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 a 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:

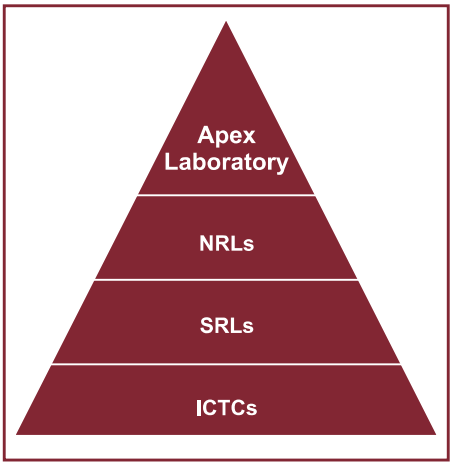
- Assesses the overall performance of a laboratory
- Provides objective evidence of laboratory quality

- 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

Figure: 2.3: Hierarchy of HIV testing laboratories



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)

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 blided 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 ^{o} 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 ^{o} 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^{O}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

Chapter 2

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 is 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.

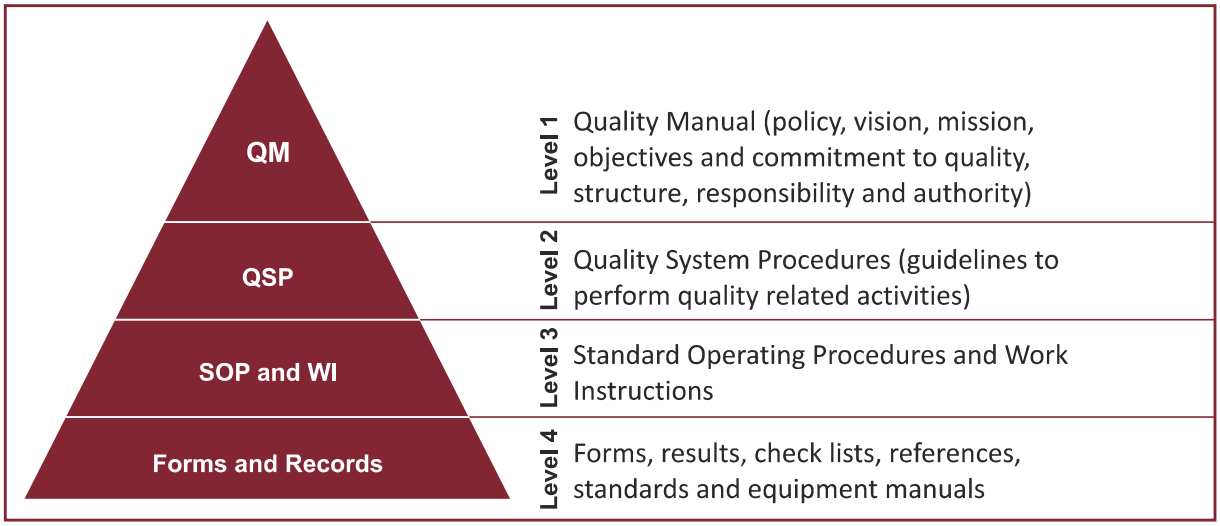
Documentation

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

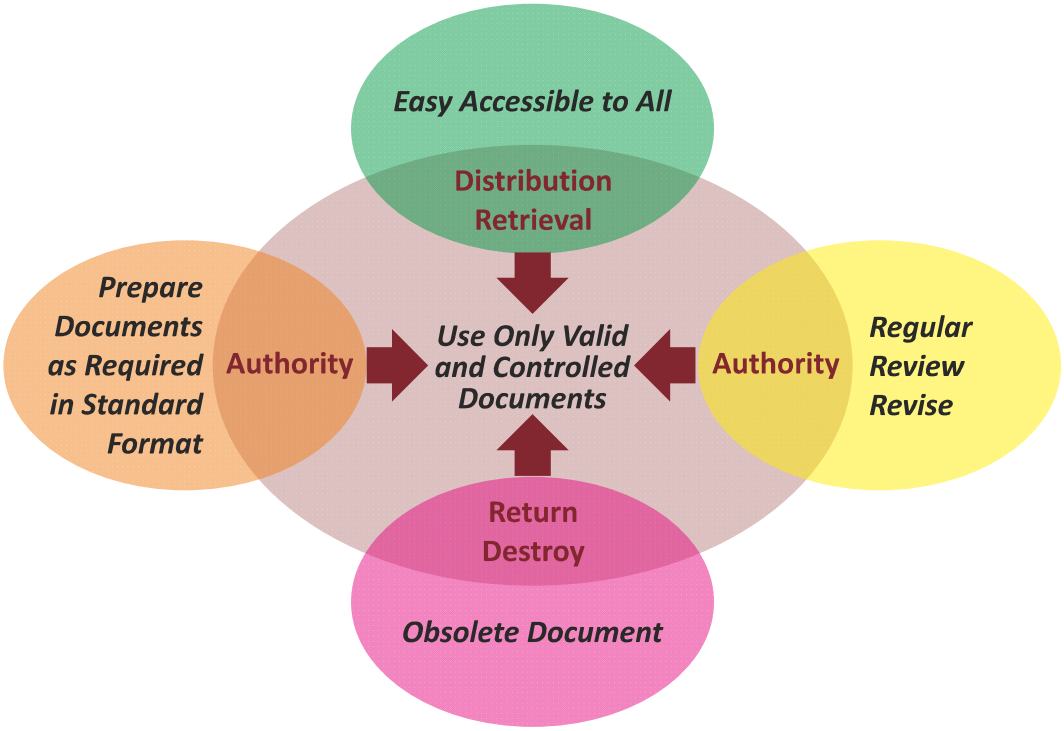
- The page number to total number of pages
- Authority for issue

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.

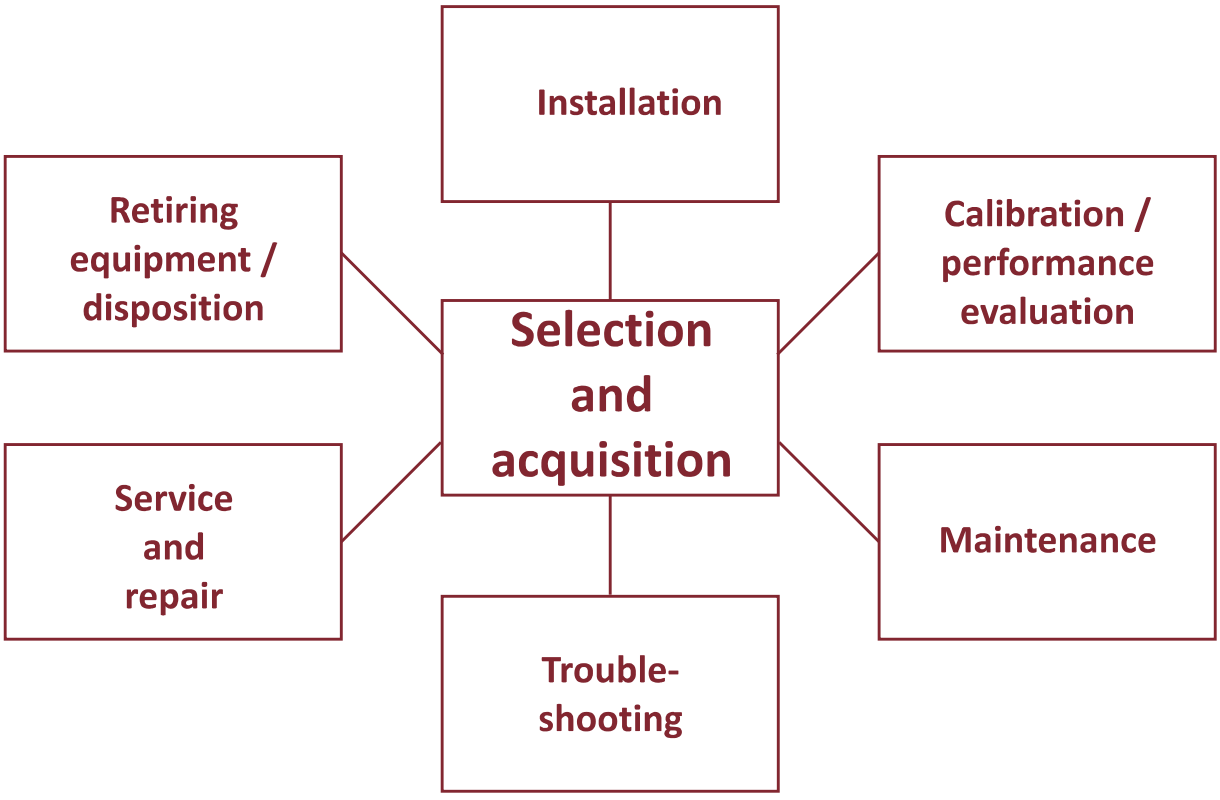
Equipment Management

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,