



National Guidelines on Quality Management Systems In HIV Testing Laboratories



National AIDS Control Organisation
Ministry of Health & Family Welfare, Government of India



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सत्यमेव जयते

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Message

Laboratory diagnosis must be accurate and reliable so that person who is HIV positive should not be labeled as HIV negative and vice versa. Therefore importance of maintaining quality and continuously improving the quality is of utmost importance.

Over the past few years, in collaboration with Centres for Disease Control and Prevention (CDC) and Project Concern International (PCI) our HIV testing reference laboratories, both national and state, have been systematically assessed for compliance with internationally recognized quality standards and have been provided technical assistance to attain these standards. This has enabled almost all National Reference Laboratories (NRLs), half of State Reference laboratories (SRLs) and some integrated Counseling and Testing Centers (ICTC) and CD4 enumeration laboratories to achieve NABL (National Accreditation Board for Testing and Calibration Laboratories) accreditation conforming ISO 15189 standards.

I congratulate Lab Services Division and thank all experts for formulation of new national guidelines in HIV testing laboratories for further mass quality across all ICTCs and other places where this testing is happening.


(K.B. Agarwal) 27.4.15



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Preface

With around 2.1 million cases of HIV in the country, HIV/AIDS remains one of the major health concerns in India. Government of India has successfully responded to the HIV epidemic from time to time. One of the cornerstones of containing HIV infections is timely and accurate diagnosis of HIV infection among various population groups. Annually more than 2.2 crore HIV tests are performed in the country. Maintaining quality of this huge number of tests is of utmost importance for accurate diagnosis.

Medical laboratory services are critical crosscutting support services and are essential to patient care, however, attaining, maintaining and improving accuracy, reliability and timeliness of test results are major challenges for health laboratories. This guideline is intended to provide a comprehensive reference on Laboratory Quality Management System in HIV diagnostic laboratories in the public and private sector. The guideline is meant for all stakeholders involved in health laboratory processes, from senior management, to middle level administration, to finally bench-work laboratorians.

The first version of guidelines published in 2007 viz. "Manual on Quality Standards for HIV Testing Laboratories" for improving quality of laboratory services was in use until recently. This mission has been taken further, towards every laboratory meeting both technical competence requirements and quality management system requirements that are necessary for it to consistently deliver technically valid results and seeking accreditation. NACO has revised the guidelines based on the international standards particular to medical laboratories' requirements for quality and competence.

Leading national experts and international agencies have contributed to the development of these guidelines and I acknowledge contributions of CDC, PCI and all contributors immensely.


(Dr. Naresh Goel)

एड्स का ज्ञान : बचाए जान
TALK AIDS : STOP AIDS

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AIDS	Acquired Immunodeficiency Syndrome
AMR	Analytical Measurement Range
BMW	Biomedical Waste Management
CAPA	Corrective Action Preventive Action
CDC	Centers for Disease Control and Prevention
CLSI	Clinical Laboratory Standard Institute
COV	Cut off value
CQI	Continual Quality Improvement
CV	Coefficient of Variation
DCGI	Drug Controller General of India
ELISA	Enzyme Linked Immuno-Sorbent Assay
EQAS	External Quality Assessment Scheme
FDA	Food and Drug Administration
FEFO	First Expiry First Out
GCLP	Good Clinical Laboratory Practice
HBV	Hepatitis B Virus
HBsAg	Hepatitis B surface Antigen
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IATA	International Air Transport Association
ICTC:	Integrated Counseling and Testing Center
IP	In Patient
IQ	Installation Qualification
ISO	International Organization for Standardization
LIMS	Laboratory Information Management System
MRA	Mutual Recognition Agreement
MSDS	Material Safety Data Sheet
NABL	National Accreditation Board for testing and Calibration Laboratories
NACO	National AIDS Control Organisation
NACP	National AIDS Control Program
NaOCl	Sodium Hypochlorite
NARI	National AIDS Research Institute
NC	Non-Conformance
NCDC	National Center for Disease Control
NCE	Non-Conforming Event
NICED	National Institute for Cholera and Enteric Disease

Abbreviations

NIMHANS	National Institute of Mental Health and Neurosciences
NML	National Metrology Laboratory
NRL	National Reference Laboratory
NRL on Q	National Reference Laboratory on Quality
OD	Optical Density
OFI	Opportunity for Improvement
OIML	International organization of legal metrology
OM	Occurrence Management
OQ	Operational Qualification
PCI	Project Concern International
PEP	Post Exposure Prophylaxis
PID	Patient Identification
PPE	Personal Protective Equipment
PQ	Performance Qualification
PT	Proficiency Testing
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
QSE	Quality System Essential
QSP	Quality System Procedure
RCA	Root Cause Analysis
RPM	Revolutions per Minute
SACS	State AIDS Control Society
SD	Standard Deviation
SI units	International System of Units
SIMS	Strategic Information Management System
SOP	Standard Operating Procedure
SRL	State Reference Laboratory
TAT	Turn Around Time
TMU	Temperature Monitoring Unit
TTI	Transfusion Transmitted Infection
UM	Uncertainty of Measurement
VIM	International Vocabulary of Metrology
WI	Work Instructions

Accident: An undesirable or unfortunate happening that occurs unintentionally

Accreditation: The process by which an independent and authorized body gives formal recognition that an organization is competent to carry out specific tasks

Amended Report: The revised version of an original report created, based on the receipt of additional information or analysis.

Assessment: A systematic process of collecting and analyzing data to determine the current, historical or projected status of an organization

Audit: A systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled (ISO 9000)

Biohazard: An infectious agent or part thereof, that presents a real or potential risk to the well-being of man, animals or plants and environment.

Biosafety: Laboratory biosafety describes the containment principles, technologies and practices that are implemented to prevent unintentional exposure to, or accidental release of, pathogens and toxins.

Biosecurity: Institutional and personal security measures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens and toxins.

Calibration: The process of comparing of a measurement instrument, kit or test system of unverified accuracy to that of a reference standard of known accuracy to detect any variation from the required performance specification.

Coefficient of Variation: The standard deviation (SD) expressed as a percentage of the mean.

Confidentiality: Confidentiality has been defined by the International Organization for Standardization (ISO) in ISO-17799 as "ensuring that information is accessible only to those authorized to have access" and by the International Code of Ethics as "Except when obligated by the law of the country concerned, a doctor shall not disclose without the consent of the patient, information which he has obtained in the course of his professional relationship with the patient"

Competence: Demonstrated personal attributes and demonstrated ability to apply knowledge and skills (ISO 9000)

Complaint: A concern lodged by any customer or client, including a patient, family member, physician, other health care staff, other laboratories, etc.

Continual Quality Improvement: A part of the quality management system focused on increasing the ability to fulfil quality requirements. It is possible to achieve continual improvement through small, incremental changes using scientific methods.

Corrective Action: An action to eliminate the cause of a detected nonconformity or other undesirable situation (ISO 9000)

Document: Information and its supporting medium. This may be paper-based or electronic.

Document Control: A system to establish and maintain the proper use of time or version sensitive documents.

Engineering controls: Well-designed work areas and equipment that minimize or eliminate exposure to hazards

Error: A deviation from truth, accuracy, or correctness; a mistake.

External Audit: Second-and third-party audits.

External Controls: Controls not included in the test kits and are used in addition to the internal controls.

External Quality Assessment: is a system of objectively assessing the laboratory performance by a designated external laboratory (organizing laboratory).

False Negative: A negative test result for a person who is actually infected.

False Positive: A positive test result for a person who is actually not infected.

Feedback: Communication from customers about how delivered products or services compare with customer expectations.

Flowchart: A graphical representation of the steps in a process. Flowcharts are drawn to better understand processes.

Form: A paper or electronic document on which information or results are captured. Once completed, a form becomes a record.

Gap Analysis: The comparison of a current condition to the desired state.

Internal Audit: Internal quality audits are audits carried-out by the laboratory's personnel (first party audit). They examine the elements of the quality management system in their laboratory to evaluate how well these elements comply with quality system requirements.

Inter-laboratory Comparison: The organization, performance and evaluation of tests for the same analyte by two or more laboratories in accordance with predetermined conditions.

Management Review: A periodic meeting of management at which it reviews the status and effectiveness of the quality management system of the laboratory.

Mean: The arithmetic average of a group of values. This is determined by summing the values and dividing by the number of values.

Medical Ethics: A system of moral principles that apply values and judgments to the practice of medicine.

Measurand: A quantity intended to be measured.

Measurement Uncertainty: A non-negative parameter characterising the dispersion of quantity values being attributed to a measurand, based on the information used.

Non-conformity: Failure to meet a requirement of the quality management system or the relevant standard. Non fulfillment of a requirement.

Occurrence: Something that happens; an event, incident, complaint, non-conformance, or accident.

Occurrence Management: A central part of continual improvement; it is the process by which errors are identified and handled.

Organizational Chart: Defines the working structure for the organization; Organizes jobs along lines of authority; defines the reporting, decision making and results accountability hierarchy and span of control; works in combination with job descriptions to define the working structure of the organization.

Path of Workflow: laboratory- sequential processes in a laboratory's activities that transform a request for examination into the laboratory information that is captured in the report of results. ISO standards group laboratory processes into pre-examination, examination and post-examination categories. Comparable terms used currently include: pre-analytic, analytic and post-analytic processes; or pre-test, test and post-test processes.

Performance Review: A periodic review and evaluation of an individual's job performance.

Personal Protective Equipment: Specialized clothing or equipment worn by an employee to protect against health and safety hazards.

Policy: a documented statement of overall intentions and directions defined by those in the organization and endorsed by management.

Post-examination Phase: Processes following an examination including the systematic review, formatting and interpretation, authorization for release, reporting and transmission of the results, and storage of samples for the examinations.

Pre-examination Phase: Chronological steps beginning with the clinician's request including the examination requisition, followed by the preparation of the patient, the collection of the primary sample, the transportation to and within the laboratory, and ending when the examination phase/process begins.

Precision: A measurement of the scatter or random error between repeated measurements expressed statistically as the standard deviation. The less variation a set of measurements has the more precise it is.

Preventive action: Proactive action/s taken to eliminate the cause of a potential non-conformity or any other potentially undesirable situation or actions taken to improve a process to prevent potential future occurrences of non-conformity.

Preventive Maintenance: Scheduled periodic work on a piece of equipment that is not a result of malfunction or failure and is intended to avert such failure.

Procedure: Specified way of carrying out an activity of a process defining in detail the work that should be done, how it should be done, who should do it, and under what circumstances.

Process: Set of interrelated or interacting activities that transforms inputs into outputs.

Proficiency Testing: The evaluation of participant performance against pre-established criteria by means of inter laboratory comparisons (ISO 17043)

Quality: Degree to which a set of inherent characteristics fulfills requirements. (ISO 9000)

Quality Assurance: A planned and systematic set of quality activities focused on providing confidence that quality requirements will be fulfilled. Quality assurance calls on laboratories to be “fit for purpose” and to “do it right the first time”.

Quality Control: A set of procedures undertaken by the laboratory staff for continuously assessing laboratory work and emergent results, in order to decide whether they are reliable enough to be released and to ensure day-to-day consistency.

Quality Indicators: Established measures (Observations, statistics, or data) defined by a laboratory to determine how well it is meeting its quality intentions, customers' needs as well as other operational and financial performance expectations.

Quality Manager: An individual with delegated responsibility and authority to oversee compliance with the requirements of the quality management system, who reports directly to the level of laboratory management at which decisions are made on laboratory policy and resources.

Quality Manual: The primary document (level 1) specifying the quality management system and quality policy of an organization.

Quality Management System: A management system of coordinated activities to direct and control an organization with regard to quality (ISO 9000); note: Systematic and process-oriented efforts are essential to meet quality objectives.

Quality Policy: The overall intentions and direction of an organization related to quality as formally expressed by executive management.

Quality System Essentials: Set of coordinated building blocks for quality management. The 12 quality system essentials are : Documents and Records; Organization; Personnel; Equipment; Purchasing and Inventory; Process Control; Information Management; Occurrence Management; Assessment/Audit both External and Internal; Process Improvement; Customer Service; and Facilities and Safety.

Random Error: the dispersion of independent test results obtained under specified conditions. It is expressed as the maximum allowable coefficient of variation (CV %) of the results in a set of replicate measurements.

Record: An evidence of results achieved or activities performed (ISO 9000).Records demonstrate traceability and provide evidence of verification, preventive action and corrective action.

Reference Laboratory: A laboratory that provides specialized expertise to other laboratories. This expertise may be in the performance of additional or specific examinations, or as consultation on submitted cases.

Regulation: A principle, rule or law designed to control or govern. A governmental order having the force of law.

Root Cause Analysis (RCA): A process for identifying the basic or causal factor(s) that underlies variations in performance, including the occurrence or possible occurrence of a nonconforming event.

Scope of Accreditation: The scope of accreditation of a testing laboratory is the formal and precise statement of activities which the laboratory is accredited for.

Sensitivity: The probability that a test will detect an analyte when it is present in a specimen. The ability of a test to correctly identify individuals, who have a given disease or condition. The sensitivity of a test is the probability of a positive test in people infected with HIV, expressed as a percentage.

Sharps: Any object that can penetrate the skin, including, but not limited to, needles, scalpels, and broken capillary tubes.

Shifts: in the mean occur when an abrupt change is followed by six or more consecutive QC results that fall on one side of the mean but typically within 95% range as if clustered around a new mean. On the sixth occasion this is called a shift and results are rejected.

Source Documents: The paper form onto which data are written.

Specification: Any requirement with which a process, equipment or other activity must conform.

Specificity: The probability that a test will be negative when an analyte is absent from a specimen. The ability of a test to correctly exclude those individuals who do not have a given disease or condition. The specificity of a test is the probability of testing negative in people not infected with HIV, expressed as a percentage.

Specimen (sample): Any sample material taken from a biological entity for testing, diagnostic, propagation, treatment or research purposes.

Standard Deviation: It shows how much variation or dispersion, there is from the average (mean or expected value). A statistical measure of variation used to describe a frequency distribution; the square root of the average of the squared deviations from the mean; to calculate a SD, the data points are first averaged, then this mean value is subtracted from each data point, giving the “difference score”; these difference scores are then each squared, and the squared difference scores are added together; the sum of the squared difference scores is then divided by the number of original data points less one, or “n-1”; a square root of the resulting quotient is the SD.

Standard Operating Procedure: Detailed, written instructions to achieve uniformity of the performance of a specific function.

Standard Precautions: An approach of infection control in which all specimens containing or contaminated with human blood and body fluids are treated as if infectious.

Supplier: Organization or person that provides a product or service.

Systematic Error: the expressed difference between the average result obtained by a procedure under specified conditions and an accepted reference value or the deviation of the mean from the target value. Bias is expressed as the maximum allowable difference (Delta diff) of an average result in a set of replicate measurements and its expected reference value.

Traceability: Ability to trace the history, application, or location of that which is under consideration.

Traceability of measurement: The property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties.

Trends: occur when values gradually, but continually, move in one direction over six or more analytical runs. Trends may display values across the mean, or they may occur only on one side of the mean. On the sixth occasion, this is determined to be a trend and results are rejected.

Turn Around Time: Length of time from when a sample arrives in the laboratory and when the final result is issued.

Uncertainty of Measurement: A parameter, associated with the result of a measurement that characterizes the dispersion of the values that could reasonably be attributed to the measurand.

Validation: Confirmation through the provision of objective evidence that the requirements for a specific intended use or application have been fulfilled (ISO 9000).

Verification: The act of determining whether products and services conform to specific requirements. Confirmation through the provision of objective evidence that specified requirements have been fulfilled (ISO 9000).

Work Instructions: A set of detailed, sequential, stepwise instructions for performing a task.

Introduction

Laboratory services are an essential component in the diagnosis and management of patients infected with the Human Immunodeficiency Virus (HIV). Universal availability and routine access to quality assured HIV related laboratory services is a key objective of the National AIDS Control Program (NACP). Good Laboratory systems are required for HIV prevention, care support and treatment, therapeutic monitoring and surveillance. National AIDS Control Organization (NACO) has established a three-tiered pyramidal HIV laboratory system to support the quality management, mentoring and EQAS, with an Apex Laboratory and National Reference Laboratories (NRLs) at the national level through the State Reference Laboratories (SRLs) down to the point of testing sites at the Integrated Counselling and Testing Centres (ICTC).

An estimated seventy percent of medical decisions are made on the basis of laboratory test results. Health outcomes depend on the accuracy of testing and reporting. If inaccurate results are delivered, the consequences can be significant and include unnecessary treatment; treatment complications; failure to provide proper treatment; delay in correct diagnosis and additional and unnecessary diagnostic testing. These consequences result in increased resource utilization costs, time and personnel effort, and often in poor patient outcomes. In an HIV testing laboratory, the results have social, medical, ethical, and legal implications.

In order to achieve the highest level of accuracy and reliability, it is essential to perform all processes and procedures in the laboratory in the best possible way. The laboratory is a complex system, involving many steps of activity and many people. The complexity of the system requires that all processes and procedures be performed properly. Therefore, the quality management system model, which looks at the entire system is very important for achieving good laboratory performance consistently.

Laboratory management needs to be firmly committed to quality assurance and adequate resource allocation. Quality is the responsibility of all staff members of the organization supported by relevant trainings, standards, procedures and documentation.

Quality standards are an integral part of the Quality system. This guideline is in alignment with the international standard by the International Organization for Standardization, “Medical laboratories- Requirements for quality and competence” ISO 15189 and the specific criteria of the National Board of Testing and Calibration Laboratories- NABL 112.

A laboratory quality system is only as good as the staff that works with it. No matter how good a quality system is, if it is not carried out consistently in daily practice, high quality cannot be achieved. Trained laboratory personnel must perform, supervise, interpret and validate

laboratory analysis at all times.

A good documentation system is necessary for the smooth functioning, good clinical laboratory practices (GCLP) and accreditation of a laboratory. Document control is an essential part of document management and involves creating, regularly reviewing and updating, distributing and maintaining all documents and information.

Health laboratories should be free from recognized hazards that may cause serious harm to their employees, the general public or the environment. Staff is expected to follow safe work practices, keep their work and material secure and follow an ethical code of conduct.

Appropriate building space, design, utilities and equipment are essential to delivering safe and effective services. Laboratory management must establish and implement an equipment management program that regularly monitors and demonstrates the proper calibration and function of instruments, reagents and analytical systems. It should also have a documented and recorded program of preventive maintenance and validation.

Assuring the quality of laboratory results is the core objective of any health laboratory and is a continuous on-going process. Participation in Proficiency Testing (PT), inter-laboratory comparison and External Quality Assessment (EQA) will ensure accurate and reliable results thereby increasing the credibility and acceptance of the laboratory. Quality Control (QC) measures should be practiced daily. The goal of QC is to detect errors and correct them before patients' results are reported.

Laboratory management should develop relevant quality indicators to systematically monitor and evaluate the laboratory's performance and contribute to the overall health services and health outcomes. Quality should be assessed through periodically scheduled audits (internal or external) the results of which should guide management in further improving the quality of laboratory services.

All these aspects have been covered in the present document which will help the laboratories to strengthen their Quality Management System (QMS) and facilitate seeking accreditation.

NACO is committed to working continually towards sustaining and improving the quality of HIV related laboratory practices and positioning the laboratory for accreditation.

Quality Assurance in the HIV Testing Laboratory

Quality is an absolute requirement for any testing laboratory. The ISO 9000:2007 defines quality as the degree to which a set of inherent characteristics fulfills requirements. Laboratory quality can be defined as the accuracy, reliability and timeliness of reported test results. To be useful and contribute in patient care appropriately, laboratory results must be as accurate as possible, all aspects of the laboratory operations must be reliable, and reporting must be timely.

For a HIV testing laboratory, the generation of false positive and false negative results is associated with social, medical, ethical and legal implications; hence it is extremely important to avoid the occurrence of inaccurate results.

To attain quality, a laboratory must have a Quality Management System (QMS) in place. QMS can be described as a set of essential building blocks for a laboratory's work operation to fulfil stated quality objectives. Such a system provides the means to direct and control the laboratory with regard to quality. Quality Management System is not limited to only testing activities in the laboratory, but extends much beyond the testing process.

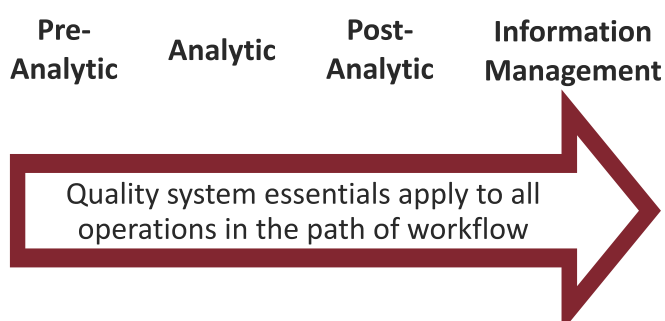
The Clinical Laboratory Standard Institute (CLSI) through a process of voluntary consensus has identified twelve Quality System Essentials (QSEs) as the foundational building blocks that function effectively to support the laboratory's path of workflow. The path of workflow comprises of sequential processes in a laboratory's activities that transform a request for examination into laboratory information that is required to report the results. It is divided into three phases (processes): pre-analytic (pre-examination), analytic (examination) and post-analytic (post-examination) phases or processes of laboratory testing.

Structure for a Quality System:

Quality System Essentials

1. Organisation
2. Customer focus
3. Facilities and Safety
4. Personnel
5. Purchasing and Inventory
6. Equipment
7. Process management
8. Documents and Records
9. Information Management
10. Nonconforming Event Management
11. Assessments
12. Continual Improvement

Path of Workflow



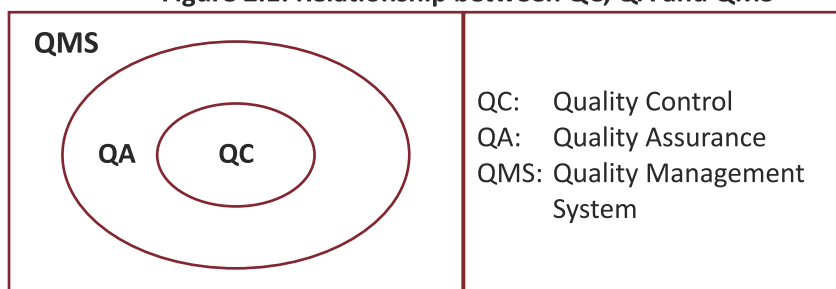
The same are defined in the international standard ISO 15189:2012 (Medical laboratories- Requirements for quality and competence) as Management requirements with 15 sub clauses (4.1 to 4.15) and Technical requirements with 10 sub clauses (5.1 to 5.10). The HIV laboratory's fulfillment of these requirements means that it meets both the technical competence requirements and the management system requirements that are essential for it to consistently deliver technically valid results.

Errors can potentially occur during the many processes that take place from the time a test is requested to the time the test results are interpreted and released. In order to mitigate or reduce the risk of errors in the laboratory, the QMS developed includes Quality Control (QC), Quality Assurance (QA) and Continual Quality Improvement (CQI).

A diagrammatic representation (Figure 2.1) explains the relationship between QC, QA and QMS.

Quality Control (QC) is defined as the activities used to monitor the testing process and ensure that the test run is valid. It refers to processes used to minimize errors during the analytical phase of testing activities.

Figure 2.1: Relationship between QC, QA and QMS



Quality Assurance (QA) is a planned and systematic set of quality activities focused on providing confidence that quality requirements are fulfilled. It is a process whereby the overall quality of the laboratory test report is assured. It is a dynamic and ongoing process of monitoring a system for reliability and reproducibility of results that provides an opportunity for corrective action when established criteria are not met. It includes minimizing errors during pre-analytical, analytical and post- analytical phases of testing.

Quality assurance is an all-encompassing activity dealing with pre-analytical, analytical and post- analytical phases, whereas quality control is specific to the analytical phase only.

The pre-analytical phase comprises of those steps involved before the actual performance of the test. This is one of the most important steps during which majority of errors can occur. The analytical phase includes various steps involved in the testing process. The post- analytical phase includes those steps involved in the interpretation and reporting of test results. The various activities occurring in each phase are listed in Table 2. 1

Table 2.1: Activities affecting the quality of test results

Pre-analytical	Analytical	Post-analytical
<ul style="list-style-type: none"> ▶ Test requisition ▶ Preparation and identification of patient ▶ Specimen selection, collection, labelling ▶ Specimen transport ▶ Specimen accession (acceptance/ rejection criteria) ▶ Specimen storage ▶ Selection and storage of test kits ▶ Performance, calibration & maintenance of equipment ▶ Trained and competent personnel 	<ul style="list-style-type: none"> ▶ Specimen processing ▶ Reagent preparation and use ▶ Test performance : adhering to test algorithms & SOPs ▶ Use of QC procedures : inclusion of internal and external controls ▶ Determine measurement uncertainty for each measurement procedure ▶ Participation in EQAS/PT ▶ Results interpretation 	<ul style="list-style-type: none"> ▶ Transcribing results from worksheet to report forms ▶ Review of results ▶ Authorized release of results ▶ Communicating the result to the appropriate person within the turnaround time ▶ Retention and storage (archiving) of specimen ▶ Retention of examination results ▶ Waste disposal

Activities like proper documentation, maintenance of quality and technical records, safety and training with competency assessments are essential in all the three phases of testing.

Benefits of a quality management system:

- ▶ Generates accurate and precise results
- ▶ Avoids inappropriate test selection, unnecessary investigations and incorrect results that can have serious health implications, and may lead to adverse events including financial and emotional burden.
- ▶ Helps the physician in quickly establishing the proper diagnosis , thus generating confidence and better health care for the patient
- ▶ Creates a good reputation for the laboratory
- ▶ Ensures inter laboratory comparability and stimulates improved performance
- ▶ Motivates staff to work better
- ▶ Ensures support in the event of legal challenge or other complications
- ▶ Saves money by getting it right at the first time
- ▶ Mandatory requirement for accreditation

The HIV network of testing laboratories at all levels (National Reference Laboratories-NRLs, State Reference Laboratories-SRLs, Integrated Counseling and Testing Centers-ICTCs) should develop, implement and maintain a QMS. Every laboratory should routinely monitor and assess the quality in the pre-analytical, analytical, and post-analytical phases/processes.

Ensuring Quality in the pre analytical phase

Test Requisition Form: Each specimen must be accompanied with a test requisition form which should include

- ▶ Name, age and gender of the patient
- ▶ Registration number: Patient Identification number (PID) and/or hospital In-Patient/Out-Patient number
- ▶ Type of specimen
- ▶ Identity of the requester
- ▶ Date and time of collection
- ▶ Identity of the person who collected the specimen
- ▶ Brief clinical information

Pre-test counseling and informed consent must precede sample collection

Labeling of specimen: The label should include following information:

- ▶ Name, Age and Gender of the patient
- ▶ Date of collection
- ▶ Patient's identification number

The requisition form (Annexure 2.1) and the label on the specimen should be compared and verified before acceptance

Accession of specimen received: All specimens must be inspected at the time of receiving and before testing to ensure that they are suitable. The quantity of the specimen should be adequate to perform the test (e.g. 2 - 5 ml of whole blood for HIV serology) to perform the test. The accepted samples must be entered into the Specimen Acceptance Register (Annexure 2.2)

▶ **Rejection criteria:**

- ▶ Insufficient quantity
- ▶ Lipaemic sera (serum is milky white from its high fat content)
- ▶ Haemolysed sera (pink to red tinged serum)
- ▶ Visually turbid serum due to contamination
- ▶ Inappropriate container
- ▶ Leaking / soiled container
- ▶ Specimen not accompanied by the requisition form
- ▶ Specimen not transported at recommended temperature
- ▶ Specimen container label absent, incomplete or illegible

A fresh specimen should be requested for testing when specimen is rejected. A note must be made in the Specimen Accession Register as to the reason for rejection. The requester/collection site must be informed of the specimen rejection and a record of this communication must be maintained.

If the specimen is irreplaceable or critical, the requesting physician takes responsibility for identifying and providing proper information. A note must be made in the accession register and in the report, for reasons of acceptance of a compromised specimen. The report should also mention that the result of the test might not be valid because of the condition of the specimen

Appropriate testing specimen: The specimen/sample used for testing with a particular test kit should meet the requirements of the kit literature and the laboratory's Standard Operating Procedure (SOP).

The laboratory must have information available for patients and users of the laboratory services. The information needs to provide the following guidance and instructions for those who order laboratory examinations : the location of the laboratory, details of which laboratory tests are available and when with the turnaround times, which test requires documentation of patient consent for HIV testing, which laboratory examination require special instructions/preparation such as pre-test and post - test counseling for HIV testing, appropriate information concerning sample required, collection containers, preservatives or anticoagulants, primary sample volumes, special precautions, turnaround time, biological reference intervals, and clinical decision values; instructions for completion of the request form, method/procedure of blood collection, labeling of samples, sample acceptance / rejection criteria, instructions for transportation and storage of samples; proper disposal of materials used in the collection; availability of clinical advice on ordering of examinations and on interpretation of examination results; the laboratory's policy on protection of personal information; the laboratory's complaint procedure.

Test equipment and environment: All equipment (including refrigerators, centrifuges, ELISA readers/ washers, pipettes) required for testing should be calibrated and checked for performance. Calibration, maintenance and equipment operation have been described in the chapter on equipment.

Specimen transport: Specimen should be packaged and transported from point of collection to the laboratory in a leak proof container using standard precautions along with the requisition form. Specimen should be transported within the required time interval, and temperature range, ensuring the integrity of the sample and safety of the person transporting the specimen and the environment in accordance with all applicable transport and safety requirements and regulatory guidelines. Details of specimen packaging and transportation is described in the Guidelines of HIV Testing

Specimen storage: Serum/ plasma to be stored at 2-8°C in the refrigerator for up to 1 week. For longer storage serum/plasma should be stored at -20°C or below.

Storage of test kits: Kits should be stored in the refrigerator or as per manufacturer's recommendations.

Selection of test kits: The National HIV Testing Strategy and algorithm should be strictly adhered to for the selection of test kits and sequence of testing.

Availability of trained and competent personnel: Trained technical personnel who have undergone regular competency evaluations are authorized to perform tests.

Ensuring quality in the analytical phase of testing:

Quality Control

Quality Control (QC) refers to the procedures undertaken for continuous and immediate monitoring of laboratory work in order to decide whether results are reliable enough to be released. Quality control procedures are a tool to detect problems that could invalidate patient results. It consists of examining "control" materials of known substances along with patient samples to monitor the accuracy and precision of the complete analytic process. The goal is to detect, evaluate and correct errors due to test system failure, environmental conditions or operator performance before patient results are reported. Different QC processes are applied to monitor quantitative, qualitative and semi-quantitative tests.

The laboratory must plan for and document its quality control plan, including the levels of quality control materials to be used, frequency of performing QC, types of QC materials and the QC acceptance/rejection criteria including possible corrective action customized for each examination procedure based on that procedure's capabilities. QC data must be reviewed periodically and all staff trained.

Internal quality control (Internal to the test Kit): These are the controls included in every test kit that is supplied by the manufacturer. These include both positive and negative controls. They are intended to be used with the same lot number of the kit with which it has been supplied in the same pack and should not be interchanged between kits. Internal controls are generally adjusted by the manufacturer so that expected results are obtained with each lot of kit.

Internal Controls in HIV ELISA are used to calculate the cut off value (COV). Even with day to day use of ELISA test kits from the same manufacturer and with identical batch numbers, some degree of variations in the internal controls (supplied with the kits) are encountered that in turn result in the variation of the calculated cut off value that is calculated on the basis of OD values of the internal controls. This is due to variation in factors like preparation of the reagents, plate to plate and well to well variation in the amount of coated antigens, incubation conditions etc. Such factors influencing the OD values of the controls would also expectedly influence the OD values of the test samples in a similar direction. But the relative reactivity of a given test sample

in relation to cut off value would not change much and standardizes the data. This relative reactivity of a test sample in relation to cut off value in a particular run is expressed and termed E ratio. This is the ratio between the sample OD and cut off OD (OD/COV).

Rapid tests also contain built-in controls integrated into the design of a test kit device automatically run with each test performed. These controls may also be referred to as procedural controls. Most built-in controls monitor only a portion of the analytical phase, and they vary from one test to another as to what is being monitored. For example, built-in controls for some kits may indicate that all the reagents impregnated into the device are active and working properly, whereas built-in controls for other kits may only indicate that a sample was added and solutions flowed through the device correctly.

Internal controls have limitations as these can be used only with the kits from which they originate and are prepared artificially in a manner that minor deterioration of the kit may not be detected by the results of the internal controls. Hence, in addition to the Internal QCs, the use of external quality controls is also necessary.

External quality control (External to the test kit): These are a set of controls not supplied with the kit. They are applied for each run/ assay to monitor the entire test system, the suitability of the physical testing environment (temperature, humidity, level workspace), and whether the person conducting the test performs it correctly.

It is important to select the appropriate control materials. When choosing controls for a particular method, values that cover medical decision points must be selected, such as one with a normal value, and one that is either high or low, but in the medically significant range. For HIV testing this would be at a minimum, positive and negative controls and additional borderline positive is recommended. The borderline positive/reactive control is capable of detecting any minor error in assay performance. This is especially important in HIV ELISA tests in order not to generate false results among test samples having an OD near the cut off value. Controls should have the same matrix as patient samples; this usually means that the controls are serum or plasma-based. Because it is more efficient to have controls that last for some months, it is best to obtain control materials in large quantity and store as small aliquots.

Control materials are available in a variety of forms. They may be frozen, freeze-dried, or chemically preserved. Control materials may be purchased, obtained from a central or reference laboratory, or prepared in-house. Purchased controls may be either assayed or unassayed. Assayed controls have a pre-determined target value, established by the manufacturer. When using assayed controls the laboratory must verify the value using its own methods. When using either unassayed or “in-house” controls, the laboratory must establish the target value and control limits of the analyte.

Steps in preparing a borderline reactive external quality control sample are:

- ▶ Selection of a high titer HIV positive plasma/serum. Source could be either an HIV infected individual or a transfusion unit of blood found to be positive for HIV.
- ▶ Serial dilution of the high titer HIV positive specimen using normal human serum. This is to keep the antibodies in natural serum protein environment. Adequate quantity of serum for use as diluent can be obtained from a transfusion blood/plasma unit negative for HIV, HBV and HCV.
- ▶ Perform two fold serial dilutions (doubling dilutions) wherein a fixed volume of HIV positive plasma/serum is mixed and transferred into successive tubes containing an identical volume of diluent (i.e. normal human serum).
- ▶ Selection of a suitable sample dilution to achieve the desired titer for use as external control with borderline reactivity. Results usually show a sigmoidal curve.
The dilution suitable for using as low positive controls are generally selected at 'E' ratio of around 2.0 times the cut off.
- ▶ Batch production: Preparation of bulk external (low positive) control sample. Volume requirement will depend on the period for which the external control of the current batch needs to be used (e.g. for one year or 6 months); the sample volume required for each assay; how often the assay is to be performed
- ▶ Batch validation to check that the batch has been sufficiently mixed and is homogenous so as to minimize the inter-aliquot as well as inter run variation
- ▶ Aliquoting and storage. Aliquots stored at -20 degree Celsius with volume per aliquot sufficient to last for one week in routine testing. One aliquot is thawed at the beginning of the week for use for that week only, following which it is discarded. It is stored at 20°C to 80°C in between during the week.
- ▶ Determination of acceptable ranges of quality control to validate each ELISA test run. This is done by employing statistical parameters like mean, standard deviation and coefficient of variation. Subsequently, the external controls, in conjunction with the internal kit controls, can be used to validate all test runs. The external QC sample is tested in at least 20 runs (e.g. in 20 consecutive days) to make statistically significant observations. The mean and standard deviation of 'E' ratio of the external controls are calculated from the set of 20 data points. The coefficient of variation (CV) calculated on different dates is minimal (i.e. <15%).

For HIV rapid tests: If the positive quality control is not positive or negative quality control is not negative, then the test should be repeated. If further investigation is needed, there are several possible causes for an incorrect control in a qualitative test. First, the reagents may be added in wrong order. Second, the test procedure may be done correctly, but the results might be read too soon or too late. Also, the reagents could be outdated or possibly have deteriorated from inadequate storage. Document that there is a problem and list the QC code and expiration date. If everything seems to be accurate and the problems are still evident, then the kit manufacturer should be informed about the problem.

Laboratories must use at least two levels of quality control material for HIV ELISA testing which is negative, positive and it is recommended to use a borderline positive/reactive (Annexure 2.4), if possible. The laboratory can prepare them in-house. To validate each ELISA test run, acceptable control limits of external quality control (positive, borderline reactive) must be determined. This is done by employing statistical parameters like arithmetic mean, standard deviation and coefficient of variation. Subsequently, the external controls, in conjunction with the internal kit controls, can be used to validate all test runs.

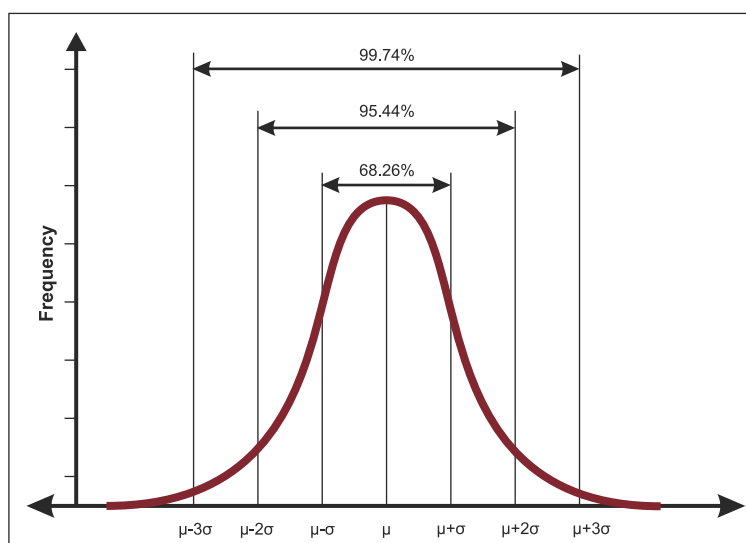
For HIV ELISA tests, statistical analysis is used for the quality control monitoring process, and Levey-Jennings charts plotted to provide a useful visual tool for this monitoring. To make statistically significant observations, at least 20 data points should be collected through intermediate precision repetitive testing over a period of 20 to 30 days for each lot number. When collecting this data, procedural variation that occurs in daily runs must be included; for example, different operators, different times of day, different reagent lot, maintenance and calibration of equipment etc. The mean and standard deviation of 'E' ratio (OD/COV) of the external controls are calculated from this set of 20 data points. Appropriate control limits are then established ($\pm 1SD$, $2SD$ and $3SD$ from the mean) to evaluate if the test run is "in control" or if the control values are not reading properly – "out of control". When only one control is used, an examination run is considered to be "in control" if a value is within $2SD$ of the mean unless a shift or trend is seen. If 2 or more levels of controls are used, Westgard multirule system is applied to evaluate the test run. The monthly coefficient of variation (CV) must also be calculated and compared to see that variation is minimal (i.e. $<20\%$).

A scientific calculator, an electronic spreadsheet, or a statistics program, all of which have functions for calculating the standard deviation of a group of measurements can be used for the statistics. The **Coefficient of Variation (C.V.)** describes the standard deviation as a percent of the mean. C.V. is used to compare the precision of a variety of determinations that have different normal values and even different units as well. Calculate the coefficient of variation (C.V.) on a monthly basis for comparison and analysis.

The Levey-Jennings control chart is used to graph successive (run-to-run or day-to-day) quality control values. A chart is created for each test and level of control. They are constructed with control values (E ratio) plotted on the y axis versus time (run date) on the x axis and lines are drawn from point to point to accent any trends, shifts, or random excursions. Control/decision limits are drawn as horizontal lines at distance from the mean measured in ± 1 , 2 and 3 standard deviations (SD). The charts are labeled to indicate name of test and control material, analytical system, lot number of control material, current mean and standard deviation, and the time period covered by the chart. Appropriate statistical QC rules are used to detect systematic (trends or shifts) and random errors.

When an analytical process is within control, since the QC data values are expected to have a normal Gaussian distribution (Figure 2.2), approximately 68% of all QC values fall within ± 1 standard deviation ($1s/1\sigma$). Likewise 95.4% of all QC values fall within ± 2 standard deviations ($2s/2\sigma$) of the mean. About 4.5% of all data will be outside the $\pm 2s$ limits when the analytical process is in control. Approximately 99.7% of all QC values are found to be within ± 3 standard deviations ($3s/3\sigma$) of the mean. As only 0.3%, or 3 out of 1000 points, will fall outside the $\pm 3s$ limits, any value outside of $\pm 3s$ is considered to be associated with a significant error condition and patient results should not be reported.

Figure 2.2: Normal Frequency Distribution (Gaussian Curve)



When the quality control sample that is used in a test run is out of the acceptable range, the run is considered to be “out of control”. When this happens, the testing process should be stopped, and the technician must immediately undertake a root cause analysis (RCA) to identify and correct problems. Possible problems to consider are degradation of reagents or kits, control material degradation, operator error, failure to follow manufacturer’s instructions, an outdated procedure manual, equipment failure, and calibration error.

Once possible sources of error have been identified, and corrections have been made, the control material should be rechecked. If they read correctly, then patient samples, along with another quality control specimen should be repeated. Do not simply repeat the testing without looking for sources of error and taking corrective action. Patient results **must not be** reported until the problem is resolved and the controls indicate proper performance.

It is important that calibrators and control materials not be confused. Calibrators are solutions with a specified defined concentration that are used to set or calibrate an instrument, kit, or system before testing is begun. Calibrators are often provided by the manufacturer of an instrument. They should not be used as controls since they are used to set the instrument. They usually do not have the same matrix as patients’ samples.

Frequency of use of quality control material: At a minimum

- For HIV Rapid tests-Minimum once a week (beginning of the week) and for HIV ELISA- with

every run/batch

- ▶ With every new test kit box when it is put to use.
- ▶ Every time these appear in the laboratory log sheet.
- ▶ New shipment of test kits
- ▶ Beginning a new lot number
- ▶ Environmental conditions exceed range needed for stability of kits
- ▶ New personnel performing the test
- ▶ New quality control lot

An Analytical Run: According to CLSI a run is “an interval (i.e., a period of time or series of measurements) within which the accuracy and precision of the measuring system is expected to be stable. In laboratory operations, control samples are analysed during each analytical run to evaluate method performance; therefore the analytical run defines the interval (period of time or number of specimens) between evaluations of control results. Between quality control evaluations, events may occur causing the measurement process to be susceptible to variations that are important to detect.”

If two or more controls are used, the Westgard rules may be considered for accepting or rejecting an analytical run. Westgard rules are multirule QC rules to help analyze whether or not an analytical run is in-control or out-of-control. It uses a combination of decision criteria, usually 5 different control rules to judge the acceptability of an analytical run. The advantages of multirule QC procedures are that false rejection can be kept low while at the same time maintaining high error detection.

Explanation of Individual Rules

1_{2s}

One control measurement exceeding 2 standard deviations of control limits either above or below the mean. This rule is used as a warning rule to trigger careful inspection of the control data.

1_{3s}

This rule is commonly used with a Levey-Jennings chart when the control limits are set as the mean ± 3 standard deviations of control limits. A run is rejected when a single control measurement exceeds the mean ± 3 control limits.

2_{2s}

The control run is rejected with 2 consecutive control measurements beyond 2 SD of control limits on the same side of mean with this rule.

R_{4s}

This rule rejects a run if two control measurements in a group exceed the mean with a 4 standard deviation difference between the 2 controls

4_{1s}

This rule rejects a run with the 4 consecutive control measurement exceeding 1 standard deviation on the same side of the mean.

10_x

This rule rejects a control run when there are 10 consecutive controls on the same side of the mean.

The steps to implement a QC program are:

- ▶ Establish written policies and procedures
- ▶ Assign responsibility for monitoring and reviewing
- ▶ Train staff
- ▶ Obtain control materials
- ▶ Run controls along with patient samples and collect data
- ▶ Set target values (mean, SD)
- ▶ Establish Levey-Jennings charts
- ▶ Routinely plot control data
- ▶ Establish and implement troubleshooting and corrective action protocols
- ▶ Establish and maintain system for documentation

External Quality Assessment (EQA)

The laboratory should participate in an inter laboratory comparison program such as External Quality Assessment Scheme (EQAS) or Proficiency Testing (PT)

EQA is a system of objectively assessing a laboratory's performance by a designated laboratory (organizing laboratory). A program where-in multiple specimens are periodically sent to a group of participating laboratories for testing. The organizing laboratory compares and analyses the results of the participating laboratories and then provides a feedback to the respective participating laboratory. If the predetermined criteria are not fulfilled the participating laboratory must implement the necessary corrective action. EQA checks for accurate, timely and clinically useful output. It is a tool to provide management with an insight into the quality of the laboratory work. It is never a substitute for, but complements QC. EQA is periodic and retrospective while QC is concurrent and daily.

Benefits of External Quality Assessment:

- ▶ Assesses the overall performance of a laboratory
- ▶ Provides objective evidence of laboratory quality

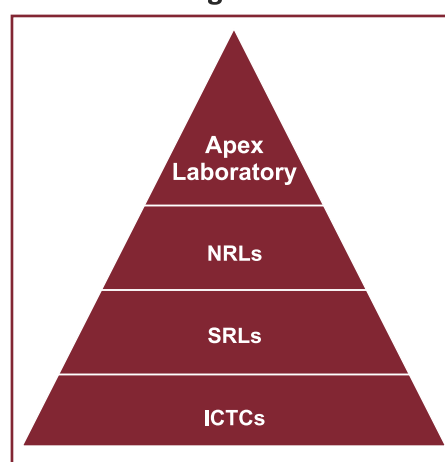
- ▶ Establishes inter-laboratory comparison
- ▶ Serves as a warning system for problems and provides an opportunity for RCA leading to corrective action and preventive action/s (CAPA).
- ▶ Indicates areas towards which efforts need to be directed for improvement of quality of results
- ▶ Identifies training needs
- ▶ Pre-requisite for accreditation

The National AIDS Control Program (NACP) supports the “External Quality Assessment Scheme” for HIV serology. It has the following components:

1. Proficiency testing
2. Rechecking
3. On site monitoring and mentoring

EQAS is supported by a three tier pyramidal structure (Figure 2.3), with an Apex Laboratory, National Reference Laboratories (NRLs) at the national level through the State Reference Laboratories (SRLs) down to the Integrated Counselling and Testing Centres (ICTCs)

Figure: 2.3: Hierarchy of HIV testing laboratories



1. Proficiency testing

It is a periodic evaluation of a laboratory's performance by the organizing laboratory using proficiency panels. A proficiency panel comprises a set of predefined validated specimen. The participating laboratory integrates the proficiency panel into the routine workflow in a manner that follows the handling of patient samples. The PT samples must be examined using the same procedures as those used for patient samples and by the personnel who routinely examine the patient samples. The results must be reported to the organizing laboratory within the stipulated time frame.

In the national PT program for HIV serology, each of the NRLs prepares a panel of both HIV positive and negative plasma samples (Annexure 2.6). The NRL sends the proficiency panel to the Apex laboratory for validation before distribution to the linked SRLs. PT is performed at six monthly intervals.

The designated NRL distributes an eight member blinded panel to the linked SRL for their proficiency testing and a bulk panel of four members blinded is given to the SRL for aliquoting and distributing to their linked ICTCs. The participating laboratories test the panel along with the routine test samples and communicate the result in the prescribed format (Annexure 2.6A) to the organizing laboratory (ICTC to SRL and SRL to NRL) for analysis within the specified time i.e. 7 working days.

The organizing laboratory analyzes data received, provides feed back to the participating

laboratories and assists in troubleshooting and RCA in case of discordance. The PT report should be reviewed by the lab in charge within seven days. The participating laboratory takes corrective action where ever needed depending on the feedback of results. The outcomes are communicated as per the reporting hierarchy. The organizing laboratory monitors for compliance to CAPA. This is recorded in a prescribed format.

The Proficiency testing of the ICTC's is conducted by the SRL and in turn the Proficiency testing of the SRL is conducted by the NRL. Similarly the Proficiency testing of the NRLs is undertaken by the Apex laboratory which in turn participates in an international EQA.

The limitations of PT are that they are spot checks in time. They represent the upper performance level and usually involve a small number of samples. Moreover, there are a limited number of assessments per year. Therefore, the test results frequently do not represent the daily, routine test performance since there is always greater care taken in testing PT samples.

2. Rechecking of Samples

Rechecking is a process by which a specified percentage of samples are collected from the routine tested samples at the test site, during a pre-determined period of time and are sent to the designated higher laboratory for verification.

Under NACP the ICTCs send 20 percent of HIV-positive and 5 percent of HIV-negative sera (0.5 ml) tested in the 1st week of each quarter of the year (January, April, July, and October) to the designated SRL by the 10th of the respective month. The samples are selected systematically e.g. for 20% positive samples, select the 5th, 10th, 15th, 20th etc. and the last sample. The samples are stored at 2 to 8 °C till they are transported. It is important that samples are selected systematically; every 5th positive sample and every 20th negative sample is selected. Serum samples are packaged and transported maintaining cold chain (2 to 8 °C) along with the requisition form (Annexure 2.7). An aliquot of the samples sent for rechecking should be kept back in the freezer compartment of the refrigerator till the results are obtained. A record of the samples sent is maintained by the ICTC.

The SRL tests these serum samples as per the algorithm followed by the ICTC. The results from rechecking are conveyed to the respective ICTC within seven days of receiving the samples (Annexure 2.8). If there are any discordant results, the SRL advises the ICTC and helps the ICTC with the RCA so that the appropriate CAPA can be taken and documented. If the discordance persists, the SRL sends the sample to the designated NRL for confirmation. The SRL prepares a consolidated report to be sent to the NRL.

Although the use of internal and external QCs and participation in EQA are the mainstay of QA in the analytical phase, the quality of the testing process can also be compromised by other factors such as dilution errors, not adhering to recommended temperatures, improper dropper use,

using improper pipette tips, inconsistent technique, use of non-calibrated and poorly maintained equipment, mixing components from different kits, and not adhering to SOPs.

3. Onsite Monitoring and Mentoring

On site monitoring and mentoring is an additional method that helps evaluate the adherence of the testing site to their QMS. An onsite evaluation program should include a standard checklist of laboratory indicators (Annexure 2.9) and evaluators should be trained to perform consistent laboratory reviews.

In the present set up, the evaluator undertakes periodic site visits for systematic assessment of laboratory practices. This helps focus in on how the laboratory monitors its operations in all three phases of testing and then the evaluator mentors for continual quality improvement.

During these visits, every aspect of the laboratory's QMS is assessed to identify gaps and to facilitate the institution of CAPAs.

Quality Assurance in the Post Analytical Phase:

- ▶ Transcribing results from worksheet to report forms or computer may result in errors. To avoid these transcriptional errors, the transcribed results should be cross-checked and signed by the authorised signatory.
- ▶ Report format should be in the prescribed form (Annexure 2.3). Results should be legible and no parameter should be left blank. A record of the report should be retained in the laboratory so that prompt retrieval is possible. A comment on the quality of sample received if it was unsuitable for examination or if it could have compromised the result should be made.
- ▶ It must be ensured that the HIV test reports are received by the appropriate individuals along with post-test counselling ensuring confidentiality, within the turn-around time.
- ▶ In the event a report needs to be amended, the amended report should be signed and released by the authorized personnel after proper documentation as per the SOP.
- ▶ The laboratory must retain copies or files of the reported results, such that prompt retrieval of the information is possible. The length of time that reported data are retained should follow national/local guidelines, whichever is longer. NACO guidelines recommend a period of five years.
- ▶ For results reported by a referral laboratory (NRL or SRL), results may be transcribed by the referring laboratory such that all essential elements of the results reported by the referral laboratory are reported without alterations that could affect clinical interpretation or the original report from the referral laboratory can be handed over to the customer and a copy retained by the referring laboratory for record purpose.
- ▶ Storage/Archiving of samples after testing: The serum/plasma samples after testing are placed in leak proof, screw capped plastic containers in the refrigerator at 2 to 8°C for at least 48 hours in case repeat testing is required.
- ▶ All samples must be discarded in 1% Sodium hypochlorite NaOCl (available chlorine) solution using standard precautions

Key points

- ▶ QA in the laboratory consists of monitoring quality in the pre-analytical, analytical and post-analytical phases of testing.
- ▶ Pre-analytical QA is the right investigation on the right sample collected in the right manner by the right technique in the right laboratory by right transportation, right labelling, right quantity and right storage.
- ▶ QA in analytical phase includes QC procedures, equipment reliability through periodic calibration and maintenance, reagent stability and efficiency, procedure reliability in terms of precision and accuracy.
- ▶ Post analytical QA consists of delivering the right report to the right person at the right time.
- ▶ Every laboratory must define, implement and monitor a QC programme and participate in an EQA/PT programme.

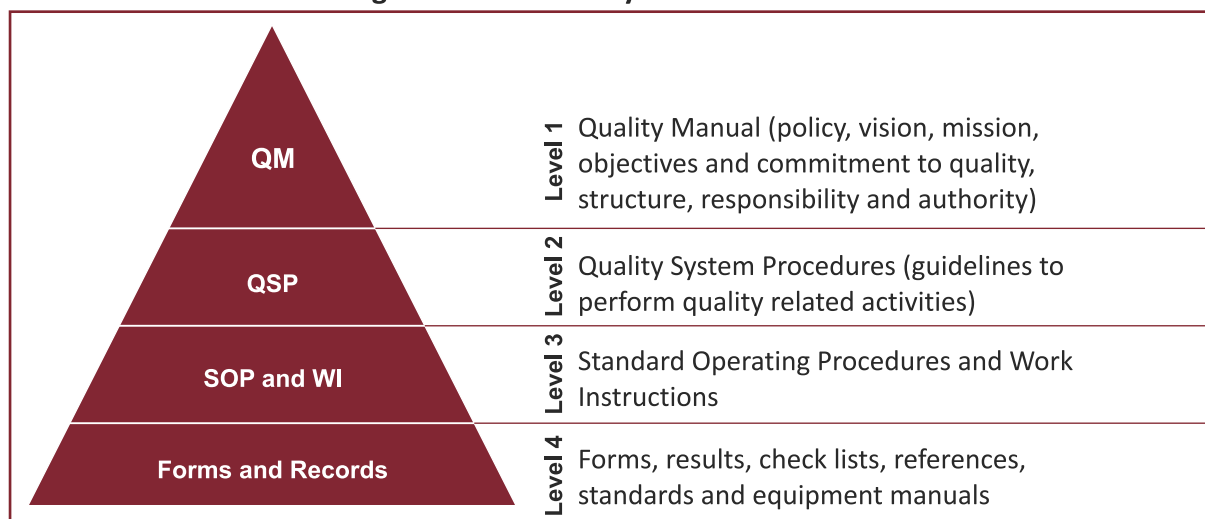
Documentation

Quality Management System (QMS) documentation is extremely important in ensuring quality practices in the laboratory. The documentation can be in any form or type of medium, provided that it is readily available and protected from unauthorized changes and undue deterioration. All policies, procedures and work instructions must be documented and communicated to the staff that understand them and agree to follow them. Since the functions, processes and procedures of laboratories are constantly changing; documents should be reviewed periodically and revised if necessary. Verbal instructions are unreliable as a means of communication as they may not be heard, may be misunderstood, may be ignored or may be quickly forgotten (particularly so, if they are complex technical information). Good documentation is the backbone for smooth functioning, GCLP and accreditation of a laboratory.

Proper documentation in a laboratory consists of creation, revision, review, control and distribution of the QMS documents and collection, review, storage and retention of quality and technical records. A document is any information that provides direction and a record is any information that provides evidence of an activity or task performed.

Document Structure: Documents are most useful when assembled according to a defined structure and a hierarchical system is helpful in arranging documents (figure 3.1).

Figure 3.1: Hierarchy of documentation



Quality Manual is the level I **document** of a laboratory that includes the quality policy; a description of the scope of the QMS; a presentation of the organization, management structure of the laboratory and its place in any parent organization; a description of the roles and responsibilities of the laboratory management, including that of the laboratory director and quality manager; a description of the structure and relationships of the documentation used in the QMS; the documented policies established for the QMS and reference to the managerial and technical activities that support them. It gives an overview of all the functions carried out by

the laboratory and provides links to all other documentation.

A Quality Policy is a written statement of overall intentions and directions defined by those in the organization and endorsed by management. It is reviewed periodically for continuing stability.

A laboratory's Quality Policy should ensure:

- ▶ The mission, goals, and purpose
- ▶ Scope of service
- ▶ Management's statement on the standard of service
- ▶ Provide a framework for establishing and reviewing quality objectives
- ▶ Commitment to good professional practice, quality of examinations and compliance with the QMS
- ▶ Management's commitment to comply with the international standards ISO 15189 and continual improvement of the quality of laboratory services.
- ▶ Be communicated and understood within the organisation.
- ▶ Is reviewed for continual stability

Laboratory management must establish and document the quality objectives, including those needed to meet the needs and requirements of the users, at relevant functions and levels within the organization. The quality objectives must be measurable and consistent with the quality policy.

Procedural Documents specify details of processes and procedures. Processes are a “set of interrelated or interacting activities that transform inputs into outputs”. Processes describe the series of steps usually occurring over a period of time and 'provide the information to carry out the intent' defined by a policy. They are easily represented in flow charts.

Quality System Procedures (QSPs): These level II documents describe major processes undertaken by the laboratory to implement the quality measures (Annexure 3.1). Some examples of QSPs are

- ▶ Document Control/Management
- ▶ Inventory Management (Management of reagents, calibration and control materials)
- ▶ Equipment Management
- ▶ Non-conforming Event/Occurrence Management
- ▶ Control/Management of Records (process, quality and technical records)
- ▶ Personnel Management
- ▶ Management of Complaints and Feedback (from users of the laboratory)
- ▶ Information and Data Management
- ▶ Control of Clinical Material (Primary sample management)
- ▶ Evaluation and improvement including Internal Audit

► Confidentiality of patient information

Standard Operating Procedure (SOP): It is a level III document that describes detailed, sequential, stepwise instructions for performing a task/activity. These are specified for each activity and should be clear, understood and implemented by the staff. An SOP describes completely and accurately the procedure that is valid and approved for use in the pre-analytical, analytical and post-analytical phases of laboratory services. All procedural documents must be easily accessible, understood, and adhered to by the laboratory staff. Examples of SOP are:

- **Pre analytical:** Specimen collecting and handling; Specimen transportation; Specimen reception
- **Analytical:** Referral to other laboratories; Examination procedures (number depends on range of examinations performed); Ensuring the quality of examinations.
- **Post analytical:** Reporting results; The amended report, Archiving of samples after testing.

Work Instructions (WI): Procedures can refer to '*working instruction's*'. These are practical day to day instructions and, for example, might describe starting up or closing down of an ELISA reader, CD4 flow cytometer or a laboratory computer. Instructions can be embedded in a procedure or can be referred to in the procedure and published separately.

The final level in the hierarchy is represented by '*forms and records*'. Recording any information or data such as patient's results, quality control data or the result of an audit should be done in a systematic way on forms of an agreed format. Records made on forms '**provide evidence of fulfilment of intent**'. If a procedure requires something to be recorded on a form, the form must be referred to in the procedure

Documents are information that provide direction, for example: Policies, processes, procedures; Specifications; Plans; Regulations and standards, National guidelines. The list of documents which form part of the laboratory's QMS include policy statements, processes/QSPs, SOPs, specifications, calibration tables, charts, text books, posters, manuals, notices, memoranda, software, drawings, plans, regulations, standards, national guidelines. A document control master list/log that identifies the distribution and revision status should always be maintained.

Master Document List/Log/Register is the master document indexing all the QMS documents both internal and external, with the current valid edition/version and their distribution. It is a document which enlists all the master documents like Quality Manual, SOPs, QSPs, Forms etc. used in the facility. It contains information on the document name, unique document ID number, version/edition number, effective date, location and working copy holder.

Documents can be classified as internal or external documents.

Internal documents include

- ▶ Quality Manual
- ▶ Laboratory safety manual.
- ▶ Primary sample collection, storage, transport instructions and procedures.
- ▶ Equipment inventory, maintenance, calibration, and monitoring document (details in section on equipment maintenance and calibration).
- ▶ Reagent and consumables inventory document.
- ▶ Standard Operating Procedures
- ▶ Quality System Procedures
- ▶ Directory of external services & supplies
- ▶ Documents detailing the contracts to perform special activities (e.g. research projects).

External documents include:

- ▶ National guidelines
- ▶ Regulations
- ▶ Specifications
- ▶ Reference text books
- ▶ Kit inserts
- ▶ Equipment user manual
- ▶ Technical standards
- ▶ Calibration certificates

Document Format: The format of documents is important for the implementation of the QMS. The main requirements of QMS documentation are that documents accurately describe the key processes in sufficient detail for all those who will use that document. Consistency in style is preferred. The following style features are suggested to comply with an institutional identity style manual. This makes the appearance of documents uniform and easier to read. The following is an example:

- ▶ Page size A4 as portrait
- ▶ Left margin 1.5 cm
- ▶ Font for body of text Times New Roman and font size 12 point
- ▶ Line spacing 1.5 lines
- ▶ Body of text justified

All QMS documents are identified to include the following information:

- ▶ Name of the organization/laboratory
- ▶ Title and identification number of the document
- ▶ Unique identifier on each page
- ▶ Edition/version/revision date and/or number

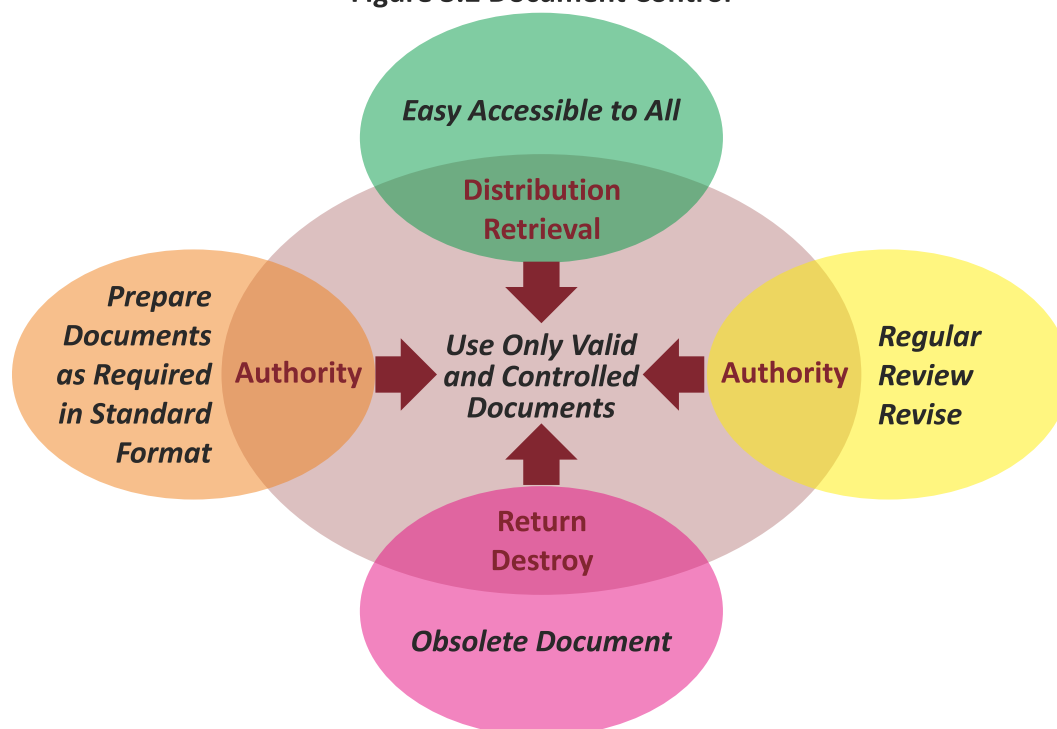
- ▶ The page number to total number of pages
- ▶ Authority for issue

The documents can have the identification in the form of a cover page and/or header and/or footer.

Document Control: A system to control the handling and management (including archiving, storing and destruction) of documents that are the part of the quality management system. The document control process/QSP must ensure that staff access and use only the most current versions of documents and that the unintended use of any obsolete document is prevented. Documents that are considered for document control are those that may vary based on changes in time or versions. They are both the internal and external documents required by the laboratory's QMS.

Document control elements are: Document unique identification; Creation, Review and Approval of new documents; Authorisation for issue of new documents and revised documents; Distribution of current authorised editions/versions at points of use and removal of obsolete documents; Master document files; Periodic review of approved documents at a predefined frequency to ensure that they remain fit for purpose; Revision and approval of changes to approved documents; Document changes and hand edits/amendments; Master index/list identifying current revision status of documents and distribution; Obsolete documents are marked, dated, archived, stored, and retention periods defined .(Figure 3.2)

Figure 3.2 Document Control



Among the many aspects of document control the laboratory must ascertain that the following conditions are met:

- ▶ All documents issued to laboratory personnel as part of the QMS are reviewed and approved by authorized personnel prior to issue;
- ▶ Master Document List/Log/Register indexing the current valid revision of documents and their distribution is maintained;
- ▶ Currently authorized versions of appropriate documents are available for active use at relevant locations;
- ▶ Documents are periodically reviewed, revised when necessary, and approved by authorized personnel;
- ▶ Invalid or obsolete documents are promptly removed from all points of use, or assured against inadvertent use;
- ▶ The master copy of the obsolete document is marked obsolete and archived
- ▶ The laboratory defines the length of time various documents pertaining to the QMS and examination results are to be retained. This is defined by national or local guidelines, whichever is longer.

New document creation: New documents are created in the prescribed format by the authorised personnel which may be the laboratory in-charge, supervisory personnel or the technical person, whenever there is a requirement for a standardised written procedure to comply with the QMS. The quality manager of the laboratory coordinates the review and approval process and assigns the unique identification number to the document as per the system. The original signed document will form the master copy and will be maintained by the quality manager. A copy of each of these controlled documents shall be archived for future reference. The documentation of equipment will be retained as long as the machine is being used or up to two years after the decommissioning of the equipment.

Document Approval: The respective technical manager or the designated quality manager or laboratory in charge reviews the documents. Documents are approved by the head of the laboratory or the designee. The quality manager should ensure that up-to-date documents are being used and that obsolete documents are removed from use. This includes materials from sources outside the laboratory such as standards, applicable regulations and specification sheets.

Distribution of Documents: The current documents should be available and accessible for use. The master list or an equivalent document control procedure identifying the current revision status and distribution of documents should be developed. Authorized copies of the appropriate documents should be made available at all locations where operations essential to the effective functioning of the laboratory are performed. References, textbooks, publications and other relevant documents should be retained as a part of document control. A copy of the

old document should be archived and the remaining copies destroyed. This is important for providing an accurate historical record. The revised/changed document must be shared/communicated to the staff.

Controlled Copies: The copies of a document that are distributed to relevant laboratory personnel are controlled and stamped or marked as “CONTROLLED COPY”. Distribution of the controlled copies is documented in the master log/list/register or in a separate document distribution log.

Uncontrolled Copies: These are informational copies that are distributed to administration, trainers or other interested parties. These are stamped or marked as “UNCONTROLLED COPY”.

Storage and Retrieval of Documents: A retention period for obsolete/ superseded documents shall be defined. While being stored for a specified or required retention period, documents should be protected from damage, tampering, loss, or degradation due to atmospheric conditions. Retention period of all documents and records is decided on the basis of national, regional or local guidelines whichever is longer. Retention period as per national guidelines is 5 years

Review and Revision of Documents: Documents need to be reviewed, amended, or revised as and when required such as when a procedure is changed, the documents such as work instructions and work sheets need to be changed too. Documents are periodically reviewed at least annually and revised when necessary to ensure suitability and compliance with necessary requirements. When persons other than the original author are designated for review, they must first familiarize themselves with pertinent background information upon which to base their review and approval. Any alteration to the text and the reason for this change is documented on the amendment sheet. If the laboratory allows for changes by hand, a single line should be drawn through the error/correction and it should be initialed and dated by the person making the correction. The line drawn should not render the deletion illegible. A revised document is formally re-issued as soon as practicable. Authorised personnel must carry out reviews and revisions/ amendments. The laboratory should have a policy to define the number of amendments allowed per document so a new edition/version can be issued when the number is surpassed. Requests for amendments can be initiated by anyone within the laboratory. It should go through established approval procedures before preparation, authorization and distribution.

Obsolete Documents: Documents that become invalid are promptly removed from all points of issue or use. The master copy of the obsolete document is archived for legal and/or knowledge preservation purposes and is marked as “obsolete”. The remaining copies are destroyed and a record of this is maintained in a separate register.

Records contain information that provides evidence of an activity, task or procedure performed by the laboratory. This information is generated through the prescribed forms listed above which are the level IV documents. A number of records are generated in the course of activities of the laboratory. These records must be organized and maintained for traceability, future reference, audit and legal purposes.

Records: any information that provides evidence, for example, Requisitions; Examination results and reports; Quality Control and EQA records; Equipment calibration and maintenance, service records; Incident/Accident reports

Control of Records:

Records of other laboratory activities should be maintained in addition to those generated/created concurrently by the performance of each activity that affects the quality of the examination results. Quality and technical records should be controlled by specifying the individual or group responsible for various elements such as record identification; Creation and legibility; Records reviews; Record collection and indexing; Records access; Changes to recorded information; Record storage and retention and Record safe disposal.

Such records include but are not limited to:

- a. Supplier selection and performance, and changes to the approved supplier list
- b. Staff qualifications, training and competency records
- c. Chain-of-custody records for specimens (test requisition, sample accession log)
- d. Information on reagents and materials used for examinations (e.g. lot number certificates of supplies, package inserts)
- e. Laboratory work books or work sheets
- f. Instrument printouts and retained data and information
- g. Examination results and reports
- h. Instrument & equipment calibration, maintenance & service records
- i. Calibration functions and conversion factors
- j. Quality control records and EQAS/PT/ILC records
- k. Incident records and action taken
- l. Accident and incident records and action taken
- m. Non-conformity identified, immediate action, corrective & preventive action
- n. Customer/User complaints/feedback records
- o. Records of internal and external audits
- p. Quality improvement records
- q. Minutes of meetings that record decisions made about the laboratory's QMS
- r. Records of management reviews

Standard Operating Procedures

Standard Operating Procedures (SOPs) are one of the most important documents in a laboratory. They ensure that correct methods are followed to generate quality results. They are written, approved procedures that describe routine activities that are specific to the daily operations at each facility. SOPs allow appropriately qualified personnel to perform a procedure once trained.

An SOP must be prepared for each activity including all tests being performed in the laboratory. Measures to monitor that SOPs are correct, understood and are followed by relevant personnel are important. For SOPs to be effective they must be written unambiguously, in exquisite detail and must be accurate. After an SOP has been prepared, reviewed and approved, the concerned staff should be trained on contents. Following an SOP is mandatory in the laboratory.

The laboratory must have procedures that describe completely and accurately all activities including management and technical activities. The procedures for management activities such as document control, occurrence management, procurement of supplies, complaint redressed, continual quality improvement are often called Quality System Procedures (QSPs). Technical SOPs cover all activities in the pre-analytical, analytical, and post-analytical phases of the laboratory. SOPs should be written with sufficient detail to serve as a resource to technical personnel in all aspects of their responsibilities and to ensure consistency of practices among all staff assigned common tasks.

Format of an SOP: An SOP should display the following information on all pages in either the header and/or footer

- ▶ Name of the organisation/laboratory with logo if available
- ▶ Title of SOP
- ▶ Unique document number
- ▶ Version/edition number and or dates of revision
- ▶ Pagination as page number with total number of pages. (e.g. page 1 of 5)
- ▶ Author's name and approving/issuing authority.

A typical SOP (Annexure 3.2) should include in addition to the above the following as a standard format

- a. Purpose of the examination
- b. Principle and method of the procedure used for examinations
- c. Performance characteristics; AMR
- d. Type of sample (e.g. plasma, serum, urine)
- e. Patient preparation
- f. Type of container and additives
- g. Equipment and reagents required
- h. Environmental and safety controls
- i. Calibration procedures (metrological traceability)

- j. Procedural steps including the quality control procedures
- k. Principle of procedure for calculating results including, where relevant, the measurement uncertainty of measured quantity values
- n. Biological reference intervals if applicable
- o. Documentation of results including calculations
- p. Laboratory clinical interpretation
- q. Precautions & safety
- r. Clinical significance, inference and limitation of the test
- s. Troubleshooting in case of breakdown of equipment
- t. Specimen preservation and storage before analysis and after analysis
- u. Records and data management
- v. References of test procedure

Key Points about Standard Operating Procedures-

- i. SOPs should be available at activity/testing site and should be followed every time an activity / test are performed.
- ii. SOPs must be simple to follow and may be in the form of flow diagram / chart, one step leading into the next and easy to interpret.
- iii. SOPs must include all the pre-analytic, analytic and post-analytic requirements for performing the test while keeping the quality issue in view.
- iv. SOPs should have a defined structure with the name of the organization, title, purpose, scope, responsibilities/authorities, description of the activity and the resources needed. (See Annexure 3.2 for a prototype SOP).
- v. SOPs should be available at all times in the immediate bench area of the personnel engaged in the collection, processing or examination of specimens and/or performing related work.
- vi. SOPs must be reviewed at appropriate time intervals (at least annually) and revised as required. A master copy of the obsolete SOP must be archived for future reference and all additional copies should be destroyed.

Key points

Documents:

- ▶ Include written policies, processes, and procedures.
- ▶ Need to be updated and maintained fit for purpose.

Records:

- ▶ Include information captured in processes and procedures.
- ▶ Are permanent, do not require updating.

A good document control program:

- ▶ Most current version used.
- ▶ Availability and ease of access.

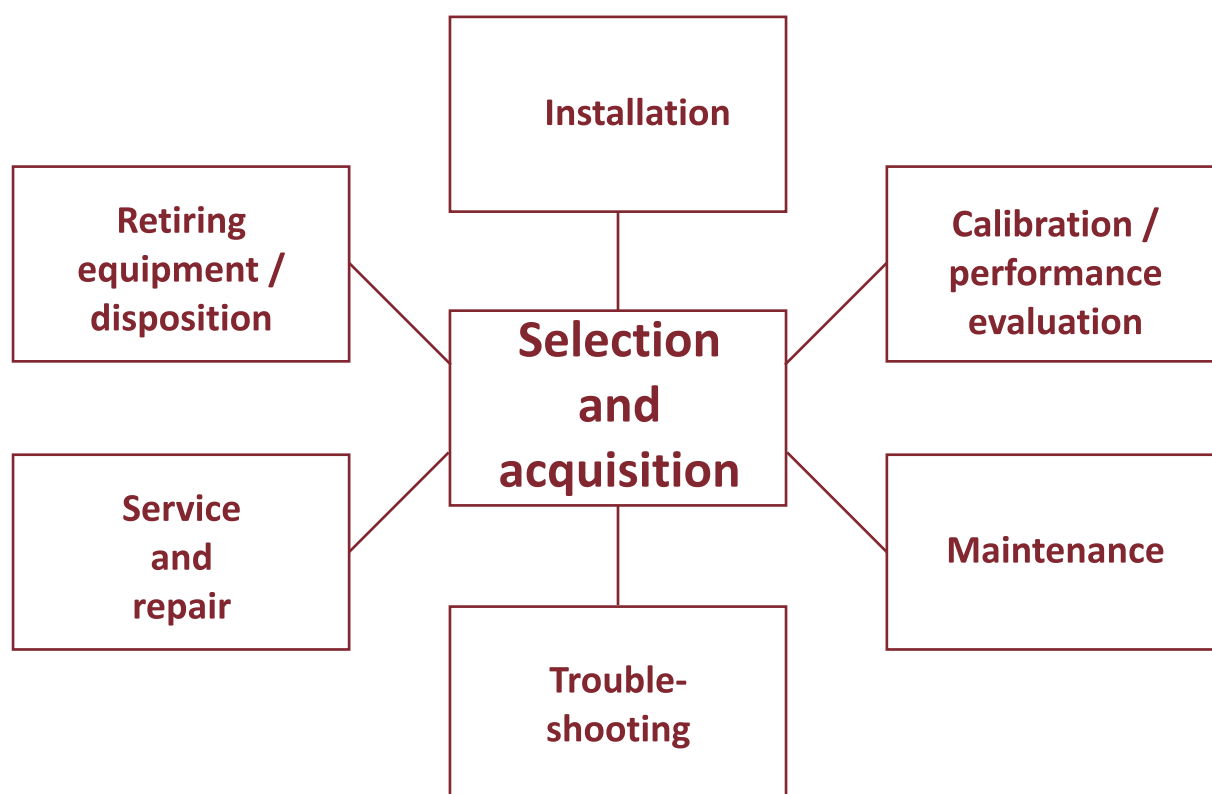
Equipment Management

Equipment used in the laboratory can be classified as instruments (units that measure) and machines (units that perform a specific function). One of the advantages of using rapid technology for HIV testing is that minimum equipment is required. Separation of serum requires a centrifuge, pipetting devices are needed for dispensing samples and reagents, refrigeration is required for storing HIV test reagents or specimens, and timers are required to ensure the reading of test results at the specified time interval. The equipment needed for conventional HIV tests are ELISA plate incubators, washers, and readers.

A good equipment management program is necessary to ensure accurate, reliable, and timely testing and thus to maintain a high level of laboratory performance. It reduces variation in test results, and improves the technician's confidence in the accuracy of testing results. It also lowers repair costs, as fewer repairs will be needed for a well-maintained instrument; lengthens an instrument's life; reduces interruption of services due to breakdowns and failures; increases safety for workers and yields greater customer satisfaction.

Equipment management comprises of (Figure 4.1)

Figure 4.1: Equipment Management



i. Equipment selection & acquisition: Lot of thought must go into selecting laboratory equipment. Cost, ease of operation, performance specifications, preventive maintenance costs and environmental requirements are important factors to consider. In addition laboratories must consider things such as the user manual, installation and training responsibilities, spare parts and the warranty including a trial period to verify that the instruments are performing as expected. The contents of the manufacturers' maintenance/service contract and whether maintenance is provided on a regular basis must be ensured. After selecting a piece of equipment, a laboratory must acquire it through purchase, lease, or rent. When the equipment arrives, the package contents must be checked to confirm that all parts are present; a copy of any software that is part of the system must be made.

ii. Equipment installation: Equipment should be suitably located in the laboratory so as to allow accessibility, smooth path of workflow and sequential utilization. This minimizes the need for frequent movement of specimens or reagents. Physical requirements such as safety checks, electrical specifications, space, ventilation, water supply and ambient temperature must be verified. It is preferable to have the manufacturer install the laboratory equipment since that will improve conditions of the warranty, and ensure that the installation is done properly and quickly.

iii. Equipment validation: It is a detailed process of confirming (by examination and provision of evidence) that the instrument is installed correctly, that it is operating effectively, and that it is performing without error. The process is broken into three different processes: the installation qualification (IQ), the operational qualification (OQ), and the performance qualification (PQ)

IQ is the correct installation as per plan and protocol. It comprises of

- ▶ Receipt check, visual inspection, assembly, site preparation, environmental requirements, and utilities verification.
- ▶ Preparation for calibration, maintenance, and cleaning requirements including their schedules.
- ▶ Identification and verification of all system elements, parts, services, controls, gauges, and other components
- ▶ Calibration of the measuring control and indicating devices against appropriate, traceable national or international standards.
- ▶ Documented records for the installation, installation qualification report must be reviewed and approved for satisfactory installation. It should include details (e.g., the supplier and manufacturer; system or equipment name, model and serial number; date of installation; spare parts, relevant procedures and certificates).

OQ looks at what the equipment/process is supposed to do and does it happen?

- ▶ Systems and equipment should operate correctly – operation verified as in the qualification

protocol by identified staff.

- ▶ Each qualification namely calibration, correlation, linear regression if applicable and reference ranges must be listed, described, acceptance criteria set.
- ▶ Studies on critical variable to include conditions encompassing upper and lower operating limits and circumstances (i.e., “worst case conditions”)
- ▶ Verification of operation for all system elements, parts, services, controls, gauges, and other components.
- ▶ Finalize and approve SOP (operation)
- ▶ Training of operators provided – training records
- ▶ The results of qualification must be documented and it must be determined if performance meet criteria. Discrepancies and action taken must be explained. OQ report must be reviewed and approved.

Systems and equipment released for routine use after completion of OQ, provided that the calibration, cleaning, maintenance, training and related tests and results were found to be acceptable

PQ is evidence that the whole process works as intended. Written instructions for the PQ activities must include test sample required, materials to be used, testing conditions to be used and data to be collected. Personnel who will perform the PQ must be identified. Draft copies of the processes and procedures must be followed. The PQ must be performed to ensure that:

- ▶ Systems and equipment are consistently performing in accordance with the design specifications – verified in accordance with a PQ protocol and results documented.
- ▶ Show satisfactory performance over a period of time. The manufacturers justify the selected period.
- ▶ It must be determined whether performance met criteria and any discrepancies explained along with action taken.
- ▶ PQ report must then be reviewed and approved and the conclusion statement must be drafted (successful as expected-why or why not), final approval signatures obtained and all records generated including instrument printouts compiled and retained.

When equipment designed for a fixed location is moved or there is a major methodology or software upgrade both IQ and OQ need requalification.

Equipment use: The laboratory needs to train and authorise selected staff to use the equipment and the staff need to follow documented operation instructions for the equipment. Instructions for use need to be kept current and readily available to staff. A record of who is authorised to use the equipment must also be maintained.

iv. Equipment Calibration and Calibration verification:

As components age and equipment undergoes changes due to variations in the environmental temperature and humidity or sustains mechanical stress, performance gradually degrades. This is called *drift*. When this happens test results become unreliable and quality of results suffer. While drift cannot be eliminated, it can be detected and either corrected or compensated for through the **process of calibration**. Any parameter of an instrument that will affect the quality of the test results has to be calibrated. E.g. in a refrigerated centrifuge – quantities to be verified are speed, time, temperature.

Calibration is the process of verification by comparing the accuracy of the quantity of a measuring (test) instrument against a reference standard within defined limits of accuracy and uncertainties in order to detect correlate or eliminate by adjustment any discrepancy in the accuracy of the test equipment being calibrated.

The laboratory needs to develop and implement calibration processes for instruments and equipment involving measurements that include the following

- ▶ A schedule for calibration and calibration verification, following at a minimum the manufacturer's recommendations or specific criteria from NABL
- ▶ Assignment of scheduled responsibilities
- ▶ Traceability of calibration standards
- ▶ Performing and recording calibration and calibration verifications
- ▶ Analysis of the results of calibration and calibration verifications
- ▶ Recording the actions taken when calibration and calibration verification results fail to meet predetermined criteria
- ▶ Posting a label of the calibration status and next due date on the calibrated instrument/equipment
- ▶ Placement of labels of any needed adjustments, tolerances or corrections.

The overall program of calibration, verification and validation of equipment must be designed and operated to ensure that measurements made by the laboratory are directly traceable to National and International standard of measurement through an unbroken chain of accredited calibrating laboratories. A laboratory must ensure that the calibration certificates indicate this traceability to the international system (SI) of units and also provide a statement on the uncertainty of measurement and standards used with their valid calibration, uncertainty & traceability (Annexure 4.1).

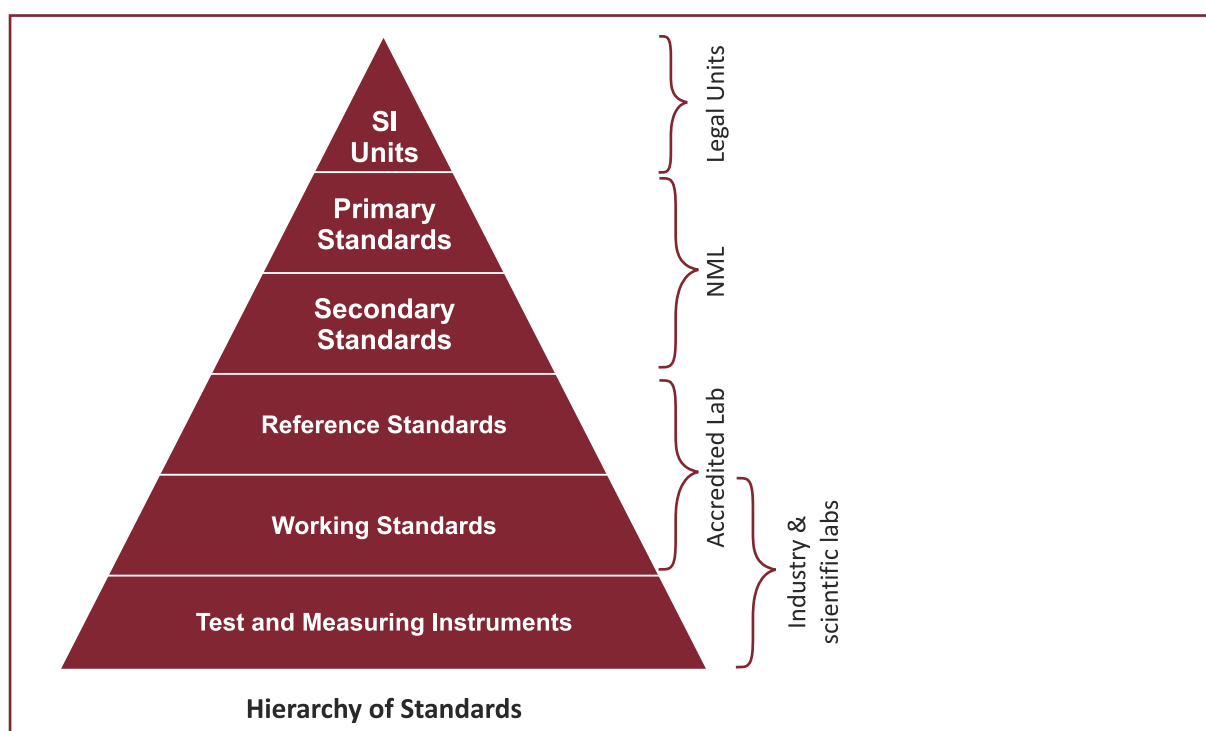
Certain basic elements to be addressed as part of calibration are calibration interval, (period of time between successive, scheduled calibrations) measurement traceability, records, labels, calibration procedures, environmental control (temperature, relative humidity, atmospheric pressure), personnel requirements. Factors deciding the frequency of calibration are usage rate,

conditions of use, skill level of personnel, degree of accuracy expected as per ISO/NABL standards, manufacturer-recommended calibration interval, before or after a major critical measuring project. The initial calibration interval for the majority of test and measuring instruments is set at 12 months.

After any calibrations, adjustments and before resuming use, the laboratory needs to verify that the equipment functions as expected.

Measurement/Metrological Traceability: Calibration has a chain-like structure in which every instrument in the chain is calibrated against a more accurate instrument immediately above it in the chain (Figure 4.2). The knowledge of the full chain of instruments involved in the calibration procedure is known as **traceability**. According to the International Vocabulary of Metrology VIM traceability is defined as *“the property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons having stated uncertainties”*. National Traceability is to the National metrology institute/laboratory, NPL New Delhi and international to the SI system of units (BIPM France).

Figure 4.2 Traceability through an established calibration program



Uncertainty of Measurement: Every measurement is subject to some uncertainty. A certain amount of variability is observed in repeat measurement results even if the measurement system is perfect. These can come from the measuring instrument, from the item being measured, from the environment, from the operator, and from other sources. A measurement

result is only complete if it is accompanied by a statement of the uncertainty in the measurement. A measurement result should therefore be specified as $X \pm U$, where X is the best estimate of the measurand and is equal to the average of repeat observants. U is the uncertainty of the measurement. Measurands are particular quantities subject to measurement (temperature, time, speed, volume etc.).

UM is defined as a non- negative parameter, associated with the result of a measurement that characterizes the dispersion of the values that could reasonably be attributed to the measurand. When the uncertainty in a measurement is evaluated and stated, the fitness for purpose of the measurement can be properly judged. The use of good practice – such as traceable calibration, careful calculation, good record keeping, and checking – can reduce measurement uncertainties

UM is evaluated from the statistical distribution/analysis of the results of series of measurements obtained under specified repeatability conditions. The repeat measurements are spread or dispersed around a specific value (arithmetic average/mean). This spread (standard deviation) is the uncertainty interval where the measurement result is expected to lie. The wider the interval, the more uncertain we are about the assigned value; similarly, if the interval is small, the uncertainty of the measurement result as an assigned value is also small.

UM is expressed as a standard deviation (or a multiple of a standard deviation) or the half-width of an interval having a stated level of confidence. Uncertainty is expressed in terms of a coverage factor, together with a size of the uncertainty interval, and state a level of confidence i.e. By using the coverage factor $k = 2$, to give a level of confidence of approximately 95 percent.

Calibration Certificate:

The result from the calibration of a measuring equipment or measurement standard is given in a calibration certificate/report. It can be in either hard copy or electronic format and at a minimum displays:

- ▶ Name and address of the calibrating laboratory.
- ▶ Unique identification of the certificate
- ▶ Name and address of the client
- ▶ The identification of the equipment calibrated (by manufacturer or brand and type and by the unique identification number, as specified by the inventory).
- ▶ Date the calibration was performed.
- ▶ The environmental conditions during calibration
- ▶ Standards used with their valid calibration, uncertainty & traceability (traceability certificate of reference standard)
- ▶ Identification of the method used
- ▶ The calibration results obtained and units of measurement including: A record of the

readings obtained during the calibration for each of the calibration values and record of the calculation of the accuracy and precision for all sets of values.

- ▶ Any use limitations on the equipment calibrated
- ▶ The correction factor (if any)
- ▶ The uncertainty of measurement result
- ▶ Coverage factor/confidentiality limits (levels)
- ▶ Validity of the latest calibration
- ▶ The authority under which the certificate is issued (The name, function and signature of the person authorizing the certificate)
- ▶ NABL symbol since calibrating lab must be NABL accredited

Calibration of equipment can be outsourced to an external accredited calibration laboratory. For in-house calibration/calibration verification of instruments in the HIV testing laboratory, use a calibrated tachometer-for rotational speed of the centrifuge; a calibrated digital temperature sensor-for checking the temperature of a refrigerator, incubator etc., a calibrated glass thermometer- for temperature checking of oven, water bath etc.; calibrated weights-for the balance which in turn is used to calibrate pipettes, calibrated timers to calibrate timers of centrifuges and those used to alert the technician to read test results in specified time intervals .

Calibration is a QA function. The quality of serviceable instruments is only verified and not upgraded directly by calibration. Upgrading is accomplished through repair, maintenance and through the action of new procurement.




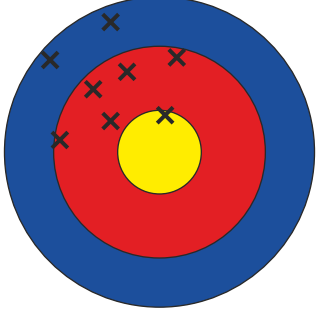
v. Performance/ Function Evaluation:

Routine checking/monitoring of instrument performance parameters verifies that the equipment has remained within specified range of accuracy & precision and that it is working according to the manufacturer's specification. This should be done before using the instrument initially as often as recommended by the manufacturer (performed periodically-daily, weekly, monthly). These function checks should also be done following any instrument repairs. Some examples of function checks are daily monitoring of temperature and checking the accuracy of wavelength calibration.

Accuracy: The closeness of agreement between the result of a measure and the true value of measurement. Calibration is used to determine the accuracy of an instrument. Accuracy is measured in terms of bias/error. (Figure 4.3).

Precision (Repeatability): Precision is the closeness of agreement between the results of successive measurements of a defined procedure several times under prescribed conditions. Precision is measured in terms of imprecision. It is evaluated statistically using standard deviation, coefficient of variation or confidence interval. (Figure 4.3).

Figure 4.3: Accuracy and Precision

	Accurate	Inaccurate (systematic error)
Precise		
Imprecise (reproducibility error)		

vi. Equipment Maintenance, Service and Repair: Equipment maintenance is the scheduled, regular and systematic cleaning, decontamination, adjustment, or replacement of instrument and equipment parts that have the potential to fail (e.g. tubing, motor brushes, and rubber gaskets). The aim is to minimize equipment malfunction or failure by detecting minor problems early and before they cause shut down or malfunction of equipment. This preventive maintenance is performed periodically viz. daily, weekly, monthly, annually but at a minimum the manufacturer's recommendations should be followed.

- ▶ **Daily Maintenance** - Assure that all equipment is clean, add controls or calibrators to each run, daily monitor temperatures of refrigerators, freezers, incubators and the room temperature, check wavelength calibration, assure that the printer paper is adequate, check that waste containers are empty, rinse sample ports with distilled water or acceptable cleaners, clean up all spills, check reagent levels, dispose of bio-hazardous waste properly and check autoclave indicator paper
- ▶ **Weekly Maintenance** - keep optical and other components free from dust and surfaces of instruments clean. Prepare fresh batches of reagents as needed, defrost refrigerators and clean water baths.
- ▶ **Monthly Maintenance** - Perform electronic or optical checks on all components. Many automated and semi-automated instruments have built-in programs for calibration.
- ▶ **Biannual Maintenance** - Clean or change filters; check fluid lines and tubing for signs of deterioration or dirt and replace as needed. Re-grease and recalibrate all pipettes as needed

and check electrical connections and wiring.

- ▶ **Yearly Maintenance** - Change all fluid lines and tubing of major instruments, recalibrate pipettes and call the factory representative (if possible) to arrange for a service visit.

Steps to implementing a maintenance program include

- ▶ Assigning responsibility for the oversight of all laboratory equipment,
- ▶ Developing written policies and procedures for maintaining equipment including routine maintenance plans for each piece of equipment that specify the frequency with which all maintenance tasks should be performed,
- ▶ Developing the format for records, creating logs and forms, and establishing the processes to maintain records,
- ▶ Training of staff on the use and maintenance of the equipment, and ensuring that all staff understand their specific responsibilities.

vii. Equipment Inventory, Documentation and Records: An equipment inventory system assists in the control of equipment. Records should be maintained for each piece of equipment contributing to the performance of examinations. Each piece of equipment should have a dedicated logbook documenting all characteristics including:

- a. Identity / name of the equipment.
- b. Manufacturer's name, type identification, serial number or other unique identification.
- c. Manufacturer's contact person with appropriate contact details.
- d. Date equipment was received and date it was implemented in laboratory service.
- e. Condition when received (e.g. new, used, reconditioned etc.).
- f. Checks that equipment complies with performance specifications e.g. analytical capability, acceptable limits for operation, troubleshooting guide, etc.
- g. Validation records to confirm that the equipment was found to be suitable for use
- h. Current location.
- i. Manufacturer's instructions manual or reference to where this can be accessed.
- j. Calibration frequencies, reminders and records.
- k. Adjustment and acceptance criteria and acceptance failures.
- l. Maintenance plan and maintenance record.
- m. Damage, malfunction, modification, repair and service records.
- n. Responsibility for equipment management.
- o. Date equipment was removed from service.

To ensure that the laboratory does not run out of spare parts, an inventory record of those used most frequently should be kept for each piece of equipment. The record should include: part name and number; average use of the part, and the minimum to keep on hand; cost, the date when the part is placed into storage and when it is used (in and out stock log) and quantity of each part remaining in inventory.

Equipment documents and records are an essential part of the quality system. The policies and procedures for maintenance should be defined in appropriate documents. Keeping good equipment records will allow for systematic evaluation of any problems that arise. Each major piece of equipment will have its own equipment maintenance document which should include: step-by-step instructions for safe handling, transport, storage and use; how to prevent contamination and deterioration; information on routine maintenance including frequency of performance and how to keep records of maintenance; instructions for carrying out function checks, frequency of performance, and how to record the results; directions for calibrating the instrument; guide for troubleshooting; any required manufacturer's service and repair and a list of any specific items needed for use and maintenance, such as spare parts.

When computers or automated examination equipment is used for the collection, processing, recording, reporting, storage or retrieval of examination data, the laboratory must ensure that:

- a) Computer software, including that built into equipment, is documented and suitably validated as adequate for use in the facility;
- b) Procedures are established and implemented for protecting the integrity of data at all times;
- c) Computers and automated equipment are maintained to ensure proper functioning and are provided with environmental and operating conditions necessary for maintaining the integrity of data;
- d) Computer programs and routines are adequately protected to prevent access, alteration or destruction by casual or unauthorized persons.

Reconstruction of the history of each piece of equipment from acquisition to decommission should be traceable from the equipment records. These records should be readily available for the life span of the equipment or for any time period required by national, regional and local regulations.

viii. Troubleshooting: Problems with equipment may present in many ways. The operator may notice small changes such as drift in QC or calibrator values, or obvious flaws in equipment function. Sometimes, the equipment fails to operate. While training operators it is important to teach them to troubleshoot equipment problems in order to quickly get the equipment functioning and resume testing as rapidly as possible. When an instrument drift is observed, it is necessary to repeat the preventive maintenance procedures as a first step to resolving the problem. If this does not work, proceed with troubleshooting processes.

Manufacturers or user manuals frequently provide a flowchart that can help determine the source of problems. Is the problem related to a poor sample? Has the sample been collected and stored properly? Are factors such as turbidity or coagulation affecting instrument performance? Is there a problem with the reagents? Have they been stored properly, and are they still in date? Have new lot numbers been introduced without updating instrument calibration? Is there a problem with the water or electrical supply? Is there a problem with the equipment?

One change should be made at a time. If the equipment is the problem, the manufacturer's instructions or SOPs must be reviewed to verify that all procedures are being followed correctly. Equipment that does not function properly must not be used. When In-house efforts have failed, find a way to continue testing until equipment can be repaired. Options for testing include referring tests to an identified accredited laboratory or using a validated, calibrated and maintained backup instrument or storing samples appropriately until the testing is possible. Help from manufacturer or other technical expert must be then sought. A malfunction label/notice must be placed on equipment so all staff are aware that it is not in use.

Documentation must be complete. A problem log record must be developed for each piece of equipment and details to be noted include the date when the problem occurred, removed from service, reason for breakdown or failure, corrective action taken, date returned to use, change in maintenance or function checks.

ix. Defective Equipment Management: Whenever equipment is found to be defective thorough function checks or other monitors of performance, protocols dictate that;

- a. It should be isolated and taken out of service
- b. It should be clearly labelled or marked as being out of service. One must examine the effect of this defect on previous examinations
- c. A list of the measures taken to reduce contamination shall be provided to the person working on the equipment
- d. Reasonable measures must be taken to decontaminate equipment prior to service, repair or decommissioning
- e. Suitable space for repairs and appropriate personal protective equipment (PPE) should be provided
- f. Equipment must be appropriately stored until it has been repaired
- g. And after repair, before being put to use again, equipment must be shown by means of calibration, verification, or function checks, that it meets specified acceptance criteria

x. Retiring Equipment / Disposition: It is necessary to have a policy and procedure for retiring older laboratory equipment. This will usually occur when it is indicated by experts that the instrument is not functioning and is not repairable, or when it is outmoded and should be replaced with new equipment. Once a piece of equipment is fully retired and it has been determined that it has no further use, it should be disposed off in an appropriate and safe manner. When disposing off equipment, salvage any usable parts, particularly if the equipment is being replaced with another similar one. Any potential biohazards must be considered and all safety disposal procedures must be followed.

xi. Oversight and Supervision: It is the responsibility of the laboratory in charge to oversee all the equipment management systems in the laboratory; ensure that all persons who will be using

the instruments have been appropriately trained and understand how to correctly operate the instrument, troubleshoot, perform all necessary performance checks and routine maintenance procedures. Specific person/s must be designated to oversee and deal with all aspects of equipment management. Oversight of equipment management includes ensuring that all procedures are followed; procedures are updated when necessary, all records are routinely reviewed.

Annexures:

4.1 Temperature Controlled Units (Refrigerators and freezers; Incubators)

4.2 Incubators

4.3 Centrifuge

4.4 Pipettes

4.5 Electronic balance

4.6 ELISA System

Key points

The laboratory should be furnished with all items of equipment required for the provision of services. Laboratory equipment

- ▶ Should be selected and shown upon installation and in routine use to be capable of achieving the performance required (validation);
- ▶ A list of working equipment should be maintained with unique identification, serial number, model, name of manufacturer, date of installation, current location, calibration status and records of maintenance, function checks and performance assessment;
- ▶ Every equipment should be labeled to indicate the unique identity, functional status, calibration or verification status and the date when next calibration or re-verification is due
- ▶ Equipment should be maintained in safe working condition, including examination of electrical and mechanical safety, emergency stop devices, and safe handling and disposal of chemical and biological materials by authorized persons.
- ▶ Laboratory management should establish a documented program that regularly monitors and demonstrates proper calibration, and preventive maintenance of equipment that, at a minimum, follows the manufacturer's recommendations.
- ▶ Up-to-date instructions and SOPs on the use and maintenance of equipment, including any relevant manuals and directions for use provided by the manufacturer, should be readily available for use by laboratory personnel. The equipment should only be operated by authorized personnel.
- ▶ Records should be maintained for each item of equipment contributing to the performance of examinations.
- ▶ Whenever equipment is found to be defective, it should be taken out of service, clearly labeled, appropriately decontaminated and stored until it has been repaired. It should be recalibrated before being put into use again.

Laboratory supplies and inventory management

For successful performance, every testing laboratory should have sufficient supplies to meet the requirements of the customer/scope of the laboratory. For an HIV testing laboratory, these supplies could be categorized as consumables, reagents and kits. Providing a dependable, uninterrupted supply of good quality kits and consumables is important for the success of the NACP.

Inventory is a stock or store of supplies. It is a part of the supply chain which also consists of storage and distribution. Inventory management includes those systems and processes that identify inventory requirements, set targets, provide replenishment techniques and report actual and projected inventory status. Inventory management thus will be successful if the storage and distribution infrastructure is efficient. A good inventory is vital for successful operation and customer satisfaction.

Inventory for HIV testing has some special characteristics. It has to deal with the different quantities required for three types of test (1st, 2nd and 3rd), their storage conditions and shelf life. HIV testing is dynamic, requiring change to be incorporated as and when directed by the national guidelines. The necessity to adhere to the testing algorithm leaves no option for substitution especially if there is a stock out of kits. On the other hand if the laboratory purchases too many supplies, then they have to redistribute the excess stock to prevent wastage.

Definitions:

- ▶ **Reagents** are chemicals and biological agents that are used in laboratory testing for detecting or measuring an analyte, the substance being measured or determined.
- ▶ **Consumables** are items that are used once while performing a test and are not reused.
- ▶ **Inventory** is a stock or store of supplies
- ▶ **Inventory management** comprises the procedures that govern how supplies are ordered, received, stored, handled, distributed and re-ordered.
- ▶ **Full supply** is a situation wherein sufficient quantities of all commodities are available to meet all needs of laboratory.
- ▶ **Standard protocol for inventory control** is when orders are placed at regular intervals. A product is ordered only if it has reached its minimum/reorder stock level.
- ▶ **Lead time** is the amount of time it takes to fill and process orders and deliver product to the receiving facility.

Inventory Management System:

Every laboratory should have a good inventory management system. The purpose of inventory management is to ensure a continuous, uninterrupted supply of quality products as and when needed. The role of this system is to:

- ▶ **Identify how much to order** or issue as much as is required to meet laboratory demands (anticipated / expected), ensure a continuous supply of reagents and consumables (at no time should a test be denied for lack of supplies) and protect against stock outs or overstock leading to expired products.
- ▶ **Understand when to change the quantity of order or issue** - Forecast a supply based on requirement (anticipate a likely increase / decrease in requisitions) so that excess stock does not lead to expired goods due to non-utilisation.
- ▶ **Know when to order or issue** - Identify / define buffer stocks and reorder levels
- ▶ **Maintain a continuum of services**

Components of Inventory Management:

The Components of Inventory management includes

- ▶ Requirement
- ▶ Procurement
- ▶ Disposal of expired stock

Requirements : includes personnel, supplies, infrastructure and documentation.

Personnel - Designate a responsible staff member for inventory management and describe his/her roles and responsibilities.

Supplies - Select products that are appropriate based on the testing protocols, cost, training of personnel, and infrastructure for storage and transportation. The designated person prepares a list of all supplies that would be required to successfully carry out the tests under the laboratory's scope. These include:

- ▶ The test kits (as applicable)
- ▶ The equipment / reagents / consumables not provided with the kit (read the kit literature under 'equipment / reagents / consumables required but not provided e.g. micropipettes, pipette tips, wash buffers etc.)
- ▶ Material required for performing the tests as per Good Clinical Laboratory Practices (GCLP).
- ▶ Material required for safety issues including Personal Protective Equipment, spill management, sharp policy, biomedical waste management and Post Exposure Prophylaxis. Though this may not directly affect the performance of the test, they form a part of the quality policy of every testing laboratory and should be complied with at all times

A comprehensive checklist based on the above can be used as a record for procurement, storage and distribution. (Annexure 5.1)

Infrastructure: Storage area and equipment - The minimum infrastructure required would be a well-ventilated and well lit storage area that can be efficiently secured, a separate storage area for chemicals as per their Material Supplies Data Sheet requirements, and cold storage for kits

and reagents as required (walk in coolers / cold room / refrigerators / deep freezers). Store the supplies in such a way that First Expiry First Out (FEFO) can be followed. Storage areas should be in a controlled environment and have adequate capacity.

Documentation: Every testing facility should maintain a 'stock register'. (Annexure 5.2) The stock register should be updated every time a supply is distributed / procured. A QSP describing inventory control should be developed and implemented.

Procurement

The key objectives of procurement are that the consumables must be of the desired specifications, in the appropriate quantities, of good quality and at competitive price.

- ▶ From whom to procure? Presently, under the programme kits are supplied by the SACS/NACO and the other supplies are purchased by the testing centres through a grant made available to each testing facility. The method of procurement should be as per guidelines of the funding agency, which should be well documented.

A typical procurement cycle consists of selecting / identifying the commodity, quantifying the commodity, re-quantifying based on budget, identifying the suppliers, procuring product brochures from suppliers, preparing specifications, placing an order to the vendor whose sample/s satisfies the specifications and who has provided the lowest quotation, inspecting samples and approving, making a payment, documenting receipt and payment, updating the stock register, distributing and collecting consumption data.

A good procurement process is transparent, accountable, provides good quality products and should be well documented.

- ▶ How much to procure? Forecast the quantity required based on the number of tests likely to be performed over a defined period, and the minimum reorder level/ buffer stock required. A minimum reorder level/ buffer stock is the minimum stock maintained to protect the testing facility against stock-outs. The defined period would depend on the storage infrastructure available at each testing centre, the shelf life of the supplies and the down time for procurement. Also, adjust the estimated quantity for products that may be lost (expiry, wastage, breakage, etc.), and those required for QC purposes. Order only as many as can be procured from the budget provided. Never order kits or consumables more than the storage space can hold.

While re-ordering (based on the lead time and buffer stock/ reorder level and the actual supplies in hand i.e. physical count), place an order to meet the requirement as described above.

- ▶ How are the supplies to be accepted, stored and used?

- ▶ Use the checklist when accepting supplies. (Annexure 5.3)
- ▶ On receipt, all materials should be inspected and approved [test if required]
- ▶ If temperature sensitive parameters are required for quality, these should be checked and ascertained
- ▶ Check the packing for integrity
- ▶ Check the expiry date and any certificate of analysis / conformity if required
- ▶ Document all the kits, reagents and consumables in the stock register
- ▶ Stack properly in the designated locations based on their requirement for temperature, storage (coolers / refrigerators are required for storage of testing kits). Store all supplies as per requirements on each supply label.
- ▶ All supplies should be used on a First-Expiry-First out (FEFO) basis.
- ▶ When to place a re-order? Whenever the kit stock reaches minimum level, place an order keeping in mind the lead time. Calculate the minimum stock level with the help of the following formula:

$$\text{Minimum Stock Level} = \frac{\text{Maximum lead time}}{(\text{In weeks})} \times \frac{\text{Maximum Usage}}{(\text{In a week})}$$

Disposal of Expired Stock:

In an efficiently managed inventory system, situation where stocks expire should not arise. A system of redistribution of close to expiry kits should be implemented. In an unlikely event of expired stock the under mentioned steps to be followed:

- ▶ During monthly stock checks, expiry dates for all supplies, must be checked to ensure that no stock is kept in circulation that is out of date.
- ▶ Expired stock must be removed from use immediately upon discovery for disposal.
- ▶ Inform the local authority for collecting/sending the expired stock.
- ▶ If stock need to be disposed of, follow the Material Safety Data Sheet (MSDS) and the national biomedical waste management rules.
- ▶ Maintain records of the same.

Key points

Inventory management involves

- ▶ Assignment of responsibility
- ▶ Analysing needs
- ▶ Establishing minimum stock needs
- ▶ Development of forms and logs
- ▶ Establishment of a system for receiving and storing
- ▶ Maintaining inventory systems in all storage areas

Personnel

The success of QMS in a laboratory regardless of the design, ultimately depends upon its human resource. Qualified, trained and motivated personnel are the backbone of the QMS. When implementing a QMS the organizational structure must be well defined in the form of an **organizational chart** which is a diagram that shows the structure of an organization and the interrelationships, designations and reporting hierarchy. Personnel policies must be documented and available to all employees.

The laboratory personnel / staff include:

- ▶ Head of the Institute
- ▶ Head of the department
- ▶ Laboratory/section in charge/s
- ▶ Quality Manager
- ▶ Safety Officer
- ▶ Technical Manager
- ▶ Technical Staff

Job descriptions that specify tasks, responsibilities and authorities for all personnel must be established and well defined. When assigning responsibilities, education, demonstrated skill, training and experience must be considered. Deputies for all key managerial and technical personnel must be specified and communicated. Authorized signatories must demonstrate knowledge and competence in the concerned speciality. The qualification norms for authorized signatories are according to NACO/NABL guidelines.

Head of the Institute provides commitment in terms of administrative support and resource mobilization so as to ensure that the laboratory is directed towards adopting the QMS approach.

Head of the Department has the overall responsibility for professional, scientific, advisory, organizational, administrative and educational matters relevant to the services offered by the laboratory and coordinates with the Head of the Institute for allocation of resources and garnering administrative support for the laboratory. The Head of the Department also designates the Quality Manager who would monitor and maintain day-to-day activities pertaining to QMS.

The Laboratory/Section In charge coordinates with the Head, Quality Manager and Technical Staff to ensure that the QA of the technical aspects of the laboratory is adequate and authorizes the release of reports. In the event of non-conformances, s/he ensures that results of test examinations are not reported until all corrective actions have been taken and the test system is properly functioning; provides training to personnel; annually evaluates and documents the performance of all testing personnel.

The Quality Manager, appointed by the HOD has delegated authority and direct responsibility to ensure processes needed for the QMS are established, implemented and maintained. S/he oversees compliance with the QMS requirements. S/he reports directly to the level of management at which decisions are made on policy and resources. The Quality Manager must be trained and experienced in medical laboratory science and trained in the quality management system. The quality manager must have undergone a four day training course on laboratory QMS from a reputed institute.

Safety Officer should be appointed wherever possible to ensure that the safety policies and programmes are followed consistently throughout the laboratory. The safety officer executes these duties on behalf of the head of the institute or laboratory. The person designated should possess the professional competence necessary to suggest, review and approve specific activities that follow appropriate bio-containment and biosafety procedure/s. S/he should apply relevant international, national and local rules, regulations and guidelines, as well as assist the laboratory in developing the safety manual/standard operating procedures. The safety officer should also be able to communicate effectively with administrative, technical and support personnel.

The Technical Manager needs to have applicable theoretical and practical background as well as experience in the examinations or interpretations on which s/he make professional decisions. S/he is responsible for day-to-day supervision of the lab operation, as well as personnel performing testing and reporting test results. Monitors examinations to ensure that acceptable levels of analytic performance are maintained; ensures that all remedial actions are taken whenever test systems deviate from the laboratory's established performance specifications;

The technical Staff must:

- ▶ Follow the laboratory's procedures for specimen handling and processing, test analysis reporting and maintaining records of test examinations
- ▶ Maintain records that demonstrate that proficiency testing samples are tested in the same manner as patient specimens
- ▶ Adhere to the laboratory's quality control policies, document all quality control activities, instrument and procedural calibrations and maintenance performed
- ▶ Follow the laboratory's established policies and procedures whenever test systems are not within the laboratory's established acceptable levels of performance
- ▶ Be capable of identifying problems that may adversely affect test performance or reporting of test results and either must correct the problems or immediately notify the supervisor or HOD; and
- ▶ Document all corrective actions taken when test systems deviate from the laboratories established performance specifications

All quality management issues can only be addressed and fully implemented if institutional head commits to and provides full support including resources to the system.

A broad outline of steps (Table 6.1) to be taken by personnel at different levels for instituting QMS is provided:

Table 6.1: Laboratory Personnel/Staff and their Roles in maintaining the QMS:

Level	Action
Head of the Institute	<ul style="list-style-type: none"> ▶ Ensures commitment for implementation of QMS ▶ Ensures commitment in terms of administrative support & resource mobilisation and allocation
Head of the Department	<ul style="list-style-type: none"> ▶ Coordination with the Head of the Institution to ensure administrative support & resources ▶ Overall responsibility for professional, scientific, advisory, organisational, administrative and educational matters relevant to the services offered by the laboratory ▶ Designates Quality Manager and Laboratory In-charge, wherever required ▶ Provides advisory services to clinicians
Laboratory/Section In charge	<ul style="list-style-type: none"> ▶ Coordinates with the Head and Quality Manager and Technical Staff to ensure the implementation of quality assurance measures in the laboratory ▶ Authorizes the release of reports ▶ Provides advisory services to clinicians
Quality/Technical Manager	<p>In consultation with the Laboratory In charge & Head of the Department:</p> <ul style="list-style-type: none"> ▶ Defines, implements and monitors standards of performance and continual quality improvement in the laboratory ▶ Plan trainings and re-trainings of staff including competency evaluations
Safety Officer	<ul style="list-style-type: none"> ▶ Biosafety, biosecurity and technical compliance discussions/meetings ▶ Periodic internal safety audits on technical methods, procedures and protocols, biological agents/materials and equipment

Level	Action
Safety Officer	<ul style="list-style-type: none"> ▶ Verifies that all staff receives appropriate safety training and continuing education ▶ Ensures proper waste management and emergency adverse incident management
Technical Staff	<ul style="list-style-type: none"> ▶ Develops documents according to document system QSP plan ▶ Carries out processes as per the documented policies & procedures

All personnel must know their roles and responsibilities in the QMS so as to collectively contribute and make it effective. Qualified and trained personnel who have the authority to provide the laboratory's services and who understand both technical and managerial aspects (Head of the department and/or Laboratory In charge) should head this effort and should direct the technical personnel. Once the Quality Management System is established, the competency of personnel must be assessed initially and periodically. It must be verified that all persons have been trained appropriately for their set of responsibilities and periodically assessed and retrained if necessary.

Personnel Training:

Laboratory management must have procedures for the training for all staff. Training must be documented for all individuals, including healthcare providers performing testing, staff engaged in the performance of supportive tasks such as data entry, accessioning and reporting, supervisory and management staff. Training programs should include the following elements:

- ▶ Job Tasks (assigned work processes and procedures)
- ▶ QMS
- ▶ Safety and Health
- ▶ Ethics including confidentiality of information
- ▶ Governmental reporting requirements
- ▶ Applicable laboratory information system including computer systems

The laboratory must introduce new personnel/staff to their assigned work processes and procedures with the applicable laboratory information system, the terms and conditions of employment, staff facilities, and orient them to the laboratory facility and safety (including prevention or containment of the effects of adverse events, fire and emergency) the QMS and the ethical code of conduct. This must be planned, documented and implemented; the laboratory in-charge/HOD must provide continuing education on an annual basis to laboratory staff commensurate with the scope of their duties. Records of all trainings must be maintained.

Competence Assessment:

To determine if staff possesses and continues to demonstrate the skill in which they were trained, an individual's competence is assessed

- ▶ After initial training and before working independently and six months thereafter
- ▶ Periodically throughout employment (at least once a year)
- ▶ Whenever job responsibilities change

Competence assessment applies to all laboratory personnel who perform responsibilities in the path of workflow. When competence assessment fail to meet established criteria, root cause(s) analysis should be performed and appropriate retraining is initiated and documented.

Competence assessment methods include but are not limited to

- ▶ Testing blinded samples, PT samples, split sample testing, replicate testing
- ▶ Periodic written test
- ▶ Compliance with policies and procedures
- ▶ Observation for compliance with safety protocols
- ▶ Direct observation of routine patient test performance, including patient preparation, specimen handling, processing and testing
- ▶ Monitoring the recording and reporting of test results
- ▶ Review of intermediate test results or worksheet, QC results records, PT results and preventive maintenance
- ▶ Direct observation of performance of instrument maintenance and function checks
- ▶ Evaluation of problem solving skills

Review of Staff Performance:

Reviews of staff performance must be undertaken at least annually. It must be ensured that these reviews consider the needs of the laboratory and of the individual in order to maintain and improve the quality of service given to the users. Productive working relationships must be encouraged.

Continuing Education and Professional Development:

A continuing education program must be available to personnel who participate in managerial and technical processes.

Personnel Records/Files:

The records listed are not required to be stored in the laboratory, but can be maintained in other specified locations, providing they remain accessible as needed.

The laboratory must maintain the following personnel records

- a. Personal information including educational and professional qualifications; previous work experience

- b. Copy of the degree/ diploma certificates
- c. Registration with local/ national authorities, wherever applicable
- d. Copy of appointment letter
- e. References from pervious employment
- f. Roles and responsibilities
- g. Job description and authorization
- h. Records of competency evaluations, training, continuing education
- i. Performance evaluation
- j. Health records including history of exposure to occupational hazards and immunization status.
- k. Hepatitis B vaccine should be offered to all the laboratory staff and the protective antibody titres subsequent to vaccination should be checked and documented.

Key points

Following personnel related aspects should be addressed while implementing QMS:

- ▶ The qualifications and experience of authorized signatories and technical staff should be followed unless otherwise specified.
- ▶ The number of staff employed should be appropriate to the workload of the laboratory.
- ▶ The roles, responsibilities and reporting hierarchy of the staff should be clearly outlined and documented. The staff should also understand the nature of work assigned to them and must be authorized to perform the tasks independently.
- ▶ A programme for technical training and updating skills on regular basis should be in place. The laboratory management should be committed for providing continuing education and professional development opportunities for staff.
- ▶ Laboratory should organize competency evaluation of staff, the frequency and method of which should be decided by the laboratory.
- ▶ Laboratory should organise performance reviews to evaluate an individual's job performance periodically.
- ▶ All personnel/staff must maintain confidentiality of information and ethical code regarding patients.

Laboratory Safety and Biosecurity

The laboratory can be a potential source of physical, chemical and biological safety hazards e.g. fire, breakage of glassware, sharps, spillages, pressure equipment and gas cylinders, extremes of heat and cold and radiation. However, with proper laboratory design and safety program these hazards can be prevented. Biosecurity is the protection of pathogens, toxins, and sensitive information from loss, theft and subsequent misuse.

The laboratory work space and services must be maintained in such a way that various tasks can be performed without compromising the quality of work or the safety of laboratory staff, other health care personnel, patients, visitors, the community or environment. All laboratories must comply with the national and state regulations.

Developing a Laboratory Safety Program:

Safety Officer

A designated laboratory safety officer must be assigned the responsibility for developing a safety program and organizing appropriate safety measures and safety trainings and drills for the laboratory. The steps for designing a safety management program include developing a safety manual to provide written procedures for safety and biosafety in the laboratory; organizing safety training and exercises that teach staff to be aware of potential hazards and how to apply safety practices and techniques, setting up a process to conduct risk assessments, as well as ongoing laboratory safety audits to look for potential safety problems. Laboratory safety audits can be undertaken using a safety checklist (Annexure 7.2).

The Safety Officer's job responsibilities include the following:

- ▶ All staff members are trained on safety and vaccinated against Hepatitis B. Records are available to corroborate this
- ▶ Ensure that there is an adequate supply of appropriate equipment for safety and biosafety, such as PPE; fire extinguishers and fire blankets
- ▶ Ensure appropriate storage and cabinets for flammable and toxic chemicals
- ▶ Provide eye washers and emergency shower; waste disposal supplies and equipment; first aid equipment
- ▶ Conduct and record weekly inspections to ensure that the laboratory is safe and in a good condition. Fire extinguishers and eye-wash stations are inspected, tested and service is up-to-date. First Aid kit is replenished when necessary
- ▶ Organize periodic (at least yearly) fire drills and laboratory evacuation procedures, handling of incidents and basic security precautions
- ▶ Ensure that the Material Safety Data Sheets (MSDS) are available in the respective laboratory sections and that the staff have read and understood them
- ▶ Ensure all incidents are documented and attended to immediately

- ▶ Conduct periodic safety audit with the help of a checklist

Safety Policies: The following safety policies must be in place to ensure the continued safety of laboratory staff and any authorized individual who may enter the laboratory:

Standard Precautions Policy:

This policy defines all human biologic specimens as potentially infectious and addresses topics of consideration when dealing with potentially infectious specimens, such as hand care, PPE, working with open lesions, handling contaminated needles and other sharp objects, autoclaving, and disposal of materials.

Chemical Hygiene Policy:

This policy addresses aspects of safe chemical handling, including storage, utilization and disposal of chemicals, with the goal of minimizing exposures and risks associated with those chemicals. MSDS provide information about the identities and hazards of chemicals, required appropriate labelling, exposure, first aid, spill management etc.

Waste Management Policy:

This policy details appropriate measures to take when disposing of waste materials to ensure continued human and environmental health.

General Safety Policies:

These policies address less specific topics as they relate to laboratory safety, such as fire and electrical safety.

Safety Equipment:

These policies typically detail all available safety equipment, their purposes, and proper utilization

Safety Training:

Training should include information about standard precautions, infection control, chemical and physical safety, how to use personal protective equipment (PPE), how to dispose of hazardous waste, and what to do in case of emergencies. Documentation related to the completion of safety trainings must be maintained. Safety trainings must be completed before any laboratory personnel begin working in the laboratory, and on a regular basis thereafter. Ongoing safety training must take place each calendar year.

Safety Incident Reporting

Safety-related incidents including injuries (needle prick, sharps injury, falls, burns, etc.); chemical exposure; malfunctioning equipment posing a safety risk (e.g. potential for electrical