Sample Collection and Management Manual

for the clinical department and local laboratory procedures within

Name study

Full name study

CLINICAL TRIAL

ND|BB COMBACTE

Universiteit Antwerpen

UMC Universitair Medisch Centrum Utrecht

imi Innovative Medicines Initiative

Sample Collection and Management Manual

for the clinical department and local laboratory procedures within

study name

Developed by	**COMBACTE LAB-Net**
In collaboration with:	
Sponsor Protocol number:	
Application Number	

This protocol has been authorized by:

Name	**Signature**	**Date**

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1. Introduction

This manual is a guideline through the sample collection and the different processing procedures that are performed within the clinical trial name study. The manual is primarily written for research staff including (sub-) investigators, research nurses, and laboratory staff involved in the execution of the study.

The clinical trial protocol and subsequent amendments are the reference in all cases. If there is a discrepancy between this manual and the clinical trial protocol then the trial protocol is the leading document.

Local SOPs might need adaptations to comply with the procedures described in this manual.

In this section a high level description of the study should be given:

Type of study: Phase 1, phase 2 or phase 3 study; dosing regimen;
Information on the interventional product
Information on target population
Number of subjects to be enrolled and/or dosed, number of sites, location of sites
Duration of the study

Name study is being conducted through the Innovative Medicines Initiative Joint Undertaking (IMI JU, 2012), which is a pan-European public-private partnership between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA), theme Combatting Antimicrobial Resistance in Europe (COMBACTE) (New Drugs for Bad Bugs [ND4BB] Subtopic 1C). Sponsor name will execute this study in conjunction with CRO name (if applicable) and the COMBACTE consortium of leading academic, clinical, and microbiological researchers in the field of antibiotic-resistant bacteria and other applicable fields.

2. Sample Collection and Management

This document gives an overview of how samples should be collected and processed during the study. More details on the clinical protocol can be found in Protocol: protocol name and number. Users of this manual should be mindful of amendments to the clinical protocol. In case of such and discrepancy between the clinical protocol and this manual, the clinical protocol will always be the leading document.

2.1 Overview of samples to be collected and handlings to be performed

This table gives a summary of the samples that should be collected and the handlings, preparations or tests that should be done on the samples. An example is given in the table.

Sample	Handling, Preparation or Test

Tracheal Aspirate	• *Gram stain*
	• *Culture for bacteria*
	• *Preparing microbanks*
	  ○ *Tracheal Aspirate isolate (microbanks)**
	• *Preparing aliquots*
	  ○ *Name aliquots**

* Should be shipped to Central Lab

2.2 Overview of samples to be taken and handlings to be done per time point:

Table indicating all the assays that need to be done and all the aliquots that need to be prepared on specific visits per sample type. An example is given in the table.

Sample Type		*Visits*				
		V1	*V2*	*V3*	*V4*	*V5*
Tracheal Aspirate	*Gram-stain*	*x*		*x*		*x*
	Culture	*x*		*x*		*x*
	Tracheal aspirate isolate	*x*		*x*		*x*
	Tracheal aspirate aliquot	*x*	*x*	*x*	*x*	*x*

Acceptance criteria need to be defined for each sample type depending on the study and the importance for the processing of these samples. I.e. acceptable volume of the sample should be defined, as well as turnaround time of transfer of the material to the lab after sampling and transport conditions of the specimens.

The acceptance criteria might be applicable for example to define the quality of a sputum sample. Prior to culturing a sputum specimen, a Gram stain should be performed to evaluate the quality of the specimen. One of two criteria are currently used to determine if the specimen is contaminated with oral flora organisms, which would make the specimen unsuitable for culture. One criterion states that the sputum specimen should be rejected if 25 or more squamous epithelial cells/low power field (SQE/LPF) are observed. The second criterion recommends a cut-off of more than 10 SQE/LPF. In either case, a minimum of 20 LPFs should be observed.

If the sample does not comply with the acceptance criteria defined for the study, this should be registered and reported. There might be need for a new specimen to be taken if feasible.

2.3 Overview of study supplies

- *Important messages on initial supply and the procedures to reorder material.*

Central lab name will provide you with the supplies required to collect, prepare and ship samples for this study.
Initial supplies include the following:

- *List of material that is provided to the site including study material (kits, microbanks,…) as documents (Sample Collection and Processing manual, Collection Flow Chart, Requisition forms, Reorder forms, other documents related to the study)*

2.3.1 Collection kits

Description of the collection kit:

- *Description of how kits need to be used: one kit to be used for every visit or visit specific collection kit*
- *Description of information on the label and a picture of a kit with label*
- *Description of kit content*
- *Acceptance criteria might need to be specified here if crucial for the study*
- *Section on toxic information if applicable to the sample kit provided for the study*

The below text can be used in case University of Antwerp is central lab but needs to be updated in case the procedure is differs for the study or the central lab is located elsewhere.

Kits will contain study sample materials for *specify visits or samples*. Sample kits are labeled with the following information:

- Study Name: name study
- Study number: *study number*
- Time point: *visit name*
- Expiration date: *month-year*
- Kit lot number: *visit name-4-digit number*

Example of a label on a kit to be used for *visit name*:

Name study
Study N°: *study number*
Time point: *visit name*
Expiry date: *month-year*
Lot: *visit name – 4-digit number*

The expiration date displayed on the label shows the last full month in which the sample kit can be used.

Each kit contains an instruction sheet specific for that time point and an investigator and laboratory requisition form (Appendix *x*).

A Collection Flow Chart (CFC) giving a global overview of all the time points and all the procedures is provided in an A3 format (Appendix *x*).

Disposal of unused collection kits: *Unused collection kits might need to be sent back to the central lab or destroyed locally. Specific garbage regulations for the kits of the study should follow.*

Description Of Study Sample Material

Table: Description of provided material and for which sample type it needs to be used. An example is given in the table.

Sample	Handling	Material provided for sample collection	Material provided for sample processing/storage
Sample type	*Handling that needs to be done*	*Description of material that is provided or if material should be used from routine setting*	*Description of material that is provided or if material should be used from routine setting*
Tracheal Aspirate	*Gram-stain*	*Tracheal Aspirate container not provided. Please use your own container*	*- Please use your local standard*
	Culture *- Isolate*		*- Microbanks to store strains* 
	Tracheal Aspirate aliquot		*- Tracheal Aspirate transfer tubes* *-* 

Disclaimer regarding use of devices supplied to the site within the study (if applicable) and samples and strains stored at the site:

- *Devices supplied to the site within the study should be used solely for the purposes of that study.*
- *The study samples are collected only for the purposes of the study. Any remaining frozen samples at the site should be destroyed after the end of the study upon instructions of the central lab. These samples cannot be used for analyses undertaken by the local lab that are not explicitly mentioned in this manual.*
- *Strains collected within the study could be preserved at site after the end of the study.*

2.3.2 Storage conditions and expiry date of unused study materials

2.3.2.1 Storage Conditions

- Unused sample kits should be stored at room temperature and protected from direct sunlight.
- *Material* needs to be stored between *x* °C to *x* °C.

If applicable:
Instructions what to do in case of excursions.
Instructions on which documents/information needs to be collected: for example Temperature Records, Calibration Certificate…

2.3.2.2 Expiry Dates

- Expiry dates are clearly marked on the label that is placed on the outside of the collection kit box. The expiry date is always reflective of the tube that expires the earliest. The kit is good to the last day of the month displayed on the label.
- *Expiry date information of other material (if applicable)*

2.3.3 Labelling and identification of samples and derivates

- *Important messages on how to use labels*
- *how labels are provided (label sets, labels in kit, pre-labelled tubes,..)*
- *labels for draw tube and labels for storage tubes (sometimes labels are not provided for all tubes, this needs to be specified)*
- *how to select labels*
- *how to use labels (in case only a part of the label needs to be used, if the label needs to be applied in a certain direction on the tube,..)*
- *things to complete on the label (if applicable)*
- *example of a label (picture) with explanation of the above described procedures*

The below text can be used in case University of Antwerp is central lab but needs to be updated in case the procedure is different for the study or the central lab is located elsewhere.

You will be provided with pre-printed labels to be used on all samples/forms. One label set will contain all labels for a single subject. The labels should be kept in the Investigator site file (ISF) until use.
Every sample, aliquot, microbank and study document (i.e. requisition forms,..) should be clearly labeled with the provided labels. Always label both collection tube and transfer vial to prevent mix-up.
The labels include the following information:

Study Name		*Name study*
Site ID	*Unique for your site*	*Example*
Subject ID	*Unique for each subject*	*Example*
Sample collection time point	*Visit name*	*Abbreviation on label (if applicable)*
	Visit name	*Abbreviation on label (if applicable)*

The following information should be written on the labels:

Sample type	*Sample type*	*Abbreviation on label (if applicable)*
	Sample type	*Abbreviation on label (if applicable)*

Example of a label for a sample collected from patient *xxxx* enrolled at site *yy* for *specify visit*:

Study name *yy-xxxx* *visit*

Be aware that sample material shipped to the Central Laboratory should not contain personal patient information (no patient name, patient initials and patient routine hospital numbers should be on the tubes)

Blinding/unblinding conditions: If applicable add section on blinding/unblinding conditions for the local site. It might be the case that samples are to be sent blinded to the local lab.

2.3.4 **Requisition Forms**

- *Important messages on how to use requisition forms*

- *Detailed description on how to use requisition forms (add a copy of the requisition forms in appendix)*
    - *Same requisition form for all visits or visit specific requisition forms*
    - *Investigator and lab requisition form*
    - *Detailed description of information that needs to be completed and how (use a label to identify patient/visit, use black pen, press firmly,..)*
    - *Detailed description of the procedure: where the requisition forms can be found, which copy needs to be retained, which copy stays with the samples*

The below text can be used in case University of Antwerp is central lab but needs to be updated in case the procedure is different for the study or the central lab is located elsewhere.

You are provided with the **Investigator Requisition Forms** (Appendix *x*), **Local Laboratory Requisition Forms** (Appendix *x*), *other requisition forms if applicable*.
Requisition forms for each subject visit must be completed on paper and in the "electronic Case Report Form (eCRF)". The requisition forms are *the same/specific* for the different time points within the study. Both the Investigator and Laboratory requisition forms are enclosed in the sample kits.

For the investigator

- At each sampling time point, the investigator or designee should complete the paper **Investigator Requisition Form.** The information on the paper Investigator Requisition Form must then be entered in the eCRF by study staff targeting *time* after sampling.
- The paper Investigator Requisition Form will be kept in the subject's file with only study staff having access to it.
- At the time the samples are transported to the local laboratory, they are accompanied by the ***unfilled*** **Local Laboratory Requisition Form,** unused materials and unused sample labels for that study time point.
- *Other instructions if applicable*

For the Local Laboratory

- The Local Laboratory should fill out the paper **Local Laboratory Requisition Form** at the time the samples arrive in the laboratory. The information on the paper Local laboratory Requisition Form must be entered in the eCRF by study staff targeting *time* after the samples arrive in the laboratory.
- The paper **Local Laboratory Requisition Form** should be kept in the subject's file with only study staff having access to it.
- *Other instructions if applicable*

Please make sure that the forms are complete and easy-to-read. If an error is made, cross out the mistake using a single horizontal line, write down the correct information, accompanied with your initials and date the change.

2.3.5 Reordering of supplies

Detailed description of the reordering procedure:

Hard copy reordering form or in online system (add a copy of the reordering form in appendix)
Who needs to be contacted (if applicable)
How confirmation will be received (if applicable)
Time needed to supply the site with study material

The below text can be used in case University of Antwerp is central lab but needs to be updated in case the procedure is different for the study or the central lab is located elsewhere.

At study start you will be provided with the study specific materials. Supply stock should be monitored by the local sites. Supplies can be reordered using the reorder forms located in Appendix *x*. A specific form is available for the supply of sample materials/sample kits, microbanks and medium. Once the form is completed, fax or email the form to the contact information displayed on that specific form. Reorders should be placed 2 weeks in advance to allow for processing and shipment of the order.

2.4 Detailed sample collection instructions

You have been provided a Collection Flow Chart (Appendix x) with your initial supplies. The chart will provide you an overview of the collections needed for this study at designated visits.

Summary of general procedure:
- Kits
- Labels
- Requisition forms
- Additional important topics to keep in mind

2.4.1 Sample type 1

Table indicating when sample type 1 needs to be collected

	Visits							
Sample type								

- *Detailed instructions per sample type how to collect the specimen. It is clearly indicated if a specific protocol needs to be followed or if routine procedures can be followed.*

- *Acceptance criteria need to be defined for each sample type depending on the study and the importance for the processing of these samples. I.e. acceptable volume of the sample should be defined, as well as turnaround time of transfer of the material to the lab after sampling and transport conditions of the specimens.*

  The acceptance criteria might be applicable for example to define the quality of a sputum sample. Prior to culturing a sputum specimen, a Gram stain should be performed to evaluate the quality of the specimen. One of two criteria are currently used to determine if the specimen is contaminated with oral flora organisms, which would make the specimen unsuitable for culture. One criterion states that the sputum specimen should be rejected if 25 or more squamous epithelial cells/low power field (SQE/LPF) are observed. The second criterion recommends a cut-off of more than 10 SQE/LPF. In either case, a minimum of 20 LPFs should be observed.

  If the sample does not comply with the acceptance criteria defined for the study, this should be registered and reported. There might be need for a new specimen to be taken if feasible.

2.4.2 **Sample type 2**

Table indicating when sample type 1 needs to be collected

	Visits							
Sample type								

- *Detailed instructions per sample type how to collect the specimen. It is clearly indicated if a specific protocol needs to be followed or if routine procedures can be followed.*

2.5 Detailed sample processing procedures

At the moment of the arrival of the samples in the local laboratory, the sample kit can contain the following samples:

- *List of samples*

Next to the samples, the kit should also contain *list of other material (labels, tubes, forms,..)*

Compare the labels on the samples with the information on the Requisition Form. If the info is not the same, contact your study investigator.

Take all available samples from the kit for further processing together with the corresponding transfer tubes. Below, every analysis to be performed for each sample type is described. After processing, the results should be reported to the *department involved in study* and the samples should be stored in the freezer until shipment *(if applicable)*.

2.5.1 **Sample type 1**

Table indicating which handlings need to be done for which visit

Sample type	Handling	Visits							

Detailed protocol of all handlings that needs to be done on this sample type from arrival in the lab over processing until storage of sample/aliquots and/or reporting results. It needs to be clearly mentioned in case routine protocol can be used.

2.5.2 **Sample type 2**

Detailed description of all handlings that needs to be done on this sample type from arrival in the lab over processing until storage of sample/aliquots and/or reporting results. It needs to be clearly mentioned in case routine protocol can be used.

Table indicating when sample type 2 needs to be collected

	Visits							
Sample type								

In case rapid diagnostic needs to be used, the following information needs to be included:

- *What the assay is detecting*
- *Who can perform the assay*
- *Maintenance instructions*
- *Detailed protocol*
- *Detailed instructions for quality control*
- *Detailed instructions on how to report results*

3. Shipping instructions

The below section describes the LAB-Net procedure. This should be updated in case the procedure has changed or the central lab is located elsewhere.

- Shipments on dry ice will be organized by the Central Laboratory upon request. To request a shipment, you will need to fill out a **Shipment Request Form** (Appendix x) that should be faxed/emailed to the Central Laboratory 15 days prior to the next scheduled pick-up.
- The form will have details on the number of samples to assess the size of the shipment and any national holidays that might fall in the fortnight of the proposed pick-up/shipment.
- At the time of shipment to the Central Laboratory, each sample kit should contain all the material from *one subject/all the material from one subject with the exception of the microbanks/other description*.
- *Other things to keep in mind when organising a shipment: for example: 1 microbank per strain will be shipped on dry ice in small boxes (one box can hold ~100 microbanks) similar to the ones in which the microbanks were sent to you by the Central Laboratory.*
- No shipments will be picked up on Fridays.
- The courier will call you to verify sample availability and to propose a pick-up date. The agreed pick-up date and time will be confirmed in writing via e-mail or fax.
- Dry ice and external packaging boxes will be provided by the courier.

Central Laboratory follow-up on the received shipment:
Upon arrival, the Central Laboratory will check the available samples. Samples will be tracked and reconciled by entering the sample types received into the Sample Tracking database.

The Central Laboratory will inform you on the presence of the samples.

4. Training and quality control (if applicable)

Training requirements for staff that will handle study samples and perform study procedures, i.e. SIV need to be followed or staff needs to be trained by someone who attended SIV: documented by PI in file.

QC information and archiving of results

QC program including suggestions as internal audit. External quality assessment information, if Central lab is sending EQA panel to the local labs

5. Q&A/Troubleshooting (if applicable)

This paragraph should address Q&A based on experience in previous studies.

Examples of Frequently asked questions:
Should all samples be labeled?
Could strains be stored at -20 °C? etc.

6. Information on CRO (if applicable)

7. Contact details

Questions concerning sample materials, shipment, data management:

Contact details

Questions concerning sample collection and management:

Contact details

Questions concerning Rapid diagnostic (If applicable)

Contact details

8. Appendices

- *Collection Flow Chart*
- *Forms:*
  - *Requisition forms*
  - *Reorder form*
  - *Shipment request form*
- *Other documents important for sample collection or sample processing*