i>Site contact details (results will be sent to this contact)</i>			
<b>Name</b>		<b>Mobile</b>	
<b>Email</b> <i>(more than one email can be entered)</i>			

<b>Patient ID:</b>		<b>Patient month and year of birth:</b>	MM/ YYYY
<b>Sample ID</b> <i>(Please stick the corresponding sample label here)</i>		<b>Date sample taken</b>	<b>Description of sample (e.g.: PAX gene tube)</b>

<b>Patient ID:</b>		<b>Patient month and year of birth:</b>	MM/ YYYY
<b>Sample ID</b> <i>(Please stick the corresponding sample label here)</i>		<b>Date sample taken</b>	<b>Description of sample (e.g.: PAX gene tube)</b>

**FOR IMPERIAL MDU LAB ONLY:**

<b>Samples received by</b> <i>(print name):</i>		<b>Date received:</b>	
<b>Comments (e.g.: if sample arrived damaged):</b>			

**FOR SEPTIC TRIAL TEAM LAB ONLY:**

<b>Samples received by</b> <i>(print name):</i>		<b>Date received:</b>	
<b>Comments (e.g.: if sample arrived damaged):</b>			

*Please email a copy of the completed form to [septic@imperial.ac.uk](mailto:septic@imperial.ac.uk)*