Laboratory User Handbook

THE AURUM INSTITUTE

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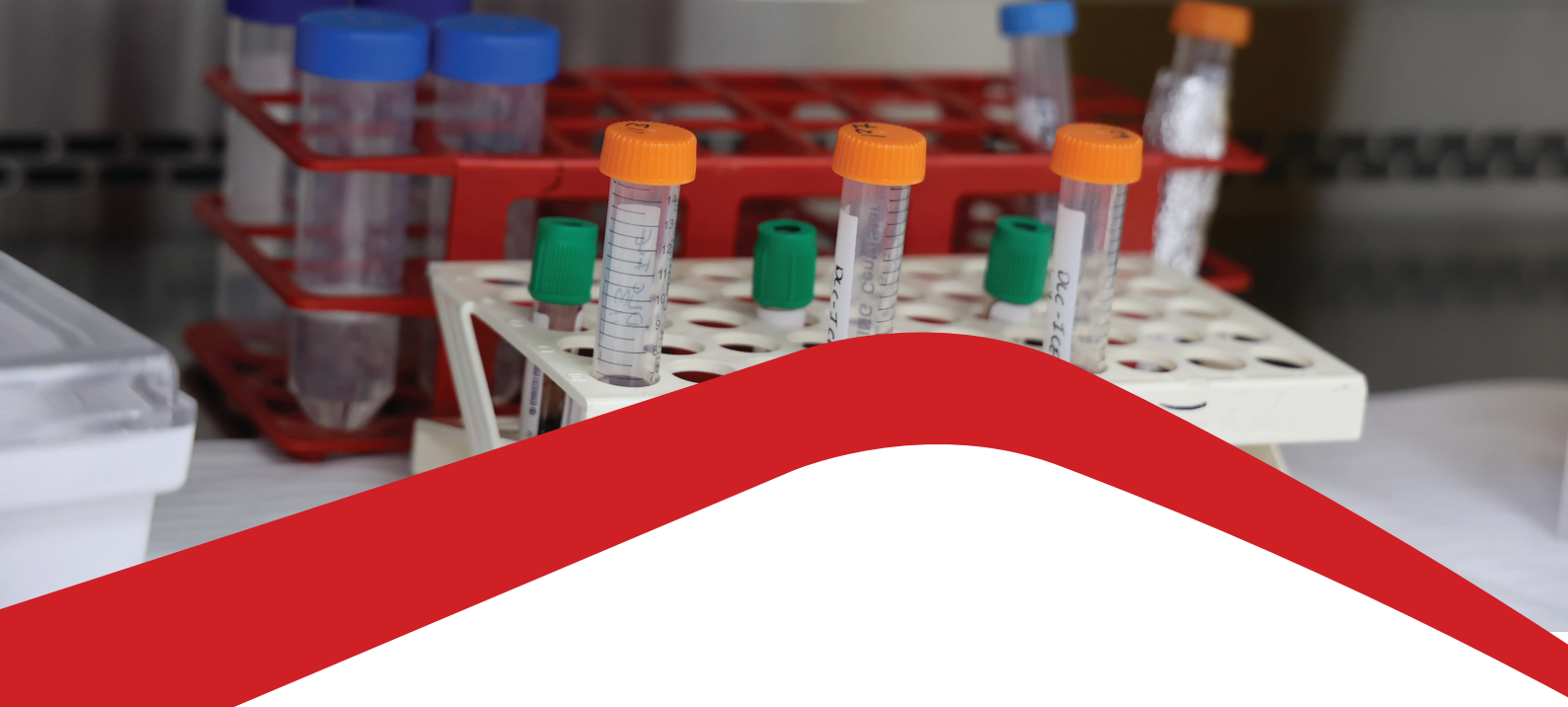

1. Introduction

This User handbook provides users and interested parties with contact phone numbers of Aurum Laboratories, information regarding selecting examination methods and interpreting examination results, information about the sample that is required for testing, storage requirements, the minimum criteria for acceptance and processing of a sample, how to handle samples, the repertoire of tests and the turnaround time target.

The Aurum Institute upholds the rights of the patients to Health care that is free from discrimination.

The analysis of samples collected from subjects participating in clinical trials forms a key part of the clinical trials process. Sample analysis or evaluation provides important data on a range of endpoints which is used. It is essential that sample analysis or evaluation is performed to an acceptable standard which will ensure participant/patient safety is not compromised and that data is reliable and accurately reported.

Clinical Research Division at Aurum Institute is non-profit organisation which conducts clinical research trials. Clinical research sites are in Gauteng and North-West Province and have site laboratories (See table 1 below) that supports clinical trials by receiving samples, testing, processing, storing and shipping of specimens to local reference laboratories, local repositories and internationally.

Clinical trial sites are responsible for participant/patient preparation for sample collection as per protocol schedule of evaluations.

Table 1: Aurum Institute Laboratory contact details

Address	Contact details and Opening Hours
Tembisa Biomedical Research Laboratory Cnr Flint Mazibuko & Rev RTJ Namane Drive Hospital View Tembisa 1632	**Lindelwa Nkangane** Laboratory Manager W: 087 135 1807 Email: lnkangane@auruminstitute.org Email: lnkangane@auruminstitute.org Opening Hours: 06:00 -18:00
Klerksdorp Laboratory The Aurum Institute 401 Jade Square Cnr OR Tambo & Margaretha Street Klerksdorp	**Letlhogonolo Seabela** Laboratory Manager W: 087 135 1413 LSeabela@auruminstitute.org Opening Hours: 06:00 -18:00
Rustenburg Laboratory Aurum Institute First Floor 50 Steen Street, Cnr Pretorius Street Rustenburg, Northwest, 0299	**Christian Kasongo** Laboratory Manager W: 087 1351578 Ckasongo@auruminstitute.org Opening Hours: 06:00 -18:00
Pretoria Laboratory The Aurum Institute Pretoria 6 Mark Shuttleworth Street Innovation Hub Pretoria 0087	**Palesa Mokoena** Laboratory Technologist W: PMokoena@auruminstitute.org Opening Hours: 06:00 -18:00

2. Purpose

The aim of this handbook is to improve, harmonize and strengthen the interaction between the clinic and the laboratory in preparation and management of specimen collection in clinical trials. This document provides requirements for all activities related to collection, labelling, sample integrity, stability, storage, packaging and transport of samples, to ensure the quality of clinical trial specimen to achieved for better health outcomes of the protocol.

3. Abbreviations

ACD	Acid Citrate Dextrose
AFB	Acid Fast Bacilli
CAT	Clot Activator Tube
CPT	Cell Preparation Tube
CRD	Clinical Research Division
CRS	Clinical Research Site
DLC-ICE	Differential Leukocyte Count and Immunophenotyping of Cryopreserved Ex vivo blood
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme Linked Immunosorbent Assay
ERP	Enterprise Resource Planning
GCLP	Good Clinical Laboratory Practice
GCP	Good Clinical Practice
HepBsAg/Ab	Hepatitis Surface B Antigen/Antibody
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HSV2	Human Simplex Virus 2
IGRA	Interferon Gamma Release Assay
KOH	Potassium Hydroxide
LN2	Liquid Nitrogen
MTB	Mycobacterium Tuberculosis
NaHep	Sodium Heparin
OHS	Occupational Health and Safety
PBMC	Peripheral Blood Mononuclear Cells
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
PI	Principal Investigator
POCT	Point of Care Testing
PPE	Personal Protective Equipment
QFT	QuantiFERON
RPR	Rapid Plasma Reagin
RT	Room Temperature
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SC	Study Coordinator
SOP	Standard Operating Procedure
SSP	Study Specific Procedure
SST	Serum Separator Tube
TAT	Turn Around Time
TB	Tuberculosis
TPHA	Treponema Pallidum Hemagglutination Assay
VL	Viral Load
ZN	Ziel Nielsen

4. Definitions

4.1 Phlebotomy: The act of drawing or removing blood from the circulatory system through an incision or puncture to obtain a sample for analysis and diagnosis.

4.2 Ambient: the air temperature of the surrounding environment. An ambient temperature is not categorized by a temperature range, as it could be any temperature.

4.3 STAT: Without delay.

4.4 TAT: The Aurum Institute CRD Laboratories Measures Turnaround Time from Samples receipt in the Laboratory until results are released.

5. Commitment by Aurum Institute Clinical Research Division

The Aurum Institute sites shall ensure activities are performed in such a way as to meet the requirements of this document. This shall include activities performed off-sites. Where collections are performed outside of the direct control of a clinical site, such as by healthcare workers or by an independent collection company the requirements of this document shall be met. There shall be cooperation between the clinical research site and the off-site facility providing collection and transport of samples, including the exchange of information, to ensure the harmonization of processes and procedures, where appropriate according to the protocol requirements.

6. Ethical conduct

Informed consent is sought from the clinical trial subject or his/her legal representative or guardian when participating in a clinical research trial. Participant/ patient should understand what the sample is to be used for and how the results of the research might impact on their interests. Consent is also obtained for storage and potential future use of samples.

Aurum Institute Clinical Research sites have a process of informed consent which ensures that sound ethical conduct is always upheld and considers undue pressure, conflicts of interest and impartiality. Each participant participating in clinical trials goes through the process of consenting for procedures of the protocol which include collection of specimens. Consent forms are based on study projects and are study specific.

If obtaining consent is not possible in emergency situations, the laboratory can carry out necessary procedures, provided they are in the best interest of the participant or Sponsor.

7. Impartiality

Participant/patient will be screened as per protocol requirements by following specified inclusion and exclusion criteria. Processes for the collection and transport of samples shall be undertaken impartially and structured and managed to safeguard impartiality.
The Aurum Institute Clinical Research site staff shall be responsible for the impartiality of its pre-examination activities and shall not allow commercial, financial or other pressures to compromise impartiality.

The Aurum Institute shall monitor its activities and its relationships to identify threats to its impartiality. This monitoring shall include relationships of its personnel. If a threat to impartiality is identified, the situation shall be eliminated or minimized so that impartiality is not compromised.

8. Confidentiality

8.1. Management of information

The Aurum Institute ensures that employees do not disclose to a third party any confidential participant/ patient information belonging to or in possession of the institute unless permitted to do so in writing by an Executive Director or authorized delegate who communicated the information to them. In some cases, the additional written permission of other parties or such as patient or other organization may be required.

8.2. Release and disclosure of information

When the Aurum Institute is required by law or authorised by contractual arrangements to release confidential information, the participant/patient concerned shall be notified of the information released and provide consent, unless prohibited by law.

Any information uncovered regarding your test results or state of health of the participant will be held in strict confidence. The participant will be informed of any finding of importance to his/her health or continued participation in Aurum studies, but this information will not be disclosed to the third party. The only exception to this rule will be cases of communicable diseases where a legal duty of notification of the Department of Health exists. In this case, the participant will be informed of any intent to disclose such information to the authorised state agency. Information about the participant/patient from a source other than the user (e.g. complainant, regulator) shall be kept confidential by the facility. The identity of the source shall be kept confidential by the facility and shall not be shared with the user, unless agreed by the source. Relevant Information about the patient/participant will only be made available to a patient/participant and any other health service provider at the request of the patient or the request of a healthcare provider acting on their behalf.

The Aurum Institute has a process for disclosure of a participant/patient safety incident, medical error, or incident related to a medical device involved in collection and/or transport of samples that did result or could have resulted in harm to that participant/patient and considers actions to mitigate the harm to the participant/patient.

8.3. Personnel responsibility

Personnel, including any committee members, contractors, personnel of external bodies, or individuals acting on the clinical research site's behalf, keep confidential all information obtained or created during the performance of the site pre-examination activities.

9. Requirements regarding participants, facility personnel and others

The site management shall ensure that the well-being, safety and rights of all participants/patients' interaction during sample collection and transport are a primary consideration.

During sample collection and transport, participants/patients and their samples are always treated in an ethical manner with care and consideration. This includes assuring privacy, being courteous and respectful and considering cultural diversity and disabilities.

10. Structural requirements

The Aurum Institute is a non-government organization which is committed in providing quality, reliable data when conducting clinical trials and any lab testing adhering to GCP, GCLP and ISO 15189: 2022.

The clinical research sites have infrastructure, adequate staff, administrative processes, adequate supplies that use applicable clinical policies, protocols and guidelines to ensure the provision of quality clinical trial conduct.

The handbook has been developed to standardize processes across clinical research division and improve quality of service delivery to participants/patients and meet protocol requirements and outcomes.

11. Site management

Clinical trial sites are under the authority of the Principal Investigator (PI) as per Good Clinical Practice guidelines. The PI is responsible for protecting the rights, safety and welfare of the participants/patients in a clinical trial. Personnel working on each clinical trial sites are delegated by the Principal Investigator.

It is the responsibility of the Principal Investigator/Clinician to ensure that specimens are correctly obtained, placed in the correct container, labelled, and transported safely. The Principal Investigator/designee is accountable for staff to which this procedure is delegated, ensuring that they have the knowledge of the process required. If a participant/patient is required to obtain their own specimens, they are given a full explanation of the process and a rationale (including the importance of hand washing prior to and on completion of the task) this information will be documented in study specific procedures and source documents for participants/patients. It is the responsibility of clinical staff to ensure that all tests are explained fully during informed consent process and before obtaining specimen. Confidentiality is always maintained to ensure sensitive information is not revealed unnecessarily on request forms by using participant identity number.

12. Advisory activities

Principal Investigator or Clinician ensures appropriate information is communicated and available to meet the needs of the participants/patients based on the protocol requirements. This is also communicated through the informed consent process when participants/patients join the clinical trial. Contact information of the responsible Principal Investigator/designee is communicated to the participant and documented in the informed consent document which the participant is provided a copy.

Clinical trial team is guided by the protocol on how to handle individual clinical cases (provided by the Consultant/Principal Investigator, Research Doctors, Senior Scientist, Laboratory Manager or Laboratory Technologist.

Regular protocol meetings between the clinic and the laboratory are conducted to communicate progress, concern between the two departments and consultation on scientific or logistical matters e.g. failure of samples to meet criteria.

12.1 Oral Requests

Clinicians can add test telephonically, however once added, this will be followed by a requisition form or amendment on the pre-existing requisition form.

13. Communication

It is the responsibility of the laboratory management to ensure that the customers' needs are met. Therefore, the laboratory has a process of receiving enquiries, comments and feedback through customer satisfaction questionnaire. Suggestions are welcomed to improve the service offered to the customer.

The laboratory communicates with users via regular meetings (Sponsor meetings, Clinic and Lab Meetings etc or completes a Laboratory/Clinic Communication Log TRIAL.LAB.SOP.QA005 FM001.

Complaints can be communicated to the laboratory by sending an email to laboratory manager. Laboratory users, participants/patients, and personnel feedback/ surveys for CRD Labs is circulated once a year by the Quality Manager.

The effectiveness of Laboratory communication with users is measured by user Feedback from the Customer survey, the outcome which is reviewed at the Annual Management Review.

14. Structure and authority

Only personnel trained in sample collection are authorized to collect specimen or assist the participant/ patient to collect specimens according to study specific procedures. Staff collecting specimens are delegated on the protocol by the Principal Investigator.

15. Training and competency

Clinical trial staff are trained and deemed competent in managing participant within the clinical trial. The phlebotomy training includes understanding the anatomy, awareness of the risk from blood exposure and the consequences of poor infection prevention and control. All health workers undertaking phlebotomy are trained in infection prevention and control procedures. Staff are expected to demonstrate proficiency on the specific methods that they will use on the job; for example, adult and paediatric sampling; and venous, arterial and capillary blood sampling.

Regular in-service training and supportive supervision is provided. The training programme provides theoretical and practical knowledge in blood sampling and blood drawing. A certificate of competence is issued upon successful demonstration of phlebotomy after completion of the training programme.

Before site staff handle participants, protocol training should have been done which include collection and packaging of specimens to the laboratory.

16. Infection prevention and control, safety equipment and best practice

All staff have a responsibility to protect themselves and others including participants/patients and the wider public, from inadvertent contamination from hazardous substances.

Always follow universal precautions. Treat all materials as infectious. Universal precautions are simple infection control measures that reduce the risk of transmission of blood borne pathogens through exposure to blood or body fluids among participants/patients and health care workers. Under the "universal precaution" principle, blood and body fluids from all persons are considered as infected with HIV, regardless of the known or supposed status of the person. Wear appropriate safety PPE such as gloves, laboratory coats and safety goggles.

16.1. Universal Precautions

A clinical specimen can be defined as any bodily substance, solid or liquid, that is obtained for the purpose of analysis. Examples include blood, sputum, pus, urine, faeces, and skin tissue. All specimens are potentially infectious, and all staff involved in collecting, handling, and transporting of specimens must follow the correct infection control precautions to reduce the risk of transmission of infection and be aware of related infection prevention and control policies, examples Personal Protective Equipment (PPE) policy and Hand Hygiene policy. Prompt, accurate laboratory reports are possible only if the specimen is properly collected and sent with the correct accompanied request form detailing participant/patient information, stored, and transported safely. It is therefore essential that staff follow the correct processes.

16.2. Personal Protection and hygiene

To prevent the complications related to unsafe practices equipment (including materials for hand hygiene) and personal protective clothing is routinely available in sufficient quantities. Items include:

a) personal protective equipment
b) safe blood-sampling equipment of high quality
c) antiseptics

16.3. Hand hygiene – before and after each participant/ patient contact and between procedures to reduce risk of cross contamination.

16.4. Gloves – a pair of well-fitting clean disposable latex or latex free gloves per participant/patient and between procedures to reduce the health care workers potential exposure and reduce the participant's risk of cross contamination.

16.5. Masks, visors – a pair of masks e.g. N95 for sputum collection to reduce exposure, and eye protection may also be needed if additional blood exposure is anticipated, for example, during arterial blood sampling.

17. Equipment and consumables

Supply chain management is a crucial aspect of running a successful specimen collection and clinical diagnostic lab. From managing inventory levels to ensuring the timely delivery of supplies, an effective Supply Chain greatly impact the efficiency and effectiveness of clinical research site. By focusing on key aspects such as inventory management, supplier relationships, and Quality Control, phlebotomy and clinical diagnostic laboratory optimize their operations and provide high-quality care to participants/patients.

As per study specific protocols, the Lab Manager prepares an annual budget for Sponsor-funded projects. The budget includes reagents, consumables, and labour. Budgets are submitted to the finance department and cost codes are assigned. The prices of tests may be requested from the laboratory by private users.

17.1. Inventory Management

Keeping track of supplies and ensuring that stock levels are optimized is crucial in specimen collection. Without proper inventory management, phlebotomists may run out of essential supplies, leading to delays in following project participant/patient which could impact on the outcome of the clinical trial.

17.2. Supplier Relationships:

Developing strong relationships with suppliers is essential in ensuring the timely delivery of supplies. By working closely with suppliers, clinical trial sites can better manage their inventory and reduce the risk of stockouts.

17.3. Ordering Processes:

Establishing efficient ordering processes help streamline the Supply Chain in specimen collection. By automating the ordering process and setting up regular deliveries, clinical trial staff can ensure that they always have the supplies they need on hand. E.g. ERP system.

The clinical trial sites follow Aurum Institute policy for ordering of stock and supplies for the clinics. Ordering of kits, stock and supplies should be in line with the clinic activities. Ordering of too much stock is avoided at all costs by managing stock inventory and usage efficiently. Study Coordinators are responsible for ordering and management of specimen collection supplies. Refer to SOP ordering of goods and supplies.

17.4. Quality Control

Ensuring the quality of the supplies used in specimen collection is essential for participant/patient safety. Supply Chain management plays a key role in verifying the quality of supplies and implementing measures to address any issues that may arise.

Procurement processes should ensure that all clinical trials unit have sufficient supplies of specimen collection and personal protective equipment. Such equipment must meet at least the minimum standards of sterility, quality and safety to prevent complications related to unsafe practices.

17.5. Blood-sampling equipment

Safety-engineered evacuated tube systems or winged needle sets are safer than a hypodermic needle and syringe, but all are effective for blood sampling. Safety features (e.g. needle covers, needleless transfer systems or adaptors, and retractable lancets) can further reduce the risks associated with manual recapping, needle removal, disassembly and transfer of blood from syringes to tubes. A needle and syringe are the most common tool for withdrawing large quantities of blood.

A sterile single-use needle and syringe should be used for each patient, and should be placed, as a single unit, into a sharp's container immediately after use. Safety-engineered equipment offers better protection to the health worker but should be appropriate for the specific task.

Capillary punctures should be performed using a sterile device – preferably with safety features that automatically retract the lancet – to help prevent both reuse and sharps injuries.

18. Risk management

The Aurum Institute has a risk management process (TRIAL.LAB.SOP.QA003) to minimise potential harm to participants/patients and site staff associated with sample collection and transport. Risk can be reduced by following best practices in infection prevention and control, after obtaining informed consent from the participant/patient.

18.1. Risks and risk reduction strategies

Participant risks	Risk reduction strategy
Exposure to bloodborne viruses through reuse of needles, syringes and lancets, contaminated work surfaces	Hepatitis B vaccine for staff Sterile single-use devices only Safety-engineered devices Clean work surfaces with disinfectant
Infection at blood sampling site	Perform hand hygiene Clean participant's skin with 70% isopropyl alcohol and allow to dry Use sterile needle and syringe removed from the packaging just before use
Pain at blood sampling site	Well-trained person should take the blood sample Venepuncture is less painful than heel-pricks in neonates Use needle of smaller gauge than the selected vein
Haematoma or thrombus	Enter vessel at an angle of 30 degrees or less Use gauge of needle smaller than the vein Apply pressure to a straight arm for 3–5 minutes after drawing blood
Extensive bleeding	Take a history to identify participants on anticoagulants and with a history of bleeding Use a gauge of needle smaller than the vein
Nerve damage	Avoid finger-pricks for children Use antecubital vessels when possible Avoid probing
Vasovagal reaction, Syncope, fainting	Hydrate participant, take postural blood pressure if dehydrated Reduce anxiety Have participant lie down if the person expresses concern Provide audio-visual distraction
Allergies	Ask about allergies to latex, iodine and alcohol before starting the procedure

18.2. Healthcare workers

Clinic staff	Risk reduction strategy
Needle or sharps injury during or after the procedure	Use safety devices such as needle covers, tube holders that release needles with one hand and safety lancets
Breakage of blood containers	Avoid two-handed recapping and disassembly
Splashes (rare)	Place sharps container in sight and within arm's reach Dispose of used sharps immediately
Exposure to blood	Hepatitis B vaccination Wear gloves Use evacuated tubes and transfer devices when drawing multiple tubes Follow protocol for exposure to body fluids and report incident, even if post-exposure prophylaxis is not desired Cover broken skin area with a waterproof dressing

19. Emergency situations

Aurum Institute has established health and safety procedures that outline the necessary steps to be taken during emergency situations like fire, bomb threats, hostage situations, earthquakes, armed robberies or public unrest. These situations may necessitate partial or total evacuation. SOP OHS 007 detail all the necessary procedures to be followed.

Each site is equipped with an emergency trolley to attend to any medical emergencies to stabilize participants before sending to hospital if required.

20. Facilities and environment conditions

Areas designated for specimen collection are situated within the clinic facility and the environmental conditions are suitable for collection of samples to ensure the quality of work, safety of personnel and participant/patient care services are not compromised. The equipment required are fit for purpose for supporting the activities of the clinic and are maintained in functional and reliable condition. Access to the examination areas is authorized to clinician working with participants for collecting samples and are controlled. The areas for sample collection provide privacy to ensure confidentiality of participants.

21. Aurum Laboratory scope of work

Each laboratory is supporting clinical trials. Each protocol has specific sample requirements based on the schedule of events. The testing in some laboratories is limited to rapid testing, processing and shipping specimens. Scope will be expanded as new research methodologies and sponsor requirements emerge.


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1. Klerksdrop Laboratory

Test offered	Type of tube or collection media	Specimen Required	Transportation Temperature	Storage Conditions and Duration.	Turn Around Time (from specimen receipt at the laboratory)
Rapid HIV	SST	Serum	Ambient Temperature	2-8 °C – 7 Days	24 hours
	EDTA	Whole Blood		2-8 °C – 7 Days	24 hours
Urine pregnancy	Specimen sterile container	Urine	Ambient Temperature	2-8 °C – 7 Days	24 hours
Urine dipstick				2-8 °C – 7 Days	24 hours
Urine microscopy				2-8 °C – 7 Days	24 hours
Vaginal wet mounts - KOH	Swab	Vaginal Swab	Ambient Temperature	-80°C freezer- SSP	24 hours
RPR/TPHA	SST	Serum	Ambient Temperature	2-8 °C – 7 Days	48 hours
SARS CoV-2 GeneXpert	Swab	Nasopharyngeal/ Oropharyngeal	Ambient Temperature	-80°C freezer- 7 Days	48 hours
HIV Viral Load PCR	EDTA	Plasma	Ambient Temperature	2-8 °C – 7 Days	48 hours
IGRA	4 x QFT	Plasma	Ambient Temperature	-80°C freezer- SSP	72 hours
Processing of samples					
Serum storage	SST, CAT	Serum	Ambient Temperature	-80°C freezer- SSP	6 hours
Plasma storage	EDTA	Plasma	Ambient Temperature	-80°C freezer- SSP	6 hours
PBMC processing	EDTA, ACD, NaHep, CPT	Whole Blood	Ambient Temperature	-80°C freezer- SSP	4 hours
DLC-ICE	NaHep	Whole Blood	Ambient Temperature	-80°C freezer- SSP	3 hours
Soft cup	50ml Falcon tube	Vaginal Excression	Ambient Temperature	-80°C freezer- SSP	2 hours


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2. Rustenburg Laboratory

Test offered	Type of tube or Sample Collection media	Specimen Required	Transportation Temperature	Storage Conditions and Duration	Turnaround Time (from specimen receipt at the laboratory)
Rapid HIV	SST	Serum	Ambient Temperature	2-8 °C – 7 Days	24 Hours
	EDTA	Whole Blood		2-8 °C – 7 Days	24 Hours
Urine pregnancy	Urine container	Urine	Ambient Temperature	2-8 °C – 7 Days	24 Hours
Urine dipstick				2-8 °C – 7 Days	24 Hours
Urine microscopy				2-8 °C – 7 Days	24 Hours
RPR/TPHA	SST	Plasma	Ambient Temperature	2-8 °C – 7 Days	48 Hours
SARS CoV-2 GeneXpert	Swab	Nasopharyngeal or Oropharyngeal Swab	Ambient Temperature	-80°C freezer- 7 Days	48 hours
HIV Viral Load PCR	EDTA	Plasma	Ambient Temperature	2-8 °C – 7 Days	48 Hours
HPV PCR	Swab	Vaginal Swab	Ambient Temperature	2-8 °C – 7 Days	48 hours
CT/NG PCR	Swab	Vaginal and Anal Swab	Ambient Temperature	2-8 °C – 7 Days	48 hours
Hepatitis Surface Antigen	SST	Serum	Ambient Temperature	2-8 °C – 7 Days	48 hours
Rapid Trichomonas	Swab	Vaginal Swab	Ambient Temperature	No storage required.	24 hours
HSV2 ELISA	SST	Plasma	Ambient Temperature	2-8 °C – 7 Days	7 days
TV PCR	Swab	Vaginal Swab	Ambient Temperature	2-8 °C – 7 Days	48 hours
Chemistry Test panels			Ambient Temperature		
Urea and Electrolyte(U/E)	SST	Serum		2-8 °C – 7 Days	24 hours
Liver Function Tests (LFT)	SST	Serum		2-8 °C – 7 Days	24 hours
Lipogram	SST	Serum		2-8 °C – 7 Days	24 hours
Glucose	Fluoride tube	Plasma		2-8 °C – 7 Days	24 hours
Haematology Full Blood Count	EDTA	Whole Blood	Ambient Temperature	2-8 °C – 7 Days	24 hours
Processing of samples					
Serum storage	SST, CAT	Serum	Ambient Temperature	-80°C freezer- SSP	6 hours
Plasma storage	EDTA	Plasma	Ambient Temperature	-80°C freezer- SSP	6 hours
Whole blood storage	NaHep	Whole blood	Ambient Temperature	-80°C freezer- SSP	6 hours
PBMC processing	EDTA, ACD, NaHep, CPT	Whole blood	Ambient Temperature	-80°C freezer/LN2 SSP	4 hours
Leukapheresis	Leucopack Specimen bag	Leukopak	Ambient Temperature	-80°C freezer LN2 SSP	4 hours
DLC-ICE	NaHep	Whole Blood	Ambient Temperature	-80°C freezer- SSP	3 hours
Soft cup	50ml Falcon tube	Vaginal excression	Ambient Temperature	-80°C freezer- SSP	2 hours
Swabs storage	Cryovial	Swab	Ambient Temperature	-80°C freezer- SSP	5 hours


RECEPTION

3. Tembisa Biomedical Research Laboratory

Test offered	Type of tube or Sample collection media	Specimen Required	Transport Temperature	Storage Conditions and Duration	Turnaround Time (from specimen receipt at the laboratory)
Rapid HIV	EDTA	Whole blood	Ambient Temperature	2-8 °C – 7 Days	24 hours
	SST	Serum		2-8 °C – 7 Days	24 hours
Urine pregnancy	Urine container	Urine	Ambient Temperature	2-8 °C – 7 Days	24 hours
Urine dipstick				2-8 °C – 7 Days	24 hours
Urine microscopy				2-8 °C – 7 Days	24 hours
Vaginal wet mounts - KOH	Swab	Vaginal Swab	Ambient Temperature	-80°C freezer- SSP	24 hours
RPR/TPHA	SST	Serum	Ambient Temperature	2-8 °C – 7 Days	48 hours
SARS CoV-2 PCR	Swab	Nasopharyngeal Or Oropharyngeal Swab	Ambient Temperature	-80°C freezer- 7 Days	24hours
HIV Viral Load PCR	EDTA	Plasma	Ambient Temperature	2-8 °C – 7 Days	72 hours
HPV PCR	Swab	Vaginal Swab	Ambient Temperature	2-8 °C – 7 Days	72 hours
CT/NG PCR	Swab/Urine Container	Vaginal Swab or Urine	Ambient Temperature	2-8 °C – 7 Days	48 hours
Trichomonas Vaginalis Routine test	Swab/Urine container	Vaginal Swab or Urine	Ambient Temperature	No storage required.	24 hours
IGRA	4 x QFT	Plasma	Ambient Temperature	Plasma can be stored-80°C freezer- SSP	72 hours
ELISPOT Quantiferon Plus	NaHep	Whole Blood/Plasma	Ambient Temperature	Plasma can be stored-80°C freezer- SSP	72 hours
TB					
Ziel Neilson AFB – Confirmatory Microscopy	Sterile Sputum Container	Sputum	ICE Gel pack 2°C - 8°)	Slides are kept at Room Temperature (17°C to 27°C) - SSP	24 hours, Reported at the same time as the MGIT/ Liquid Culture
Auramine Stain- Presumptive Microscopy				Slides are kept at Room Temperature (17°C to 27°C) - SSP	48 hours
GeneXpert Xpert MTB/RIF Assay (semi –quantitative nested real-time PCR				No Storage	48 hours
TB Culture				TB Isolates -80°C freezer- SSP. TB Cultures – Room Temperature (17°C to 27°C)- SSP	42 days

3. Tembisa Biomedical Research Laboratory *(Continued)*

Test offered	Type of tube or Sample collection media	Specimen Required	Transport Temperature	Storage Conditions and Duration	Turnaround Time (from specimen receipt at the laboratory)
Rapid Identification MTB complex	Sterile Sputum Container	Sputum	ICE Gel pack (2°C - 8°C)	No storage required.	24 hours Reported at the same time as the MGIT/Liquid Culture, unless otherwise requested by Client.
Drug Susceptibility Testing DST/ MGIT 960 system				No storage required.	42 days
Whole Blood Bactericidal Assay/ MGIT 960 System	NaHep- Tube at different time points	Whole- blood	Ambient Temperature- on a rotator	No storage required.	96 hours
Processing of samples					
Serum storage	SST, CAT	Serum	Ambient Temperature	-80°C freezer- SSP	6 hours
Plasma storage	EDTA, ACD, CPT	Plasma	Ambient Temperature	-80°C freezer- SSP	6 hours
Whole blood storage	NaHep	Whole blood	Ambient Temperature	-80°C freezer- SSP	6 hours
PBMC processing	EDTA, ACD, NaHep, CPT	Whole blood	Ambient Temperature	-80°C freezer/LN2 SSP	6 hours
Leukapheresis	Leukopak Specimen bag	Leukopak	Ambient Temperature	-80°C freezer/LN2 SSP	4 hours
DLC-ICE	NaHep	Whole blood	Ambient Temperature	-80°C freezer SSP	3 hours
Soft cup	Falcon tube	Vaginal excression	Ambient Temperature	-80°C freezer SSP	4 hours
Swabs storage	Cryovial	Swab	Ambient Temperature	-80°C freezer SSP	4 hours
RNA Isolation DNA Extraction DNA Cloning Plasmid DNA Purification	EDTA, NaHep,	Whole Blood/Plasma	Ambient Temperature	-80°C freezer -20°C freezer SSP	1 week (Research)


ENTERPRISE BUILDING


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DO NOT TURN BOX UPSIDE DOWN

4. Pretoria Laboratory

Test offered	Type of tube	Specimen required	Transport Temperature	Storage Conditions and Duration	Turnaround Time (from specimen receipt at the laboratory
Rapid HIV	EDTA	Whole Blood	Ambient Temperature	2-8 °C – 7 Days	24 hours
	SST	Serum		2-8 °C – 7 Days	24 hours
Urine pregnancy	Sterile Urine container	Urine	Ambient Temperature	2-8 °C – 7 Days	24 hours
Urine dipstick				2-8 °C – 7 Days	24 hours
Urine microscopy				2-8 °C – 7 Days	24 hours
Vaginal wet mounts - KOH	Swab	Vaginal Swab	Ambient Temperature	-80°C freezer- SSP	24 hours
Processing of samples					
Serum storage	SST, CAT	Serum	Ambient Temperature	-80°C freezer- SSP	4 hours
Plasma storage	EDTA, ACD, CPT	Plasma	Ambient Temperature	-80°C freezer- SSP	4 hours
12hr Whole Blood Assay processing and Storage.	NaHep	Whole blood	Ambient Temperature	-80°C freezer- SSP	12 hours

22. Instruction for pre-collection activities

22.1 Site Laboratories collection kits

Specimen collection kits are prepared based on the protocol schedule of events. The laboratory staff will give guidance to the clinical staff. Specimen collection kits include laboratory requisition forms specific to the visit based on the protocol schedule, blood collection tubes and or specimen transfer tube if required. The kits prepared indicate the name and number of the protocol, the visit name or number and the first expiry date of the collection tubes.

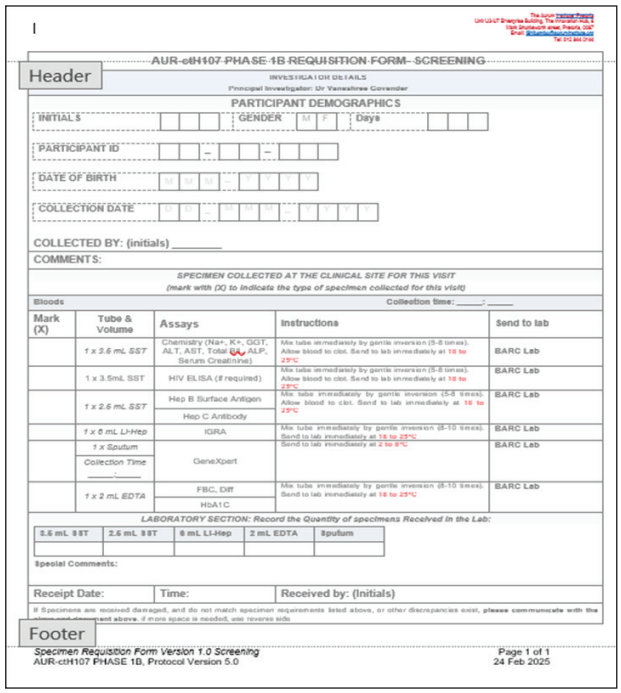
22.2 Referral Laboratory collection kits

Where samples are to be sent to an external laboratory for safety testing, a contract must be in place prior to any sample shipment. Referral laboratory specimen collection kits are provided by the reference laboratory. The site clinic is responsible for ordering, keeping the inventory and usage of specimen collection kits. The collection kits include the laboratory requisition form, blood collection tubes and supplies and specimen transfer tube if required. Each kits indicate the name/number of the protocol, name of the visit and the earliest expiry date of the collection tubes.

23. Laboratory Requisition Forms

23.1 Laboratory requisition forms (See figure 1) are prepared based on the project between the laboratory staff and the study coordinator. The laboratory requisition is visit specific. Minimum information required include: -

- Demographics
- Project name and number
- Participant Identity
- Date of birth if required
- Gender
- Collection date and time
- Visit code/number
- Phlebotomy information
- Specimen collection section
- Number of tubes required
- Type of tubes to be collected
- Instructions on how to collect
- Location where samples will be processed or shipped – optional



Laboratory Requisition Form (Figure 1)

23.2 Receiving section – Laboratory

- Number of tubes received
- Date and time received
- Initials of the laboratory staff
- Comments section

24. Instructions for Specimen collection and labelling

Clinical Trial Samples are collected and processed in accordance with the approved protocol, Participant Information Sheet & Consent form and in accordance with documented consent given by the participant/ patient. Specimens are collected based on the schedule of evaluations of the protocol.

Clinic staff prepare their working stations with the correct laboratory requisition and the correct specimen collection kit for each protocol to avoid missing important specimen collection time-points. Specimen collection kits are pre-packed for convenience. Mix-matching of specimen collection kits are avoided at all costs. Instruction on the preparation of the participant before collection is important e.g. before or after a meal. Expiry date of the specimen collection kits is checked before collection of specimens. Extra specimen collection materials are available in case of difficult phlebotomy or collapse vein.

Samples are labelled with the correct participant/ patient identity, the name of the protocol, collection date. Use the protocol specific primary label if available. For handwriting labelling, each tube must be labelled at the time of the collection by the information required. Information must be verified to match the information written on the laboratory requisition form.

Labels should be applied to the specimen tube or container in a manner that allows a clear vertical view of the tube contents to facilitate specimen use or processing by the laboratory. If the blood tube has a blank tube label, apply the primary local or any other label over the blank label so that the tube contents can still be viewed through a vertical strip opening.

25. Specimen collection procedures

25.1 There are four steps involved in obtaining a good quality specimen for testing:

- preparation of the participant/patient,
- collection of the specimen,
- processing the specimen, and
- storing and/or transporting the specimen.

25.2 Preparation

Prior to each collection, review the appropriate test description, including the specimen type indicated, the volume, the procedure, the collection materials, participant/patient preparation, and storage and handling instructions and verify and record that participants meet pre-examination requirements [e.g., fasting status, medication status (time of last dose, cessation), sample collection at predetermined time or time intervals.

25.3 Preparing the Patient

Provide the participant/patient, in advance, with appropriate collection instructions and information on fasting, diet, and medication restrictions when indicated for the specific test.

25.4 Preparing the Specimen

Verify the participant/patient's identification. Proper identification of specimens is extremely important. All primary specimen containers must be labelled with at least two identifiers at the time of collection. Submitted slides may be labelled with a single identifier, but two identifiers are preferred. Examples of acceptable identifiers include (but are not limited to): participant identity, test request form number, accession number.

26. Pre-analytical Factors

26.1 Principle

There are multiple pre-analytical factors associated with the handling and processing of laboratory specimens that can lead to test result inaccuracy. Strict adherence to all phases of proper collection and processing is essential for accurate test results.

26.2 Pre-Analytical Factors:

- Improper Patient Identification
- Incorrect Order of Draw
- Incorrect Tube Selection
- Traumatic draws leading to haemolysis
- Inadequate mixing or insufficient sample

26.3 Specimen Handling/Processing:

- Serum tubes not thoroughly clotted before centrifugation
- Delay in Centrifugation
- Storing specimens in incorrect temperatures
- Specimen Transportation
- Frozen specimens thawing during transport
- Unspun specimens transported >2 hours from collection

26.4 Which tubes are used for which Test:

26.4.1 Blood specimens and Preservatives.

This is the basic sample types that are collected for protocol specific requirements. Over and above, the sites will follow protocol specific instructions.

Tube type	Volume	Determination	Instructions
Sodium Citrate 	4ml	Coagulation	Mix well by gently inversion 8 to 10 times
Clot Activator Tube 	2ml 4ml	Chemistry Serum storage	Mix well by gently inversion 8 to 10 times. Allow to clot at room temperature for 30 minutes.
Heparin 	4ml 6ml 10ml	IGRA PBMC processing	Mix well by gently inversion 8 to 10 times
EDTA 	2ml 4ml 10ml	Full Blood Count Rapid HIV Dried Blood Spot Plasma storage Other processes	Mix well by gently inversion 8 to 10 times

ACD	8.5ml	PBMC and plasma storage	Mix well by gently inversion 8 to 10 times
QuantiFERON TB Gold Plus  NIL, TB antigen1, TB antigen 2, Mitogen.	1ml each	IGRA	Collect 1 mL of blood into each tube. Shake tubes 10 times firmly enough to ensure inner surface of tubes is coated. Do not spin and keep at room temperature.
Paxgene 	2.5ml	RNA Sequencing	Mix well by gently inversion 8 to 10 times
Tempus Tube 	3ml	RNA Gene Expression	Shake vigorously or vortex for 10 seconds.

26.4.2 Other specimens

Urine	60ml 120ml	Urinalysis, Pregnancy, CT/NG Storage	
Sputum	60ml 120ml	MTB GeneXpert TB culture	
Swabs	ea	SARS-CoV-2 HPV Storage	

26.4.3 Blood collection procedure

Best practices in phlebotomy involve the following factors:

- planning ahead
- using an appropriate location
- quality control

26.4.4 Standards for quality care for participants/ patients and health workers include:

- availability of appropriate supplies and protective equipment
- availability of post-exposure prophylaxis (PEP)
- avoidance of contaminated phlebotomy equipment
- appropriate training in phlebotomy
- cooperation on the part of participant/patients
- quality of laboratory sampling

26.4.5 Quality assurance of phlebotomy

- Education and training are necessary for all staff carrying out phlebotomy.
- Standard operating procedures are required for each step or procedure and should be written and readily available to healthcare workers.
- Correct identification of the participant/patient and the protocol should be done through matching the participant/patient binder, protocol and laboratory requisition form.
- The condition of the sample should be such that the quality is satisfactory.
- Transporting of specimen safely should be part of the best practices to improve the quality of results from testing laboratory.
- Incident report system is required for reporting all adverse events. A register should be established with accurate details of the incident, possible causes and management of adverse events.

26.4.6 Quality of care for participants/patients and clinical staff.

26.4.6.1 Availability of appropriate supplies and protective equipment

- Hand-hygiene materials (soap and water or alcohol rub), well-fitting non-sterile
- gloves, single-use disposable needles, and syringes or lancing devices should be provided in sufficient numbers to ensure that each participant/patient has a sterile needle and syringe or equivalent for each blood sampling.
- Make available sufficient laboratory sample collection kits.
- Availability of post exposure prophylaxis (PEP). PEP should be readily available in case of accidental exposure. Refer to OHS SOP 003-Post Exposure Prophylaxis for Occupational Exposure to HIV and Hepatitis B.
- Hepatitis B immunization should be provided to all health workers in contact with blood products.

26.4.6.2 Avoidance of using contaminated phlebotomy equipment.

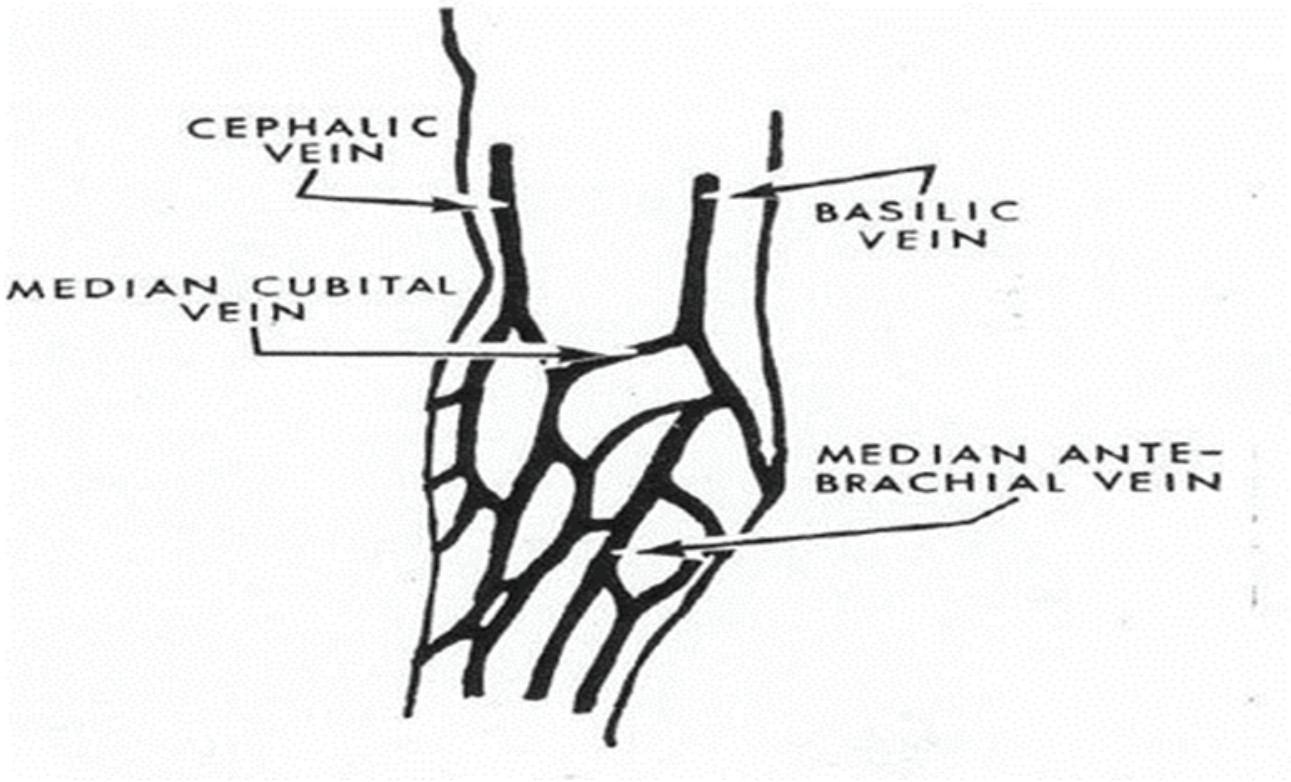
- To avoid contamination, any common use items such as glucometers should be visibly clean before use on a participant/patient and single use items should not be reused.
- Training in phlebotomy to prevent unnecessary risk of exposure to blood and to reduce adverse events to participants/patients.
- Participant/patient cooperation is one of the essential markers of quality care in phlebotomy. Clear information either written or verbal should be available to each participant/patient who undergoes phlebotomy.

26.4.6.3 Pre-collection requirements based on the protocol

- Aseptic technique is necessary to prevent the possible transmission of homologous serum hepatitis and HIV.
- It is most important that the correct technique be practiced avoiding unnecessary pain to the participant/patient, prevent tissue damage, secure a good representative blood specimen, and prevent contamination of the specimen or infection of the participant/patient.
- If difficulty is experienced in entering the vein or a hematoma begins to form, release the tourniquet and promptly withdraw the needle and apply pressure to the venepuncture site.
- When repeated venepunctures must be performed on one participant/patient, it is advisable to select different sites for blood withdrawal.
- Remove the tourniquet as early as possible once a good flow of blood has been established. Prolonged application of the tourniquet results in partial stasis of blood and lead to changes in quantitative values of blood components.
- For blood drawn by venepuncture, certain general precautions must be followed to ensure a valid analysis. Blood containers should be tightly stoppered to prevent drying or contamination.

26.4.6.4 Participant/patient identification and preparation

- Introduce yourself to the participant/patient and ask the participant/patient to state the full names, study and participant identity number.
- Check that the participant/patient binder matches the participant's identity to ensure accurate identification.
- Ask whether the participant/patient has allergies, phobias or has ever fainted during previous injections or blood draws.
- If the participant/patient is anxious or afraid, reassure the person and ask what would make them more comfortable.
- Make the participant/patient comfortable in a supine position (if possible).
- Place a clean paper or towel under the participant/patient's arm.
- Discuss the test to be performed and obtain verbal consent. The participant/patient has a right to refuse a test at any time before the blood sampling, so it is important to ensure that the participant/patient has understood the procedure and has consented.
- To obtain blood by venepuncture, draw the specimen directly from a participant/patient's vein with a sterile vacuum blood sample device.
- **In adults use the veins located in the proximal forearm or antecubital space as illustrated in the figure below.**



- The vein selected should be large, readily accessible, and sufficiently close to the surface to be seen and palpated.
- Venepuncture may pose a problem due to the age of the participant/patient, sclerotization due to repeated venepuncture, or any other unusual circumstance, e.g. healed burn areas; the phlebotomist should consult a physician concerning the procedure after two attempts were made.
- Veins can become distended and easier to enter by allowing the arm to hang down for 2 or 3 minutes. Slapping the site of puncture can haemolyze the surrounding blood cells and render some tests inaccurate.
- Young and vigorous persons usually have elastic veins well filled with blood. Elderly or debilitated persons can have sclerosed or fragile veins, which are hard to enter, or which collapse easily.

26.4.6.5 Hand hygiene

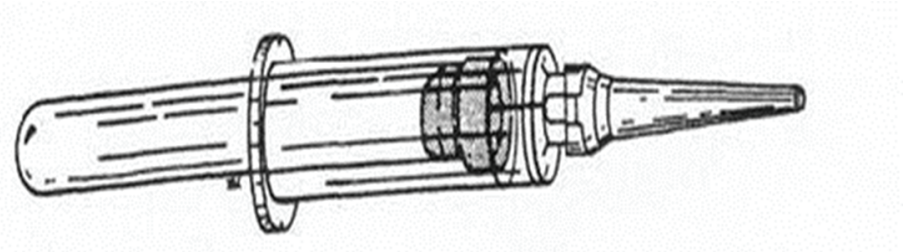
- Perform hand hygiene by washing hands with soap and water, and dry with single use towel or if hands are not visible contaminated, clean with alcohol rub.

26.4.6.6 After performing hand hygiene, put on well-fitting nonsterile gloves

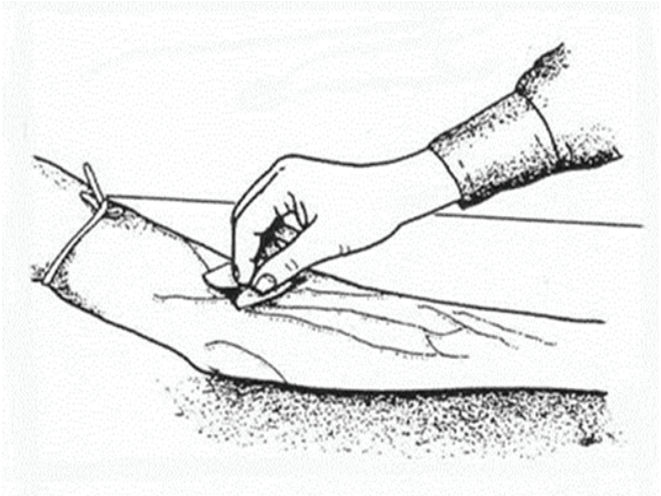
- Assess the participant/patient
- Position the participant/patient

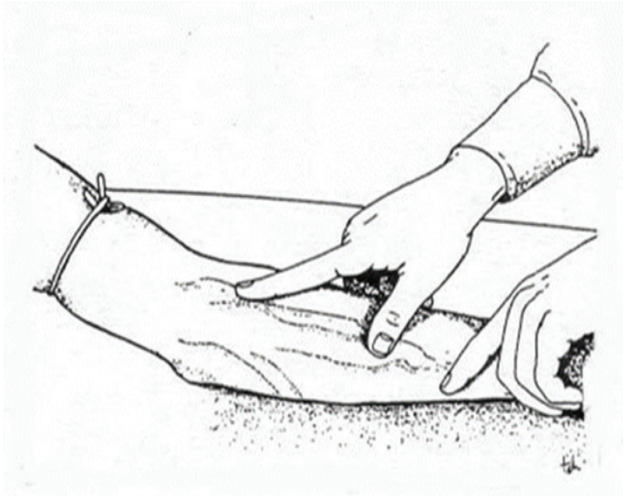
26.4.6.7 Specimen collection

- Place the Vacutainer tube in the holder until the rubber stopper reaches the guideline. The short needle should be embedded in the stopper, but the needle must not break the vacuum.



- Place a tourniquet around the participant/patient's arm above the elbow tightly enough to check venous circulation, but not so tight as to stop arterial flow. Place it approximately 5 centimetres above the proposed venepuncture site.
- **CAUTION:** Do not allow the tourniquet to remain in place for more than 2 minutes.
- Check the pulse at the wrist to make sure that arterial circulation is not cut off. If a pulse is not detected, release the tourniquet, check the pulse and re-site the tourniquet.
- Instruct the participant/patient to make a tight fist.
- By inspection and palpation locate the desired vein, determine the direction of its course, and estimate its size and depth.
- Cleanse the skin over the selected vein with prep pads in 70% percent isopropyl alcohol. Wipe off excess alcohol with sterile dry gauze (if required). Do not contaminate the area after cleaning.

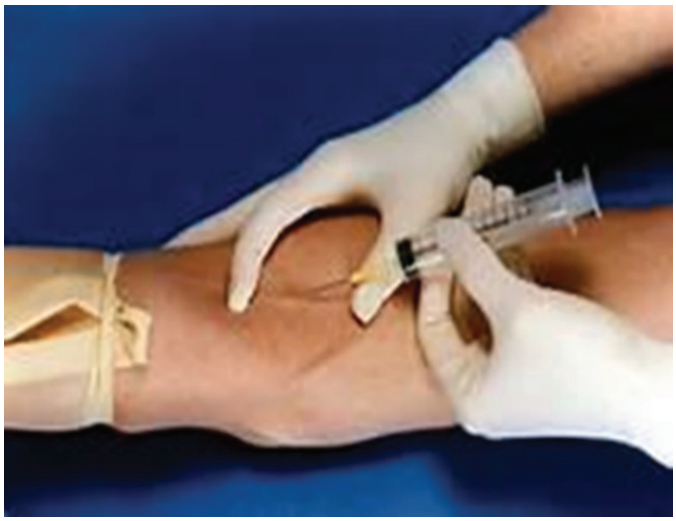


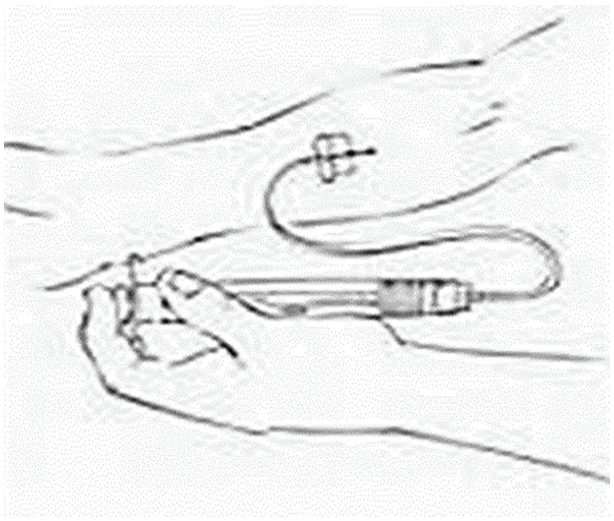


- Put on rubber/latex gloves.
- Do not remove the top cap of the needle until venipuncture is done to ensure sterility.
- For venipuncture, hold the vacutainer device between the dominant thumb and index finger. Enter the vein with the needle parallel to and alongside the vein. Probing or horizontal movement of the needle while under the skin must be avoided.
- After venipuncture change position of hands by fixing the venipuncture system with the thumb and index finger of the non-dominant hand. The non-dominant hand now serves to keep the needle immobilized in the vein during different actions.
- After entry into the vein push the tube all the way into the holder; the vacuum is broken, and blood flows freely into the tube. Release the tourniquet at this time.
- If more than one tube is required, release the tourniquet after the first tube is filled; remove the filled tube and insert the next one.
- **CAUTION:** Ensure the needle is not moved while tubes are being changed.
- After all samples have been drawn, place a sterile gauze pad/cotton wool over the point where the needle enters the skin and deftly withdraw the needle, placing pressure on the site.
- Have the participant/patient extend the arm and maintain light pressure on the gauze pad/cotton wool over the venipuncture site. Apply increased pressure for at least 2 minutes.
- Do not recap needle after use.
- Discard the vacutainer and needle immediately after use in the sharps container. Use the port on the sharps container to unscrew the needle from the needle holder to be automatically discarded.

26.4.6.8 Venepuncture procedure using a syringe:

- Place a sheathed needle or butterfly on the syringe.





- Remove the cap and turn the bevel up.
- Pull the skin-tight with your thumb or index finger just below the puncture site.
- Holding the needle in line with the vein, use a quick, small thrust to penetrate the skin and vein in one motion.
- Draw the desired amount of blood by pulling back slowly on the syringe stopper.
- Release the tourniquet.
- Place a gauze pad over the puncture site and quickly remove the needle. Immediately apply pressure. Ask the participant/patient to apply pressure to the gauze for at least 2 minutes. When bleeding stops, apply a fresh bandage, gauze or tape.
- Transfer blood drawn into the appropriate tubes as soon as possible using a needleless BD Vacutainer Blood transfer device, as a delay could cause improper coagulation.
- Gently invert tubes containing an additive 5-8times.
- Dispose of the syringe and needle as a unit into an appropriate sharps' container.

26.4.6.9 After Collection:

- Pack laboratory samples safely in a plastic leak-proof biohazard bag with an outside compartment for the laboratory requisition form. Placing the requisition on the outside compartment helps avoid contamination.
- If there are multiple tubes, place in a rack or padded holders to avoid breakage during transportation.
- Label the blood tubes with the appropriate labels.
- Blood will be handled according to individual protocol and laboratory manual requirements, e.g. at room temperature, on ice, etc. and transported to the laboratory within the specified period.

26.4.6.10 Troubleshooting Hints

a) If a blood sample is not attainable:

- If the venipuncture proves difficult because of a hard-to-find vein, pre-warming the antecubital area or rotating the wrist might help distend the vein and make it easier to find.

b) Reposition the needle.

- Ensure that the collection tube is completely pushed onto the back of the needle in the hub.
- Use another tube as vacuum may have been lost.

c) Loosen the tourniquet.

- Probing is not recommended. In most cases, another puncture in a site below the first site is advised.
- A participant/patient should never be stuck more than twice unsuccessfully by a phlebotomist.
- The Supervisor should be called to assess the participant/patient.

26.5 Paediatrics blood collection

- Venepuncture is the preferred method of blood sampling for term neonates and causes less pain than heel-pricks.

26.5.1 Equipment and supplies for paediatric participants/patients

- Use a winged steel needle, preferably 22 or 23 gauge, with an extension tube (a butterfly)
- Avoid gauges of 25 or more because these may be associated with an increased risk of haemolysis.
- Use a butterfly with either a syringe or an evacuated tube with an adaptor; a butterfly can provide easier access and movement, but movement of the attached syringe may make it difficult to draw blood.
- Use a syringe with a barrel volume of 1–5 ml, depending on collection needs, the vacuum produced by drawing using a larger syringe will often collapse the vein.
- When using an evacuated tube, choose one that collects a small volume (1 ml or 5 ml) and has a low vacuum; this helps to avoid collapse of the vein and may decrease haemolysis.
- Where possible, use safety equipment with needle covers or features that minimize blood exposure.
- Auto-disable (AD) syringes are designed for injection and are not appropriate for phlebotomy.

26.5.2 Preparation

- Ask whether the parent would like to help by holding the child. If the parent wishes to help, provide full instructions on how and where to hold the child; if the parent prefers not to help, ask for assistance from another phlebotomist.

26.5.3 Immobilize the child as described below:

- Designate two phlebotomist, or one phlebotomist and parent to immobilize the child.
- Ask the two adults to stand on opposite sides of an examination table.

26.5.4 Ask the immobilizer to:

- stretch an arm across the table and place the child on its back, with its head on top of the outstretched arm.
- pull the child close, as if the person were cradling the child.
- grasp the child's elbow in the outstretched hand.
- use their other arm to reach across the child and grasp its wrist in a palm-up position
- (Reaching across the child anchors the child's shoulder, and thus prevents twisting or rocking movements; also, a firm grasp on the wrist effectively provides the phlebotomist
- with a "tourniquet").
- If necessary, take the following steps to improve the ease of venepuncture.
- Ask the parent to rhythmically tighten and release the child's wrist, to ensure that there is an adequate flow of blood.
- Keep the child warm, which may increase the rate of blood flow by as much as sevenfold by removing as few of the child's clothes as possible and, in the case of an infant, by:
- Swaddling in a blanket; and having the parent or caregiver hold the infant, leaving only the extremity of the site of venepuncture exposed.
- Warm the area of puncture with warm clothes to help dilate the blood vessels.
- Use a transilluminator or pocket pen light to display the dorsal hand veins and the veins of the antecubital fossa.

26.5.5 Drawing blood

Follow the procedures given in Section above

- hand hygiene.
- advance preparation.
- patient identification and positioning.
- skin antisepsis (but **DO NOT** use chlorhexidine on children under 2 months of age).
- Once the infant or child is immobilized, puncture the skin 3–5 mm distal to (i.e. away from) the vein (66); this allows good access without pushing the vein away.
- If the needle enters alongside the vein rather than into it, withdraw the needle slightly without removing it completely and angle it into the vessel.
- Draw blood slowly and steadily.

26.6 Finger pricking method

26.6.1 Adult patients

- Prepare the skin
- Apply alcohol to the entry site and allow to air dry.
- Puncture the skin with one quick, continuous and deliberate stroke, to achieve a good flow of blood and to prevent the need to repeat the puncture.
- Wipe away the first drop of blood because it may be contaminated with tissue fluid or debris (sloughing skin).
- Avoid squeezing the finger or heel too tightly because this dilutes the specimen with tissue fluid (plasma) and increases the probability of haemolysis.
- When the blood collection procedure is complete, apply firm pressure to the site to stop the bleeding.
- Take laboratory samples in the correct order to minimize erroneous test results
- With skin punctures, collect the specimens in the order below, starting with
  1. haematology specimens
  2. chemistry specimens.
  3. Other as per study specific procedures

26.6.2 Paediatric and neonatal participants patients

26.6.2.1 Immobilize the child

First immobilize the child by asking the parent to:

- sit on the phlebotomy chair with the child on the parent's lap.
- immobilize the child's lower extremities by positioning their legs around the children in a cross-leg pattern.
- extend an arm across the child's chest, and secure the child's free arm by firmly tucking
- it under their own.
- grasp the child's elbow (i.e. the skin puncture arm) and hold it securely.
- use his or her other arm to firmly grasp the child's wrist, holding it palm down.

26.2.2 Prepare the skin

- Prepare the skin as described above for adult participant/patients.
- DO NOT use povidone iodine for a capillary skin puncture in paediatric and neonatal
- patients: instead, use alcohol, as stated in the instructions for adults.

26.6.2.3 Puncture the skin:

Puncture the skin as described above for adult participant/patients. If necessary, take the following steps to improve the ease of obtaining blood by finger-prick in paediatric and neonatal patients:

- ask the parent to rhythmically tighten and release the child's wrist, to ensure that there
- is sufficient flow of blood.
- keep the child warm by removing as few clothes as possible, swaddling an infant in a
- blanket, and having a mother or caregiver hold an infant, leaving only the extremity of
- the site of capillary sampling exposed.

Avoid excessive massaging or squeezing of fingers because this will cause haemolysis and impede blood flow.

26.6.2.4 Cleaning of blood spills and body fluids:

If blood spillage has occurred (e.g. because of a laboratory sample breaking in the phlebotomy area or during transportation, or excessive bleeding during the procedure), clean it up using the spill kit following safe procedure below:

- Put on gloves and a gown or apron if contamination or bleaching of a uniform is likely in a large spill.
- Mop up liquid from large spills using paper towels, and place them into the infectious waste.
- Remove as much blood as possible with wet cloths before disinfecting.
- Assess the surface to see whether it will be damaged by a bleach and water solution.
- For cement, metal and other surfaces that can tolerate a stronger bleach solution, flood the area with an approximately 5000 parts per million (ppm) solution of sodium hypochlorite (1:10 dilution of a 5.25% chlorine bleach to water). This is the preferred concentration for large spills. Leave the area wet for 10 minutes.
- For surfaces that may be corroded or discoloured by

a strong bleach, clean carefully to
- remove all visible stains. Make a weaker solution and leave it in contact for a longer period. For example, an approximately 525 ppm solution (1:100 dilution of 5.25% bleach) is effective.
- Prepare bleach solution fresh daily and keep it in a closed container because it degrades over time and in contact with the sun.

27. Urine Specimen collection

27.1 Materials for collection:
- Sterile plastic cup with lid (50 ml or more)
- Clean, screw-top specimen transport containers ("universal" containers are often used
- Gauze pads
- Soap and clean water (or normal saline) if possible.

27.2 Clean Catch Urine – Instructions for Women
- Provide a participant/patient with a clean container and that it is appropriately labelled with the study identification number.
- Participant/patient must wash their hands with soap and water.
- Open the container provided without touching the inside of the lid or cup and place it on the counter next to you.
- Open the anti-bacterial toilettes provided, removing both wipes and discard the wrapper.

27.2.1 Cleaning:
- sit as far back on toilet as possible, spreading your legs apart.
- while sitting, spread the lips of your vagina apart with one hand, keeping them spread apart with this same hand for the remainder of the collection process.
- with one of the toilettes, wipe from front to back only in a downward fashion only.
- discard the first toilette and repeat this with the second toilette.
- After cleaning and without closing the lips of your vagina, please urinate a small amount into the toilet (We do not want to collect this first small amount of urine).
- Continue to urinate into the cup, stopping collection of urine before you have finished urinating.
- Finish urinating in the toilet (We do not want to collect this final small amount of urine).
- Cover the container with the urine tightly.
- Place the urine in the designated area as instructed by the clinic staff.
- Flush the toilet and wash your hands thoroughly.

27.3 Clean Catch Urine – Instructions for Men
- Please confirm that you have a clean container and that it is appropriately labelled with study identification number. If you have any questions, please ask one of the clinic staff.
- Wash the hands with soap and water.
- Open the container provided without touching the inside of the lid or cup and place it on the counter next to you.
- Open the anti-bacterial toilettes provided, removing both wipes and discard the wrapper.

27.3.1 Cleaning:
- if applicable, pull the foreskin of your penis back.
- with one of the toilettes, wipe the head of the penis thoroughly.
- discard the first toilette and repeat this with the second toilette.
- After cleaning, please urinate a small amount into the toilet (We do not want to collect this first small amount of urine).
- Continue to urinate into the cup, stopping collection of urine before you have finished urinating.
- Finish urinating in the toilet.
- Cover the container with the urine tightly.
- Place the urine in the designated area as instructed by the clinic staff.
- Flush the toilet and wash your hands thoroughly.

28. Sputum Specimen collection

Tuberculosis (TB) is a disease caused by the organism Mycobacterium tuberculosis (MTB). Proper sputum collection is not only critical for optimizing detection/ recovery of MTB, but it is also extremely important for infection control, since this specimen is highly infectious. Accurate detection of MTB through screening tests is important for determining eligibility of participant/patients for clinical trials. Once enrolled and receiving anti-tuberculosis treatment in a clinical trial, the time when the participant/patient converts his/her sputum from culture positive to culture negative is the basis for determining efficacy of the treatment regimen.

28.1 Collection material required
- Sterile Sputum Container

28.2 Sputum Collection Procedures
- The ideal sputum specimen is produced by repeated deep inhalation and exhalation of breath followed by a cough as deep within the chest cavity as is possible for the participant/patient.

- Sputum should consist of thick, mucoid, white yellow,

sometimes blood-tinged, material from the lower airways and lungs (not saliva or oral/nasal secretion).
- Collection of early morning specimens is preferred due to overnight accumulation of secretions. However, specimens may be collected at any time from participant/patients who have a deep cough that is readily productive.

28.3 Supervised collection by Clinic or Study StaffF

- When collected in the clinic, collection staff should remain within viewing distance of the participant/patient during the procedure to help as needed; and to ensure that he/she is isolated from others until sputum collection is complete.
- Specimens should be collected in a well-ventilated area.
- Clinic staff collecting the sputum, regardless of the setting, must observe the appropriate infection control precautions, i.e. wear a N95 mask and wear gloves when hand contact with blood or other potentially infectious materials is anticipated.
- Collect sputum specimen in a sterile disposable, wide-mouth container or in a 50mL conical tube.
- Prior to collection, label the specimen container with the appropriate identifying label; including study number, participant ID, visit, protocol, and date and time of collection.
- Positively identify the study number and patient ID number.
- Inform the patient that saliva and upper respiratory/nasal secretions are not sputum and are not acceptable specimens.
- After the specimen is collected, place specimen container in refrigerator or a cooler with pre-chilled ice packs unless it is being transported to the laboratory within 1 hour.

NOTE: Specimens must be packaged in sealed zip lock biohazard bags with sufficient absorbent material and marked with appropriate biohazard labelling before transporting the specimen.

28.4 Collection, Clinic Storage and Transport of (Expectorated) Sputum Specimens

- Demonstrate to the participant/patient how to properly rinse his or her mouth and how to collect a sputum specimen using a demonstrator bottle/cup of water (from commercial source, boiled, sterile or distilled) and container/tube.

28.5 Instruct the patient to:

- Thoroughly clean his/her hands with soap and water. Provide the participant/patient clean disposable paper towels to dry his/her hands.
- Rinse his/her mouth with water (from commercial source, boiled, sterile or distilled) prior to collection of sputum. Provide a new, clean, disposable cup for each participant/patient.
- Breathe deeply several times and then cough from deep down within the lungs.
- Lean forward, breathe in and out slowly twice, hold breath for 2-3 seconds each time, and on third time forcefully cough to bring up the sputum.
- Collect the sputum in the sterile container provided and avoid touching the inside or edge of the specimen container or lid with their fingers.
- Once collection has been completed, thoroughly clean his/her hands with soap and water. Provide the participant/patient with a clean disposable paper towels to dry his/her hands.
- Repeat the above sequence until an adequate amount of sputum is collected. This may take up to 1 hour.
- If the participant/patient is unable to produce enough sputum within 1 hour, decide if the participant/patient is "unable to expectorate", requires rescheduling for another attempt at collection, or needs to undergo sputum induction.
- If collection is attempted and successful at another time, do not pool this sputum (unless instructed by the protocol) with the sputum collected at a different time.
- Tighten the lid/cap on the container/tube and to avoid leakage.
- Estimate the volume of sputum collected by comparison with container/tube with markings.

NOTE: As a rule, a minimum volume of 1 mL of sputum must be collected.

After the specimen is collected, place specimen container in refrigerator or a cooler with pre-chilled ice packs unless it is being transported to the laboratory within 1 hour.

NOTE: Specimens must be packaged in sealed zip lock biohazard bags with sufficient absorbent material and marked with appropriate biohazard labelling before transporting the specimen.

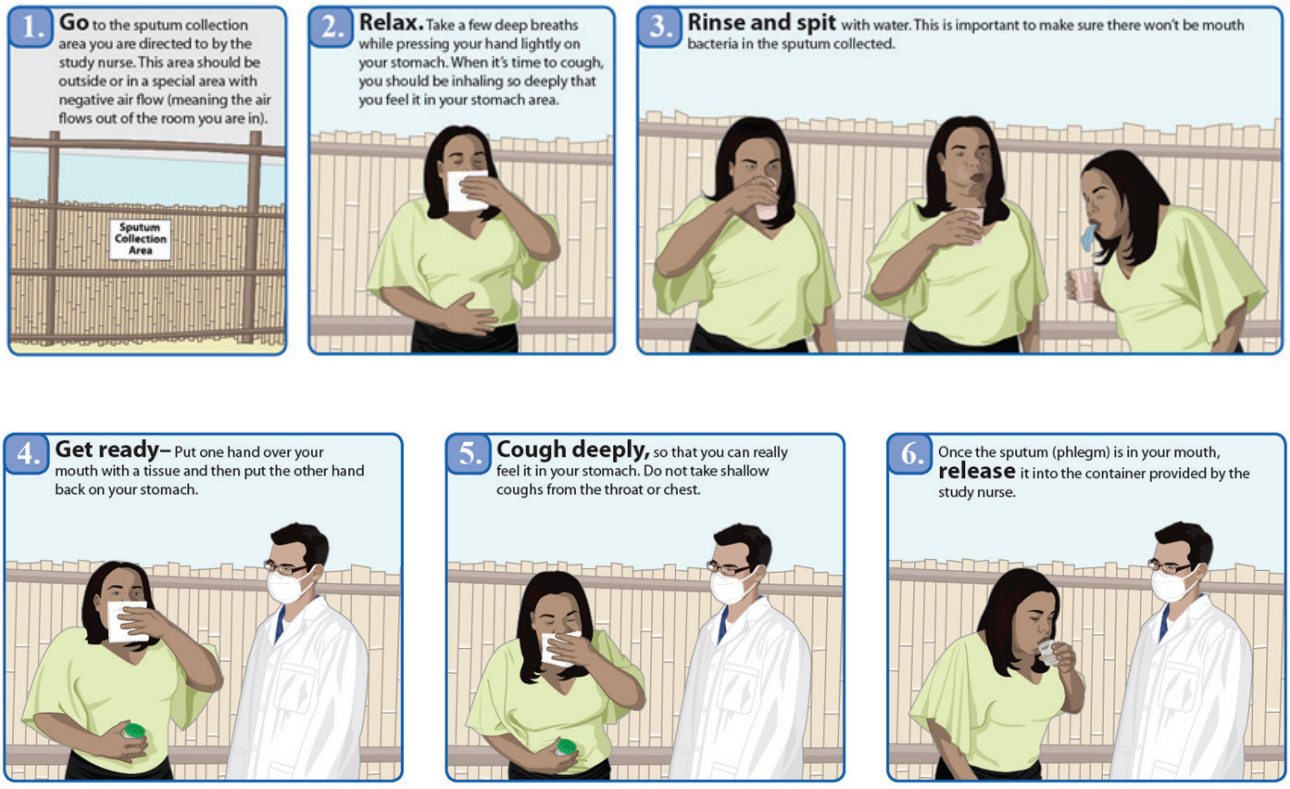
28.6 Home Collection, Clinic Storage and Transport of (Expectorated) Sputum Specimen

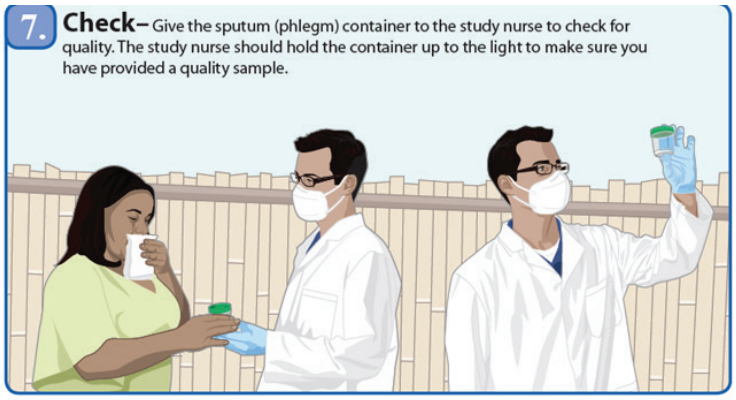
- Provide the participant/patient with a labelled specimen container with the appropriate identifying information; including study/screening number, patient ID number, visit number, and date of collection.
- Mark container/tube 'HOME' to indicate the specimen was collected at home.
- Provide the participant/patient a bottle of water (commercial source) or container with boiled, sterile or distilled water.
- Provide the participant/patient with a zip lock storage bag and absorbent material.
- Inform the participant/patient that saliva and upper respiratory/nasal secretions are not sputum and are not acceptable specimens.

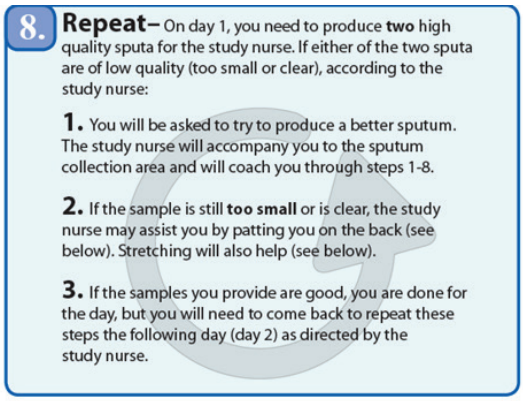
28.7 Instruct the patient to:

- Collect the sputum after getting out of bed, before the morning meal, and prior to taking any medications.
- Suggest placing the water bottle/container and specimen container in a place that will remind the participant/patient to collect the specimen first thing in the morning upon rising.
- Collect the sputum in a well-ventilated area such as by an opened window or outside.
- Thoroughly clean his/her hands with soap and water.
- Rinse his/her mouth with bottled or boiled water prior to collection of sputum.
- Breathe deeply several times and then cough from deep down within the lungs.
- Lean forward, breathe in and out slowly twice, hold breath for 2-3 seconds each time, and on third time forcefully cough to bring up the sputum.
- Collect the sputum in the sterile container provided and avoid touching the inside or edge of the specimen container or lid with their fingers.
- Replace the lid/cap after collection and close tightly to avoid leakage.
- Once collection has been completed, thoroughly clean his/her hands with soap and water.
- Store the container in a zip lock bag with absorbent material in the refrigerator or cooler with chilled ice packs, if provided.
- Bring the specimen container to the clinic as soon as possible, preferably in insulated cooler.

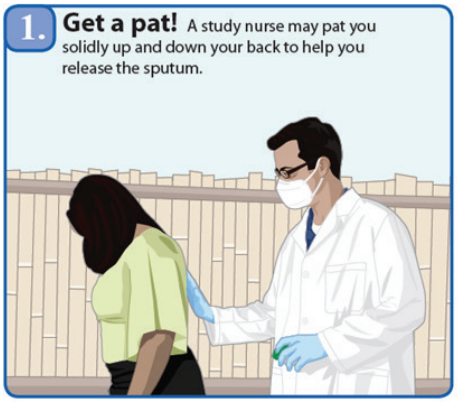
28.8 Instructions on collecting expectorated sputum:

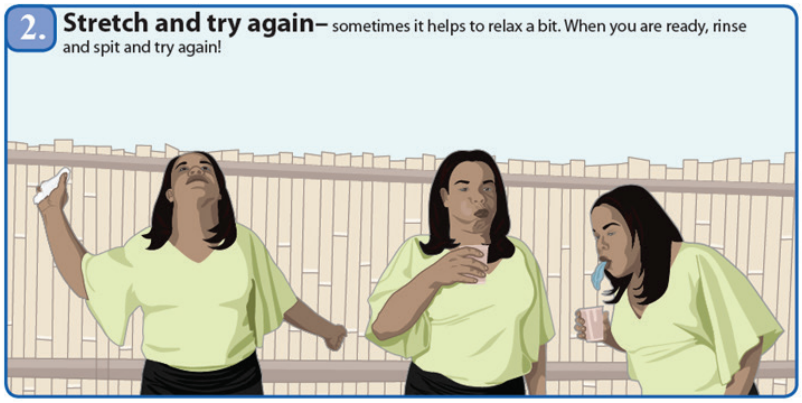






28.9 If you struggling to get a specimen, follow the instructions: -





29. Swabs Collection

29.1 Material required:

- PPE (gloves, medical mask, gown)
- Ice packs/cooler box
- field collection forms
- An alcohol-resistant pen or marker for labelling samples
- sterile Dacron or rayon swabs
- 1–2 mL viral transport medium
- Specimen collection containers

29.2 Procedure

- Disinfect bottles.
- Swab with rigid (plastic) shaft for throat and nasal specimens.
- Use tongue depressors for throat swabs.
- Use sterile saline (0.9% NS) for nasopharyngeal aspiration.
- Use sputum or mucus trap for nasopharyngeal aspiration (also require negative pressure).

29.3 Nasopharyngeal swab technique

29.3.1 Required materials

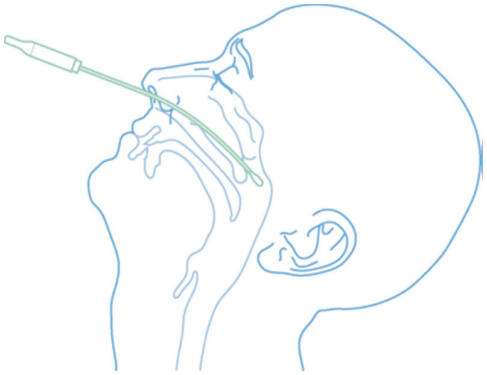
- Swab with flexible (aluminium) shaft.

29.3.2 Procedure

- Apply standard, contact and droplet precautions.
- Insert swab into one nostril and back into the nasopharynx.
- Leave swab in place for a few seconds.
- Then slowly remove swab while rotating it over surface of posterior nasopharynx.
- Withdraw swab from collection site; insert into transport tube or container with viral transport medium.
- Repeat procedure with another swab for the second nostril to deliver optimal combined sample.
- Label specimen container. After collection, immediately transport specimen to the laboratory for viral PCR testing and viral antigen detection. If transport to the laboratory is delayed, place specimen on ice or in refrigeration.

29.3.3 In case of nasopharyngeal swab in infants and young children:

- Use a swab of appropriate size: measure the distance from the nose to the ear (philtrum to the tragus).
- Insert the swab half to full amount of that distance, stopping if you encounter resistance.
- Insert the swab horizontally, below the inferior turbinate, not diagonally up the nose.



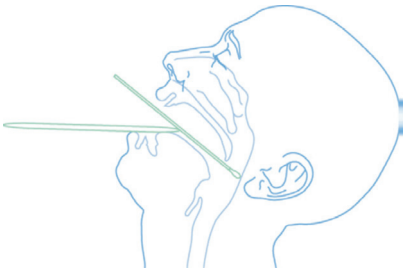
29.4 Posterior pharyngeal swab or throat swab technique

29.4.1 Required materials

- Swab with rigid (plastic) shaft
- Tongue depressor.

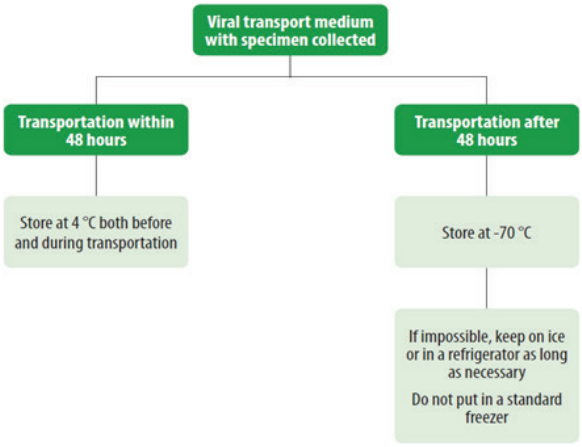
29.4.2 Procedure

- Apply standard, contact and droplet precautions.
- Ask the subject to open his or her mouth and say “ah” to elevate the uvula.
- Depress the tongue to hold out of way with tongue depressor.
- Swab the posterior pharynx and avoid tonsils and do not touch tongue with swab.
- Insert into transport tube or container with viral transport medium.
- Break applicator tip to ensure closure of vial.
- Label specimen container.
- Immediately transport specimen to the laboratory for viral PCR testing and viral antigen
- Detection.
- If transport to the laboratory is delayed, place specimen on ice or in refrigeration.



- Viral transport medium is used immediately after the collection of samples for viral isolation and testing. It prevents the specimen from drying out and prevents bacterial and fungal growth.
- Although specimens should be sent in viral transport medium to the laboratory as soon as possible, it is important to properly store them before sending them to a laboratory if there is a delay.

Figure 3: Swab -storage after collection.



30. Waste Disposal

30.1 Waste disposal

a) Waste (chemical, biological and other) is segregated and disposed according to national regulations on waste disposal.
b) Clinicians and Phlebotomy staff are trained to handle biohazardous waste: Storage and removal of waste.
c) Toxic chemical waste is collected by the outsourced facilities company Dynamic Enviro Clean.

31. Packaging of specimens

- For safe handling of specimens, biohazard bags with two pockets are provided. Specimens are placed in the zip-locked pocket along with any extra labels, and the requisition put in the outside pocket. One bag is used for each participant/patient.
- For specimen containers with lids, the label must be placed on the container itself, NOT the lid. Lids are removed from containers and participant/patient identification is compromised if the lid contains the label.
- Before placing specimens, ensure that all specimen container caps and lids are properly tightened to prevent leakage. Laboratory requisition forms must be properly completed. Double check the expiry dates of specimen containers.

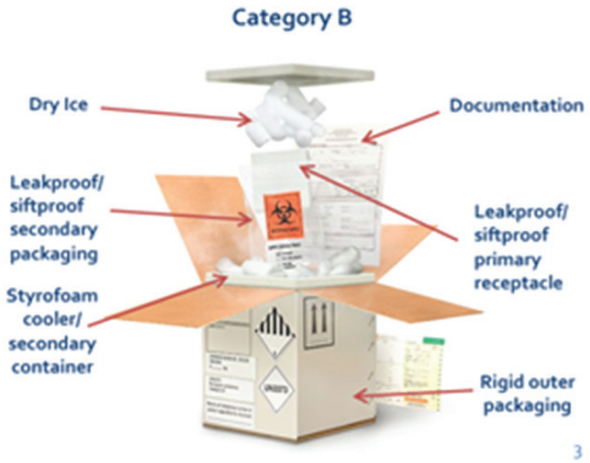
31.1 Minimum requirements for packaging specimens

31.1.1 There are different ways of packaging specimens from the clinic to the local laboratory:

1. Packaging of specimens in a biohazard plastic bag

2. Packaging of specimens by placing them upright in a rack and transporting them to the laboratory

3. Packaging of specimens using approved UN3373 container for category B samples



32. Samples Transportation

32.1 Some specimens require different transport conditions and temperature monitoring, therefore temperatures and study-specific conditions must be documented or ticked on the study-specific requisition form.

32.2 Specimens are transported from the clinic to the site laboratory immediately after collection (within oner hour) for testing and forwarding to safety laboratory where applicable. Some specimen procedure requires special processing and storage instructions. Communication between the clinic and the site laboratory is critical to maintain integrity of the sample and accurate outcome.

32.3 All specimens must be placed in a designated secure collection area until ready for collection. All specimens must be placed in a specimen bag with the laboratory requisition form in a separate pocket or attached to the adhesive strip of the bag and folded. After collection, the specimens will be placed in a **rigid, sturdy, non-breakable, closable bio-hazard specimen container, see picture below** (which is used to transport specimens safely to the laboratory).

Specimen Contain

32.4 Ambient Temp Requirements: Protocol specific requirements will be adhered to for all specimen requiring to be transported at Ambient temperature. If the specimen does not have a specific storage requirement, it will be stored at room temperature before transported to the laboratory for testing. Place the specimen in a sealed biohazard labelled specimen bag.

32.5 Refrigeration: Specimens requiring refrigerated temperatures during transport will be place in a biohazard labelled specimen bag immediately after collection. Place the specimen in rigid, sturdy, non-breakable, closed biohazard specimen container containing ice packs or crushed Ice. Specimen transport containers for refrigerated samples will be labelled as such. Temperature monitoring device is recommended or follow study specific procedure.

32.6 Urgent: All research samples are treated as urgent as they are not allowed to be kept at the clinic for more than an hour after collection. After they reach the laboratory, they are processed immediately.

32.7 Transport of samples to the referral laboratory

- Shipping of samples to referral laboratory for safety testing will be packed by the laboratory staff following study specific procedures. Referral laboratories provide the shipping containers meeting all the temperature control requirements.
- For specimens transported directly from the clinic to the referral laboratory, always review specific documentation and requirements for individual laboratories and other facilities, whether transporting to or from, to ensure that you're following any unique rules regarding their facility. Labelling requirements instructions must be followed e.g. colour coding, or other handling precautions.

32.8 For the Safety of the driver and the Public When using Aurum Institute vehicles for transporting human laboratory specimens, drivers and the vehicle must meet specific requirements:

- Trained on transporting biological specimen and handling.
- Only using the vehicle for delivery during transportation
- Proof of legal insurance coverage
- Official driver license
- Maintaining a spill plan
- Not allowing passengers during deliveries

32.9 Transport of Sputum

- Sputum specimens should be placed in a leak proof biohazard bag with sealed lids and absorbent material and transported to the laboratory in a cooler with chilled ice packs as soon as possible after collection. Within 1km distance temperature monitoring will not be required. Samples will be placed in 2-8°C refrigerator upon receipt in the lab.
- If delay is unavoidable (> 1h), the specimens should be refrigerated at 2-8°C to inhibit growth of undesired microorganisms.
- Processing requirements for sputum testing will be outlined in the protocol. Sputum must be handled per the requirements in the protocol to ensure quality specimens are obtained for testing.

- Sputum specimens must be delivered to the laboratory as soon as possible and within 24 h of collection; however, delays up to 3 days in transport from clinic to laboratory may be allowable if the transport distance is long, the sample is chilled, and the extended transit time is agreed upon by the study/protocol team.
- Notify the testing laboratory of all shipments in advance of transport.
- Provide the date and time that specimens are expected to be delivered. This ensures that laboratory personnel are prepared to receive and process the specimens.
- All specimens should be transported in compliance with local and national regulations governing the transport of potentially infectious materials.
- These rules must be followed, no matter how short the transport distance is.
- The Aurum Institute will periodically evaluate and establish adequacy of sample transportation systems.

33. Sample receipt procedure

33.1 Sample receipt procedure is well documented in Laboratory specific specimen Management/Chain of Custody SOP.

33.2 The laboratory staff will verify/QC that the information on the sample tubes/container corresponds with the information on the onsite lab requisition and results form/outsourced lab requisition form. The lab staff will then acknowledge receipt of the sample and record the sample receipt time and their initials: More information is available Laboratory specific specimen Management/Chain of Custody SOP.

33.3 Sample acceptance exceptions

33.3.1 Aurum Institute laboratories shall consider the best interests of the patient in receiving care, when a sample has been compromised due to:
33.3.2 Incorrect patient or sample identification,
33.3.3 sample instability
33.3.4 due to, for example, delays in transport,
33.3.5 Incorrect storage or handling temperature,
33.3.6 Inappropriate containers(s), and
33.3.7 Insufficient sample volume.

33.4 When a compromised clinically critical or irreplaceable sample is accepted, after consideration of the risk to patient safety, the final report shall indicate the nature of the problem and were applicable, advising caution when interpreting results that can be affected.

33.5 If the integrity of a sample has been compromised and there is a health risk, is the clinic or site where the samples was collected is notified immediately and so that action is taken to reduce the risk and to prevent recurrence will be taken.

33.6 Sample Rejection Criteria

33.6.1 Aurum Institute laboratories have established written specimen/sample acceptance and rejection criteria for each test offered and provides this information to its customers, as applicable. All specimens/samples are inspected according to these acceptance/rejection criteria.

33.6.2 The following examples are considered unacceptable specimens and will be further investigated or rejected by the Laboratory Staff (LS):
33.6.2.1 Unlabelled or mislabelled specimens
33.6.2.2 Broken or leaking specimens.
33.6.2.3 Clotted anticoagulated specimens.
33.6.2.4 Haemolysed specimens
33.6.2.5 Incorrect anticoagulant or specimen type
33.6.2.6 Specimens older than allowable for tests required.
33.6.2.7 Incorrect specimens collected for that visit.
33.6.2.8 Samples collected in an expired vacutainer.
33.6.2.9 Samples that are not accompanied by a lab requisition form will not be tested by the LS until the requisition form is presented by clinic staff to the lab.

34. Additional requirements

34.1 Sample stability

34.1.1 Refrigerated sputum (2-8°C) samples can remain stable for several days, often up to 7 days, depending on the diagnostic method.
34.1.2 Culture viability is better preserved under refrigeration compared to ambient storage.

34.2 Addition of Test Requirements

34.2.2 Addition of test depends on stability of the analyte in the primary sample, time between sample collections and testing of an added examination. Stability of Haematology, Chemistry, Microbiology and Mycobacteriology is 7 days at 2-8°C. For specialised research Test stability and storage is study specific.

34.2.3 When adding a test:
a. Add commend on Lab requisition Form
b. Add, Test added,
c. who added the test,

d. when was the test added- Date and Time Test was added.
e. Indicate if Criteria for Adding test is accepted – Yes/ NO
f. Comment on suitability of the sample.
g. More information will be provided in the Study Specific Procedure.

35. Criteria for additional examination requests

35.1 Additional examination procedures depend on the type of sample and storage conditions.

36. Handling of laboratory results

36.1 Delivery of results (internal)

- Designated personnel will deliver the results to the clinician in an envelope. The envelope must display the study name and or number, the name of the Principal Investigator/Study Coordinator.
- Results are also emailed to clinicians

36.2 A log/electronic spreadsheet will be signed when results the clinician receives results.

36.3 External results

- Results from referral laboratories will be sent by email to the designated study alias emails. When printed in the laboratory, the results will be delivered to the clinician following the process above.

36.4 Electronic results

- An arrangement is made between the clinic and the referral laboratory on designated individual to have access to be result portal. An access is granted to the designated clinicians and laboratory staff members.
- Results will include interpretation and reference ranges communicated to the clinical research site before the study begins. Any other requirements for interpretation prescribed per protocol will be included in the results.
- Amended results will be indicated on the report and the clinical research site will be informed.
- Provisional results will be available as appropriate.
- Reporting results that can adversely affect patient safety must always be considered and discussed with the sponsor and the health care provider. These events are documented as they occur.

37. Reference ranges

37.1 Rustenburg Laboratories Reference Ranges

37.1.1 Chemistry tests and reference ranges

Test	Gender	Age	Reference Ranges	Units	Method
Bicarbonate	Male/Female	≥ 13 years	21 to 31	mmol/L	Enzymatic PEP MD
Triglyceride	Male/Female	≥ 13 years	<1.70	mmol/L	GPO-POD
Chloride	Male/Female	≥ 13 years	101 to 109	mmol/L	ISE (Indirect) Oriented PVC Membrane
Potassium	Male/Female	≥ 13 years	3.5 to 5.1	mmol/L	ISE (Indirect) Oriented PVC Membrane
Sodium	Male/Female	≥ 13 years	136 to 146	mmol/L	ISE (Indirect) Oriented PVC Membrane
Anion Gap	Male/Female	≥ 13 years	8 to 20	mmol/L	Calculated
Cholesterol	Male/Female	≥ 13 years	<5.2	mmol/L	CHO-POD
HDL Cholesterol	Male/Female	≥ 13 years	1.03 to 1.55	mmol/L	Enzymatic Immuno-inhibition
LDL Cholesterol	Male/Female	≥ 13 years	<2.6	mmol/L	Enzymatic Selective Protection
Urea/BUN	Male/Female	≥ 13 years	2.8 to 7.2	mmol/L	GLDH, Kinetic Assay
Glucose	Male/Female	≥ 13 years	4.1 to 5.6(fasting	mmol/L	Hexokinase
			4.1 to 7.8 (Random)		
Direct Bilirubin	Male/Female	≥ 13 years	≤3.4	mmol/L	DPD
Total Bilirubin	Male/Female	≥ 13 years	5 to 21	mmol/L	DPD
Creatinine	Male	≥ 13 years	72 to 127	mmol/L	Modified Jaffe, Kinetic
	Female		58 to 96		

37.1.1 Chemistry tests and reference ranges (continued)

Test	Gender	Age	Reference Ranges	Units	Method
Total Protein	Male/Female	≥ 13 years	66 to 83	g/L	Biuret
Albumin	Male/Female	≥ 13 years	35 to 52	g/L	Bromocresol Green (BCG)
Aspartate Aminotransferase (AST)	Male	≥ 13 years	<50	U/L	IFCC (with/without pyridoxal phosphate activation)
	Female		<35		
Alanine Aminotransferase (ALT)	Male	≥ 13 years	<50	U/L	IFCC (with/without pyridoxal phosphate activation)
	Female		<35		
Alkaline Phosphatase (ALP)	Male	≥13	43 to 115	U/L	IFCC AMP buffer
	Female		33 to 98		
Gamma-glutamyl transferase (GGT)	Male	≥ 13 years	<55	U/L	IFCC
	Female		<38		

37.1.2 Haematology tests and reference ranges

Test	Gender	Age	Reference Range	Unit	Method
Erythrocytes	Male	≥ 13 years	4.5 to 6.5	$x10^2$ /L	DXH 500
	Female		3.8 to 5.5		
Haemoglobin	Male		13.8 to 18.8	g/dL	
	Female		12.4 to 16.7		
Haematocrit	Male		40 to 50	%	
	Female		36 to 46		
Mean Cell Volume	Male/Female		79 to 100	fL	
Mean Cell Haemoglobin	Male/Female		32 to 36	Pg	
Mean Cell Haemoglobin Concentration	Male/Female		32 to 36	g/dL	
Platelets	Male/Female		150 to 450	$x10^9$/L	
RDW	Male/Female		11.0 to 16.0	%	
Leucocytes	Male/Female		4.0 to 12.0	$x10^9$/L	
Neutrophils	Male/Female		2.0 to 7.5	$x10^9$/L	
Lymphocytes	Male/Female		1.0 to 4.0	$x10^9$/L	
Monocytes	Male/Female		0.2 to 1.0	$x10^9$/L	
Eosinophils	Male/Female		0.00 to 0.50	$x10^9$/L	
Basophils	Male/Female		0.00 to 0.30	$x10^9$/L	

37.1.3 Rustenburg Rapid Testing Reference Ranges

37.1.3.1 Urine Dipstick

Siemens Multistix 10SG	Range
SG	1.000 -1.030
pH	5 – 8.5
Leucocytes	Negative to 3+
Nitrite	Negative or Positive
Protein	Negative – Trace to 4+
Glucose	Negative to 4+
Ketones	Negative to 4+
Urobilinogen	Normal to ≥8
Bilirubin	Negative to 3+
Blood (non-hemolysed or hemolysed)	Negative to 3+

37.1.3.2 Urine pregnancy

Test kit	Range
QuickVue One Step hCG	Negative/Positive
Clinitest hCG using Clinitek Status+	Negative/Positive
SAS Pregnancy Urine	Negative/Positive
SAS Serum/Urine Pregnancy	Negative/Positive

37.1.3.3 Urine microscopy

Variable	Range
WBC	0-2/hpf
RBC	0-2/hpf
Epithelial cells	0-5/hpf
Crystals	None seen/Present
Casts	None seen/Present
Organisms	None seen/Present
Parasites	None seen/Present

37.1.3.4 Rapid HIV

Test kit	Range
Abbott Determine HIV 1/2	Negative/Positive
Abbott Determine HIV 1/2 Ag/Ab Combo	Negative/Positive
Unigold Biotech Trinity HIV 1/2	Negative/Positive
Insti HIV 1/2 Antibody Test	Negative/Positive
Chembio Sure Check HIV 1/2	Negative/Positive

37.1.3.5 Rapid Trichomonas

Test Kit	Range
Osom Trichomonas	Negative/Positive

37.1.3.6 Rapid COVID-19 Test

Test Kit	Range
Ecotest Covid-19 IgG/IgM test	Negative/Positive

37.1.3.7 Rapid RPR Test

Test Kit	Range
Pulse RPR Carbon Antigen Test	Negative/Positive

37.1.3.8 Vaginal Wet Mount

Saline	Range
Clue cells	Negative/Positive
Hyphae/Budding Yeast	Negative/Positive
Trichomonas Vaginalis	Negative/Positive
10% KOH	Range
Hyphae/Budding Yeast	Negative/Positive
Whiff Test	Negative/Positive

37.1.3.9 Quantiferon test

QFT Test	Range
QFT TB Gold Plus	Negative/Positive

37.1.3.10 GeneXpert Test

PCR Test	Range
Covid-19 PCR	Negative/Positive
HIV Viral load PCR	Negative/Positive

35.2. Tembisa Biomedical Research Laboratory Reference Ranges

37.2.1 MGIT Liquid Culture Assay

Assay	Reference
Acid-Fast Fluorescent Microscopy Auramine O smear	Normal Value: No AFB seen Pathological Value: Scanty AFB, 1+, 2+, 3+
MTB Culture (BACTEC MGIT)	Normal Value: **1. Negative for MTBC** (If no growth after 42 days) **Pathological Value, Report as follows** **1. Positive for MTBC:** MGIT = Growth TTP = X days and X hours ZN smear = Positive Blood Agar = No growth MTBc Rapid Antigen = Positive **2. Possible for MTBC (repeat ZN)** MGIT = Growth TTP = TTP = X days and X hours ZN smear = Negative Blood Agar = No growth MTBc Rapid Antigen = Positive **3. Possible NTM** MGIT = Growth TTP = Do not report TTP ZN smear = Positive Blood Agar = No growth MTBc Rapid Antigen = Negative 4**. Positive for MTBc and contamination:** MGIT = Growth TTP = Do not report TTP ZN smear = Positive Blood Agar = Growth MTBc Rapid Antigen = Positive **5. Possible NTM and Contamination** MGIT = Growth TTP = Do not report TTP ZN smear = Positive Blood Agar = Growth MTBc Rapid Antigen = Negative **6. Contaminated** MGIT = Growth TTP = Do not report TTP ZN smear = Negative Blood Agar = No growth MTBc Rapid Antigen = Negative **7. Positive for MTBc and Contaminated:** MGIT = Growth TTP = Do not report TTP ZN smear = Negative Blood Agar = Growth MTBc Rapid Antigen = Positive **8. Contaminated:** MGIT = Growth TTP = Do not report TTP ZN smear = Negative Blood Agar = Growth MTBc Rapid Antigen = Negative

37.2.1 MGIT Liquid Culture Assay (Continued)

Assay	Reference
Zeihl Neelson smear –for confirmation	Normal value: Negative Pathological Value: Positive
Blood Agar - to check for contamination	Contamination: Growth Not Contamination: No Growth
MTBc Rapid antigen – for confirmation	Normal value: Negative Pathological Value: Positive

37.2.2 Solid Culture Assay

Assay	Reference
Solid Culture (Lowenstein – Jensen medium)	Normal Value: **Negative** (No growth after 42 days) Pathological Values: a. Solid culture result is valid: i. If visible growth after 3-6 weeks **b. Results will be reported as:** i. MTB growth (1-19 colonies) **= Scanty** ii. MTB growth (20-100 colonies) = **1+** iii. MTB growth (more than 100 colonies) = **2+** iv. MTB growth (innumerable or confluent) = **3+** v. If there is growth of MTB Complex and visible contamination = **MTB growth and contaminated.** c. If there is No growth for MTB complex, but visible growth for other mycobacteria = NTM d. Culture contaminated = **Contaminated**
Drug Sensitivity Test (DST)	**Normal Value:** Streptomycin – Sensitive Isoniazid – Sensitive Rifampin – Sensitive Ethambutol – Sensitive **Pathological Value** Streptomycin – Resistant Isoniazid - Resistant Rifampin - Resistant Ethambutol - Resistant

37.2.3 GeneXpert Assay

Assay	Reference
GeneXpert	**Normal Value:** MTB NOT DETECTED **Pathological Value:** a. MTB DETECTED. Rif Resistance DETECTED b. MTB DETECTED. Rif Resistance NOT DETECTED c. MTB DETECTED. Rif Resistance INDETERMINATE

37.2.4 SARS CoV- 2 (COVID -19) Assay

Assay	Reference
SARS CoV-2 RT PCR Assay	Normal Value: Negative Pathological Value: Positive

37.2.5 Basic Science Testing

Assay	Reference
WBA Assay	Results Interpretation – as per PI discretion (For Research Purposes)
PBMC Isolation	Results Interpretation as per PI discretion ((For Research Purposes)

37.2.6 BRL POCT Laboratory reference ranges

37.2.6.1 Urine Pregnancy

Test Kit	Range
Quick Vue One Step HCG	Negative/Positive
Alere Test pack plus with OBC HCG	Negative/Positive
CliniTest HCG	Negative/Positive

37.2.6.2 Urine dipstick

Siemens Multistix 10SG	Range
SG	1.000 -1.030
pH	5 – 8.5
Leucocytes	Negative to 3+
Nitrite	Negative or Positive
Protein	Negative – Trace to 4+
Glucose	Negative to 4+
Ketones	Negative to 4+
Urobilinogen	Normal to ≥8
Bilirubin	Negative to 3+
Blood (non-hemolysed or hemolysed)	Negative to 3+

37.2.1 MGIT Liquid Culture Assay (Continued)

Assay	Reference
Zeihl Neelson smear –for confirmation	Normal value: Negative Pathological Value: Positive
Blood Agar - to check for contamination	Contamination: Growth Not Contamination: No Growth
MTBc Rapid antigen – for confirmation	Normal value: Negative Pathological Value: Positive

37.2.6.3 Rapid HIV

Test Kit	Range
Abbott Determine HIV 1/2	Negative/Positive
Abbott Determine HIV 1/2 Ag/Ab Combo	Negative/Positive
Unigold Biotech Trinity HIV 1/2	Negative/Positive
Insti HIV 1/2 Antibody Test	Negative/Positive
Chembio Sure Check HIV 1/2	Negative/Positive

37.2.6.4 Rapid Trichomonas

Test Kit	Range
Osom Trichomonas	Negative/Positive

37.2.6.5 Vaginal Wet Mount

Saline	Range
Clue cells	Negative/Positive
Hyphae/Budding Yeast	Negative/Positive
Trichomonas Vaginalis	Negative/Positive
10% KOH	**Range**
Hyphae/Budding Yeast	Negative/Positive
Whiff Test	Negative/Positive

35.2.6.6 Urine microscopy

Variable	Range
WBC	0-2/hpf
RBC	0-2/hpf
Epithelial cells	0-5/hpf
Crystals	None seen/Present
Casts	None seen/Present
Organisms	None seen/Present
Parasites	None seen/Present

37.3 Klerksdorp Laboratory Reference Ranges

37.3.1 Siemens Multistix 10SG

	Range
SG	1.000 -1.030
pH	5 – 8.5
Leucocytes	Negative to 3+
Nitrite	Negative or Positive
Protein	Negative – Trace to 4+
Glucose	Negative to 4+
Ketones	Negative to 4+
Urobilinogen	Normal to ≥8
Bilirubin	Negative to 3+
Blood (non-hemolysed or hemolysed)	Negative to 3+

37.3.2 Urine pregnancy

Test kit	Range
QuickVue One Step hCG	Negative/Positive
Clinitest hCG using Clinitek Status+	Negative/Positive
SAS Pregnancy Urine	Negative/Positive
SAS Serum/Urine Pregnancy	Negative/Positive

37.3.3 Urine microscopy

Variable	Range
WBC	0-2/hpf
RBC	0-2/hpf
Epithelial cells	0-5/hpf
Crystals	None seen/Present
Casts	None seen/Present
Organisms	None seen/Present
Parasites	None seen/Present

37.3.4 Rapid HIV

Test kit	Range
Abbott Determine HIV 1/2	Negative/Positive
Abbott Determine HIV 1/2 Ag/Ab Combo	Negative/Positive
Unigold Biotech Trinity HIV 1/2	Negative/Positive
Insti HIV 1/2 Antibody Test	Negative/Positive
Chembio Sure Check HIV 1/2	Negative/Positive

37.3.5 Rapid Trichomonas

Test Kit	Range
Osom Trichomonas	Negative/Positive

37.3.6 Rapid COVID-19 Test

Test Kit	Range
Ecotest Covid-19 IgG/IgM test	Negative/Positive

37.3.7 Rapid RPR Test

Test Kit	Range
Pulse RPR Carbon Antigen Test	Negative/Positive

37.3.8 Vaginal wet mount

Saline	Range
Clue cells	Negative/Positive
Hyphae/Budding Yeast	Negative/Positive
Trichomonas Vaginalis	Negative/Positive
10% KOH	Range
Hyphae/Budding Yeast	Negative/Positive
Whiff Test	Negative/Positive

37.3.9 Quantiferon Test

QFT Test	Range
QFT TB Gold Plus	Negative/Positive

37.3.10 GeneXpert Test

PCR Test	Range
Covid-19 PCR	Negative/Positive
IV Viral load PCR	Negative/Positive

37.4 Pretoria Laboratory

37.4.1 Siemens Multistix 10SG

	Range
SG	1.000 -1.030
pH	5 – 8.5
Leucocytes	Negative to 3+
Nitrite	Negative or Positive
Protein	Negative – Trace to 4+
Glucose	Negative to 4+
Ketones	Negative to 4+
Urobilinogen	Normal to ≥8
Bilirubin	Negative to 3+
Blood (non-hemolysed or hemolysed)	Negative to 3+

37.4.2 Urine pregnancy

Test kit	Range
Clinitest hCG using Clinitek Status+	Negative/Positive
SAS Pregnancy Urine	Negative/Positive
SAS Serum/Urine Pregnancy	Negative/Positive

37.4.3 Rapid HIV

Test kit	Range
Abbott Determine HIV 1/2	Negative/Positive
Abbott Determine HIV 1/2 Ag/Ab Combo	Negative/Positive
Unigold Biotech Trinity HIV 1/2	Negative/Positive

37.4.4 Rapid RPR Test

Test kit	Range
Pulse RPR Carbon Antigen Test	Negative/Positive

38. Storage of specimens

38.1 Specimens collected from participant/patient might need to be processed, stored and shipped to designated repository based on the protocol schedule of evaluations. Some samples or specimens collected from participants/patients during clinical trials are often not tested at the clinical trial site and may have to be sent nationally or internationally to another testing laboratory

38.2 Informed consent is required from the clinical trial participant or his/her legal representative or guardian when participating in clinical research which includes consent for sample storage for research purposes. Consent must also be obtained for storage and potential future use of samples. Participant should understand what the sample is to be used for and how the results of the research might impact on their interests.

38.3 Instructions and processes for key activities relating to the management of samples may be detailed in the protocol or separate laboratory manual, work instruction, analytical protocol or analytical plan.

38.4 Samples may be stored temporarily in the laboratory and shipped to the end point testing laboratory or shipped to the repository for long term storage. A system for recording the storage conditions within the fridge/freezer or other containment method are in place to ensure storage conditions are kept within defined limits and meet protocol requirements.

38.5 Automated specimen management system is used in the laboratory to track the specimens, specimens can be retrieved and located.

39. Shipment of specimens to the repository

39.1 Specimens that require to be shipped according to the protocol requirement are packaged and shipped according to the International Air Transport Association regulations (AITA) which are stringent in its requirements for packaging, declaration and paperwork.

39.2 The laboratory ensures that clinical samples reach their destination safely, securely, and at the right temperature which is a critical element in the clinical trial process. Cold chain or temperature control are maintained.

10. Sample destruction

40.1 At the End of Study notification has been submitted. All remaining samples will be disposed of or transferred for long term storage, in accordance with the trial protocol, ethical approval and each participant's consent status.

40.2 If consent has been given for storage for future research or biobanking, relevant samples will be transferred to suitable storage. Consent forms will be retained for the duration of sample storage.

40.3 Sample disposal will be documented and retained by the laboratory. A destruction log template is available in the BRL Biorepository. All documents pertaining to sample management are retained by the laboratory.

41. REFERENCES

41.1 IMPAACT ACTG SOP LTC 70 V1: Collection, Clinic storage and Transport of Sputum

41.2 Emergency situations SOP OHS 007

41.3 ISO 20658 2022 Medical Laboratory Requirements for collection and transport of samples

41.4 NHLS Handbook 2015

41.5 NICD Laboratory Handbook NIC0104

41.6 Primary Healthcare Laboratory Handbook 2018

41.7 Respiratory Specimen collection and processing transportation

41.8 Specimen collection, Handling and transport – Dpt of Pathology and Laboratory Medicines Lexington Medical Centre

41.9 Specimen collection and transport guide 2018-2019 Quest diagnostic

41.10 Sputum Collection guide – CDC

41.11 NHS The collection, handling and transport of specimen policy

41.12 WHO guidelines on drawing blood: Best practices in phlebotomy

33 Wrench Road, Isando, 1600, South Africa
Tel: (+27) 10 590 1300
Email: info@auruminstitute.org

www.auruminstitute.org