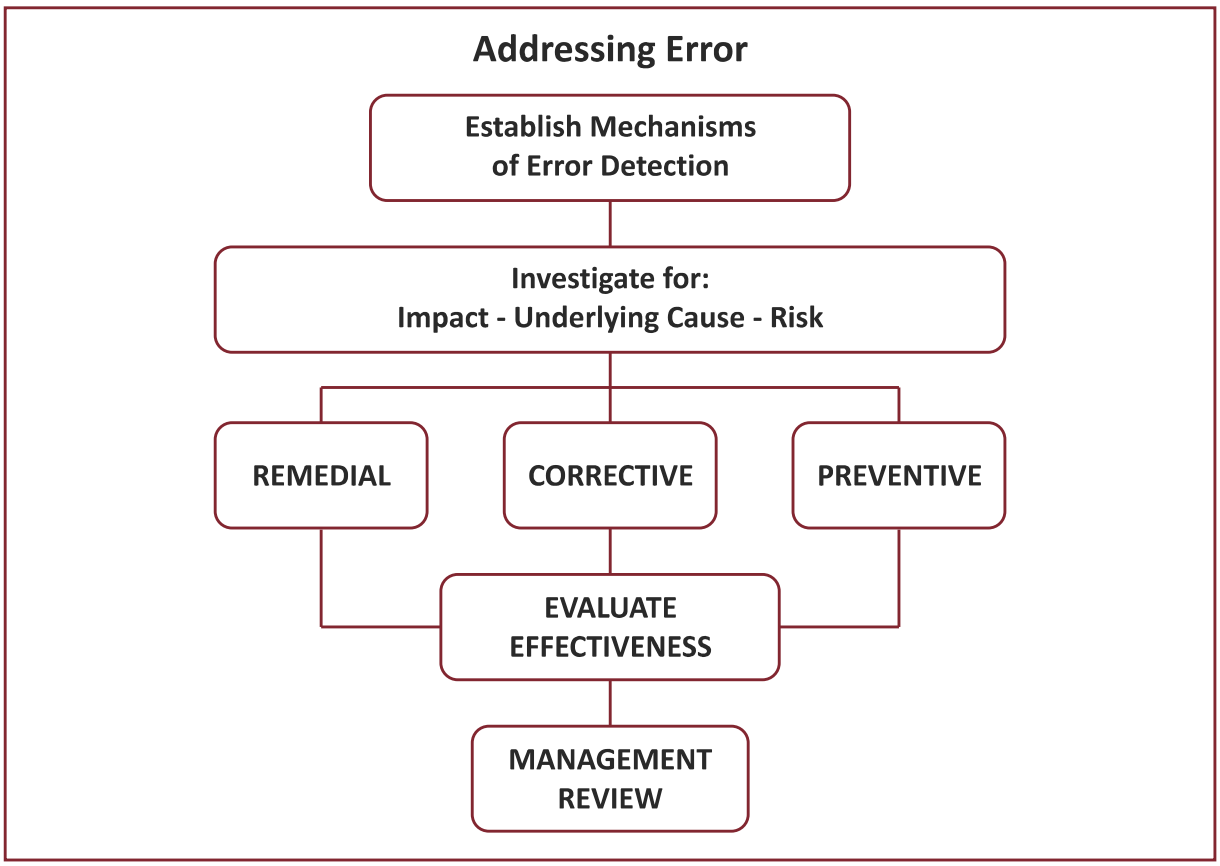
Identifying, investigating, and classifying occurrences in the implementation of the QMS leads to rapid identification of:

- The lack of a documented process, procedure, or instructions
- Documented processes or procedures not being followed; and
- Which QSE or work operations process (es) is/are causing the most problems?

Figure 8.4: Summary of NCE management



Resolution of Complaints & Feedback Management

Since the laboratory is a service organization, it is necessary that customers of the laboratory receive what they need. In HIV testing, customers include the healthcare providers who order the tests, the patients/clients who will eventually receive care based on the test results, caregivers, staff and other healthcare bodies. Methods to evaluate how well the testing site is serving the needs of its customers should be put in place to measure and assure quality of service, satisfaction, and fulfillment of program goals. These methods are address and resolve complaints, suggestions and feedback.

Customer complaints, suggestions and active feedback offer good opportunities for improvement. This way the laboratory will be able to know their shortcomings and the expectations of the customer. Complaints are negative comments about the organization's activities or service, received from the users of laboratory services, while feedback is actively

sought from the service users and customers on a periodic basis and may be adverse or satisfactory. Policies and procedures should be established for responding to customer suggestions and complaints or other feedback received. Complaints may be lodged by various means such as in writing, electronically through e-mail, by telephone, and in person. It is important to have a complaint/ suggestion register/box provided at the reception of the laboratory so that clients can have the opportunity to document the complaints as and when they visit the laboratory. Any suggestions and or complaints during telephonic conversation with the clinicians and the clients should also be noted down.

There should be periodic generation of feedback from the users of laboratory services including patients, clinicians and staff. Feedback from external customers such as referring laboratories or other healthcare services must also be sought. A feedback form can be generated with all the critical steps which form the three phases of the quality system.

A procedure for receiving, reviewing, classifying, investigating, analyzing and reporting complaints, feedback or adverse incidents must be in place. Records of these complaints, feedback and of investigations leading to corrective action with timelines and subsequent review by management must be maintained for the prescribed time period as per guidelines.

Audits / Assessments

Assessment of quality or quality audit is integral to achieving it. It is the means to determine the effectiveness of the quality management system. Assessment/Audit is a tool for examining the performance of a laboratory and comparing it to standards, benchmarks or the performance of other laboratories. Audits/ Assessment may be internal (performed within the laboratory using its own staff) or it may be external, conducted by a group or agency outside the laboratory such as accreditation by NABL. International standard ISO 15189:2012 Medical laboratories—requirements for quality and competence and the NABL document 112 are an important part of the audit/assessment process, serving as benchmarks for the laboratory.

Internal audit

The laboratory's monitoring of the QM program must include an internal auditing program. Internal audits involve an individual or a group of laboratory personnel performing a self-assessment comprising of a comprehensive comparison of the actual practices within the laboratory against the laboratory's QMS policies and procedures both management and technical e.g. personnel files, training documentation, QC performance, review of SOPs. These audits may also compare the laboratory's practices against a standard set of guidelines or standards. All findings, both compliance and noncompliance, or deficiencies that result from the internal audit should be documented in an organized format to allow for appropriate corrective actions and follow-up through resolutions.

Chapter 8

An internal audit is a valuable management tool which allows the laboratory to evaluate its own processes to assess level of conformance to requirements, to correct any deviations and thus assure on-going improvement of their quality system. When the actual practices followed in the laboratory or the findings are in concordance with the laboratory's policies or the standard guidelines then it is called conformity and if there is any deviation then it is termed as Non-Conformity (NC - The non-fulfillment of specified requirements). Non-Conformity can be related to the quality system, related to technical activities, failure to do something required and/or difference between work practices and documented instructions.

Requirements for Internal Auditing:

Internal audits should be conducted at intervals defined in the QMS (minimum once a year) to verify that operations continue to comply with the quality management system, both managerial and technical. The process and procedures for internal audits are to be defined and documented. Each of the main elements in the quality management system should be included. The internal audit should be scheduled well in advance and made known to all the staff in the laboratory (Table 8.1).

- Personnel should not audit their own work. The laboratory nominates a competent person, or persons independent of the area being audited, to be responsible for conducting audits; The auditor should have basic qualification as defined in the laboratory policy , training from recognized sources and knowledge of the QMS (quality manual, laboratory procedures and other documents)
- The audits should be carried out as per the designed agenda and time schedule for the specified scope. A checklist is helpful while carrying out an audit. The audit must begin with an opening meeting. The purpose of this meeting is to review the audit process and schedule, clarify all details, and establish a tone of cooperation and open dialogue. The primary focus of the audit is to look for intent (has it been said?), implementation (has it been done?), and effectiveness (can it be proven?). A review of previous audit results is also undertaken. The audit closes with a formal summation meeting, and a report summarizing the findings with details of sample ID, equipment, location, specific record reviewed, as prepared by the audit team.
- Analysis of internal audit findings are to be presented at management review meeting
- When deficiencies and opportunities for improvement are noted from the internal audit, the laboratory undertakes appropriate corrective and/or preventive actions, which are documented and carried out within an agreed time.
- Follow-up, monitoring activities to verify and record the implementation and effectiveness of the corrective action taken.
- A complete record of the audit must be retained. Records should include audit plan and agenda, records of the opening and closing meetings, audit report that includes the names of the auditors, the date of the audit, the scope of the audit and each of the non-

conformances identified, corrective and preventive action report that includes an assessment of the root cause(s), the corrective action(s) required and appropriate time frames for completion, and the responsible person for carrying out the action, audit follow-up report that includes evidence of review by laboratory management, evidence of verification of the effectiveness of corrective actions taken, auditor competence and performance evaluation.

- The audit is considered to be complete only when corrective actions have been taken and auditor has verified them.

Table 8.1: Outlines the four phases of the audit cycle.

Phase of internal Audit	Steps
Phase 1 : Planning and Preparation	▸ Develop and document processes and procedures or review current ones ▸ The compilation of an audit/agenda/plan ▸ The development of an effective checklist ▸ Selection of auditors ,independent to the area being assessed
Phase 2: Conduct of audit	▸ Hold an opening meeting ▸ Conduct the audit ▸ A review of previous audit records ▸ Hold a closing meeting
Phase 3: Recording and reporting the audit findings	▸ Audit plan and agenda ▸ Records of the opening and closing meetings ▸ Audit report ▸ CAPA report that includes an assessment of the RCA, the corrective action(s) required , appropriate time frames for completion, and the responsible person for carrying out the action ▸ Audit follow-up report that includes evidence of review by laboratory management, evidence of verification of the effectiveness of corrective actions taken
Phase 4: Follow up and confirmation of the corrective action	▸ Document and address NCs ▸ Take corrective and preventive measures for each NC ▸ Validate the effectiveness of actions taken ▸ Maintenance of records ▸ Retain a complete record of the audit even if no NCs are found during the audit

It may be necessary for laboratories to carry out additional unscheduled audits whenever there is reason to doubt the effectiveness of the management system. For example, when a non-conforming testing work has been detected or the laboratory has received a complaint which raises a doubt on the tests results. The additional audit may then be confined to only that area where the non-conformity has been detected or the complaint has been received. The procedure followed is similar to that of the full audit.

Management Review:

A management review is an official meeting of key members of senior management to review the status, effectiveness, and potential improvements of the QMS. It provides a platform for management to evaluate and analyze practices, for the purpose of improvement. Following the meeting, a list of action plans for improvement is created.

There should be a documented process outlining how the laboratory will conduct its management review including participants, schedule, frequency (at least once annually), inputs/agenda with action items to be addressed, follow up monitoring, output and records of MRM, communication of outcomes to staff. All action items must be described with defined responsibilities and timelines.

The personnel empowered with taking policy decisions and allocation of resources for the laboratory should participate in management reviews. The participants may include head of the institute, head of the laboratory, technical management, the quality manager and the section heads. The quality manager or laboratory in charge should be responsible for ensuring that all reviews are conducted in a systematic manner according to the established procedure, and that the management review is thoroughly minuted. Responsibility should be allocated for ensuring that any action identified during the review is implemented within the agreed time limit.

Review input :

a. Follow-up of previous management reviews and status of the previous management review action items;
b. Reports from managerial and supervisory personnel;
c. The outcome of recent internal audits, external audits and status of corrective actions taken and required preventive action;
d. The outcome of EQAS, proficiency testing, and other forms of inter laboratory comparison;
e. Any changes in the volume and type of work undertaken;
f. Feedback, including complaints and other relevant factors, from clinicians, patients, laboratory personnel and other parties;
g. Review of quality indicators for monitoring the laboratory's contribution to patient care; such as turn-around times, specimen rejection rates and customer satisfaction;
h. Review of non-conformities, including the status of corrective actions taken;

i. Evaluation of suppliers.
j. Review of training requirements.
k. To review the adequacy and suitability of the quality assurance system for current and future operations.

Review activities:
The management team must analyze all information to determine if the objective has been realized, action has been adequate or if further improvement can be achieved. When need for further improvement has been identified an action plan must be designed, documented, implemented and adhered to. The action plan must adequately identify the issue/s to be resolved, assign key responsibility for follow-up, indicate timelines for completion and define a mechanism to evaluate its effectiveness, i.e., mini audits. Timelines should be adequately assigned according to the urgency of the issue being addressed, i.e., any patient safety issues must be addressed and contained immediately.

Review output:
All management reviews should be documented. Records of the management review should include but not be limited to the agenda; minutes with attached files of information provided, and action plans with delegated responsibility and defined timelines with any supporting documents attached. Compilation of follow-up information will need to be adequately completed and documented to ensure a smooth and productive presentation at subsequent management review meetings. . Reports of management review should be retained for the prescribed time period as per guidelines.

Findings and the actions that arise from quality system audits and management reviews must be summarized, and laboratory staff informed of these findings and the decisions made as a result of the review. This is done so that they can realize the contribution their data collection is making to the betterment of the laboratory.

Management reviews thus allow the laboratory to utilize current data being collected to discover what is working; uncover problems; identify risks; plan for the future, and; determine resource requirements.

The benefits of CQI are that staff are more process focused and think globally, there is increased accountability with clear definitions of responsibilities, improved training leading to customer and employee satisfaction and finally development of a team attitude.

Key points

The useful tools / techniques for CQI are

- Quality Indicators
- Occurrence Management
- Customer Satisfaction
- Audits/ Assessments both internal and external
- Management Review

The following steps are important when adverse incidents, errors, and problems occur:

- Identification of potential sources of any system weakness or error
- Investigation of the error or problem to determine its cause and development of a plan to implement improvement;
- Take action to address the cause of the problem. Corrective actions may result in changes in policy or procedures to help ensure that the error will not recur.
- Communication with all those affected by the error or problem, for example, the staff, physician, nurses and/or client.
- Keeping a record of all circumstances related to the error or problem, including corrective action taken and any communications with affected persons.
- Reviewing the effectiveness of the action through the process of focused review and audit and if necessary adjusting the action plan and modification of the QMS.

Laboratory Information Management System

Results and information are the products of a medical laboratory. Laboratory Information Management System (LIMS) provides guidance for managing the information generated and entered into a paper-based or electronic record keeping system and disseminated to the users of laboratory services. It offers a set of key features that support and smoothen the functioning of a laboratory including issuing of test reports and operation of the quality management system. LIMS is used for the collection, processing, recording, reporting, storage and retrieval of examination data and information.

Some important elements to consider when planning and developing the key elements of LIMS are

- Standardised test request forms
- Unique identifiers for patients (PID) and specimen (Unique lab sample accession ID number)
- Logs, registers or worksheets that capture all required results from performing the process or procedure
- Checking/Verification processes to ensure accuracy of manual data entry, data recording and transmission including date and time
- Protection against loss of data
- Maintenance of confidentiality of protected patient information
- Effective and timely reporting systems and communication
- Storage space and conditions to ensure the continuing integrity of all data and information (records) that affect the quality of examination results
- Contingency plans to maintain services in the event of failure or downtime in information systems that affects the laboratory's ability to provide service

Information systems can be damaged or tampered with in a variety of ways; therefore it is important to establish policies and procedures to identify which staff member/s are authorized to access and use the data and information; protect from unauthorized access; protect data integrity and safeguard against tampering, loss or change of data.

In order to establish a computerized LIMS in a hospital/ laboratory the requirements are:

- A protected and well maintained location to keep the computers and other equipment with uninterrupted power supply is needed. The computer system must be secured.
- All the software and hardware should be appropriately validated and be demonstrably fit for purpose and verified for functioning by the laboratory before introduction.
- Appropriate training should be given to the laboratory personnel. A complete computer procedure manual, which may be electronic, should also be readily available to all authorized computer users.
- Each user account is protected by security mechanisms such as a user id and a password. The access to the data can be also restricted to different category of staff for example; a

laboratory manager might have full access to all of a LIMS functions and data, whereas technicians might have access only to data and functionality needed for their individual work-tasks. Strict policies should be established for authorizing use of the computer system. Policies should define those authorized to access patient data and those authorized to enter patient results, change results, change billing or alter computer programs.

- Data entered into the computer system either manually or by automated methods should be checked for correctness of the input data before final acceptance and report generation by the computer. All data alterations must be traceable to the person carrying them out. Stored patient result data should be easily and readily retrievable within a time frame consistent with patient-care needs.
- There should be written procedures for actions necessary to protect the data or computer equipment or both in case of fire/flood or hardware/software failure. Efficient back-up should be in place to prevent loss of patient result data in case of hardware or software failure.

A simple computerized LIMS works as follows in a hospital system: Once the test is ordered electronically the specimen is collected with a barcode given and sent to the lab for processing. On receipt of the specimen in the testing lab, either manual or automated lab work can begin. Many tests are nowadays performed by automated analyzers. Most LIMS systems can be configured to download the specimen data to an analyzer either after the order is placed or when a specimen is received in a testing lab. When the specimen's barcode is read by the instrument, the unique ID from the specimen label is matched with the order previously downloaded to the instrument. When results of lab tests are available, they are entered into the system manually or automatically, downloaded from the analyzer to the LIMS and the report is generated after verification by the authorized signatory.

Strategic Information Management System (SIMS)

To make certain robust reporting and monitoring, Strategic Information Management System (SIMS), a web-based integrated monitoring and evaluation system has been developed and rolled out by NACO. The roll-out of SIMS is on-going and will be established nationwide at all levels including over 15,000 reporting units, to collect, analyze and use the program data for planning, implementation, monitoring and measuring of programmatic impacts. Simple analytical tools will be developed to assist in day-to-day requirements of decision making. Relevant, measurable and verifiable indicators will be identified and used appropriately.

This system will enable individual level data collection for key program areas (e.g., ICTC, ART, Laboratory services) and has built-in real-time analytic, triangulation and data validation capabilities. The elements of laboratory related information are:

- Input Formats
- Output Reports

Figure 9.1: Strategic Information Management System

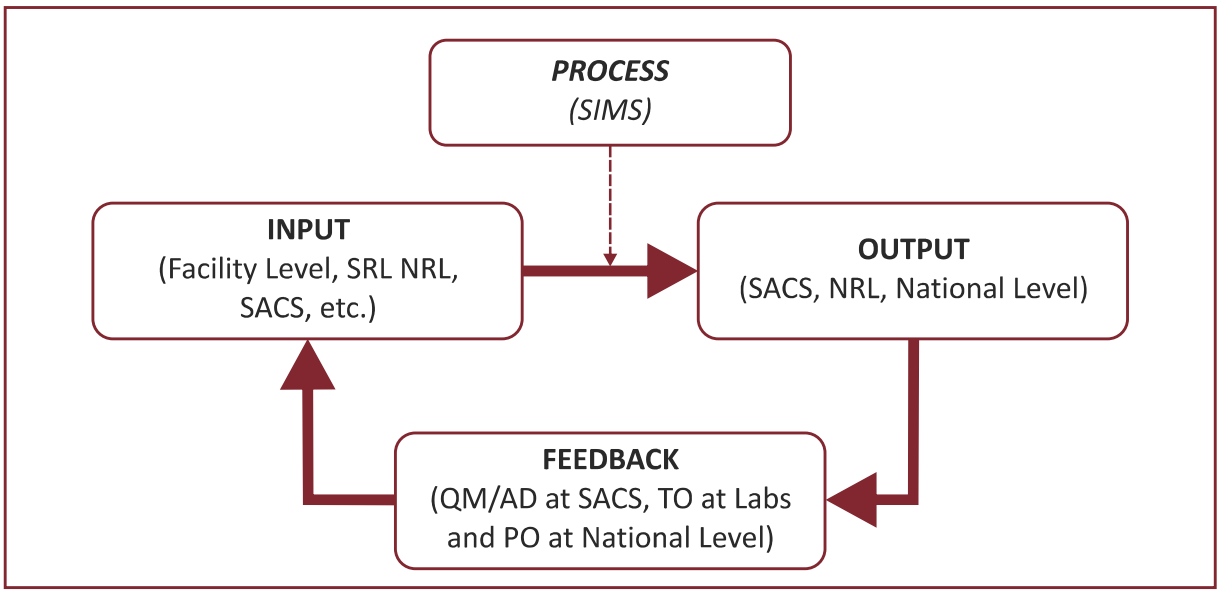


Table 9.1: Input Formats to report data at individual facility level:

S No.	Name of Format	Institution responsible	Person responsible
1	SRL SIMS Format	SRL	TO/LT
2	NRL SIMS Format	NRL	TO/LT
3	SACS SIMS Format	SACS	Quality Manager
4	HIV 2 SIMS Format	HIV 2 Lab	TO/LT
5	EID testing laboratory	EID Lab	TO/LT
6	CD4 SIMS Format	CD4 Lab	LT
7	HIV VL SIMS Format	HIV VL Lab	LT
8	EID designated ICTC Format	EID designated ICTC	LT
9	EID designated ART Centre Format	EID designated ART Centre	LT

Output Reports: Formats to consolidate data reported by individual facilities and present it to DAC/SACS/NRLs at regular time intervals:

1. National SRL Report (NRL wise)- Monthly
2. National SRL report (NRL wise) – Quarterly
3. National SRL report NRL wise - Semi Annual

4. National SRL Report SACS wise – Monthly
5. National NRL Report
6. NRL EQAS Report
7. National HIV 2 Lab Report – Monthly
8. National HIV 2 Consumption Lab Report Monthly
9. National HIV Viral Load Testing Labs Report – Monthly
10. National EID DNA PCR Test Report –Monthly
11. National EID DNA PCR Stock report – Monthly
12. National EID DBS Collection Kits Consumption Report
13. National EID Whole Blood Collection Kits Consumption Report
14. National CD4 Lab Report – Monthly
15. National CD4 Stock Report - Monthly

Additionally some analytical reports will also be generated through SIMS.

With the implementation of SIMS application, efficiency of computerized M&E system and quality of program data is improving since there are fewer opportunities for manual errors and more accountability and responsibility to reviewing units in the hierarchy. Data gets reported in a timely manner, and data accuracy and reliability is significantly enhanced.

SIMS provides tools for better decision making through data triangulation from different sources and thereby facilitates ease of evaluation and monitoring for the following purposes:

- To provide feedback to take corrective action from time to time
- To have internal and external accountability of the resources used and the results obtained
- To learn from experiences to improve practices and activities in the future
- The effective utilisation of all available information for evidence-based planning and implementation

Key points

- LIMS provides direction for managing data and information contained in both computerized or non-computerized systems
- It assists with functions of test request, unique number generation, sample delivery, worksheet generation, order information transmission to analysers, translation of instrument output into usable results, storage of data and report generation.
- Implementation of LIMS requires certain standards like secure location of the equipment, training of the staff, traceability to the person who handled the data and archival of the data at a later period.
- SIMS is a web-based integrated monitoring and evaluation system rolled out by the Department of AIDS Control (DAC). The objective is to collect, analyze and use program data for planning, implementation, monitoring and measuring of programmatic impacts.

Troubleshooting

Troubleshooting is a form of problem solving, often applied to repair failed processes and procedures. It is a logical, systematic search for the source of an error so that it can be solved, and so that the process can be made operational again. Errors can be classified into three main categories namely technical, systematic and random errors (Figure 10.1).

Technical Errors: Technical errors occur as a result of human error that range from poor education/ technique, to carelessness or failing to follow recommended guidelines that are designed to prevent errors. These errors usually can be detected when a different technologist performs the same test and gets different results or by evaluation using quality assessment programs/proficiency testing.

Systematic Errors: Systematic errors usually are due to a problem with certain aspect of testing process. Variations with instruments due to poor maintenance or malfunction often manifest by subtle changes that may not be readily apparent until catastrophic failure occurs. Pipetting errors may be technical because of carelessness or improper training of personnel but may also be systematic as a result of slow changes in a pipette's calibration leading to inaccurate volume delivery. Systematic errors usually occur regardless of the technologist performing the test. Without having a proper QA and QC measures, trends may not be identified and systematic errors may go unnoticed.

Random Errors: Random errors occur periodically for unknown reasons but may also be caused by inconsistent technical or systematic errors. An example of random error is if one well of a microtitre plate was defective, thereby producing one random error. Repeat testing by the same technologist using the same test and equipment resolve most of the random errors. However, the cause of most random errors cannot be determined and are thus difficult to prevent. Though the random errors cannot be excluded, the technical and systematic errors can be minimized thorough a properly functioning QMS.

Figure 10.1: Why do laboratory errors occur

Troubleshooting

Troubleshooting refers to the measures used to determine why an error has occurred and to provide guidance for resolving those errors. Some of the common errors, which have been categorized, based on their origin, and their resolution method(s) are given in Table 10.1 below:

Table10.1: Common errors and their troubleshooting techniques

Specimen-related Errors	
Error	**Resolution**
Insufficient volume	Collect the appropriate volume depending upon the objective of testing
Hemolysed/ lipaemic sample	Collect the sample again. In case this is not possible, record "sample hemolysed/ lipaemic" in the result.
Improper storage leading to microbial contamination	Refrigerate the sample for short storage (one week), in case of long storage, keep at -20°C or below
Repeated freeze/ thaw cycles may alter the results of borderline positive samples	Avoid repeat freeze/ thaw cycles as far as possible by aliquoting
Labeling errors	Follow a uniform method of labeling of the samples including aliquots thereof and organize in the racks systematically.

Specimen-related Errors	
Error	**Resolution**
Logging in specimen (mixing of the names/ accession numbers)	Record the details of the client and give the unique identifier to the sample in a uniform way Transcribe the result from the print out sheet to the worksheet carefully. Resolve by repeating the test. Supervision by a second person can minimize the errors. Each staff member's clerical skills should be reviewed periodically and improved if necessary
Transcription of results from print out to worksheet	
Transcription of results from the worksheet to report form	
Report sent to the wrong person or communicated without post-test counseling	Report the results to the correct person after verification only after post-test counseling while maintaining confidentiality.

Kit-dependent Errors	
Error	**Resolution**
Kit is defective (determined if one kit performs adequately whereas another from the same lot does not)	Review the test procedure and the kit specifications to ensure that the procedure is being followed correctly and that nothing else has changed (e.g. equipment) A different technologist should perform the test to be sure that the cause is not technologist-dependent. Another laboratory that uses the same lot number should be contacted to see whether the problem may be dependent on a particular lot of kits. In case a lot of kit is found to be performing sub optimally, the laboratory in charge is to perform a root cause analysis. A set of 20-25 known samples are to be tested on the kit in question and a detailed report with all kit details is communicated to the respective referral laboratory/ State AIDS Control Society. The manufacturer along with NACO and the licensing authorities are informed of further necessary action and if required after inquiry the batch is withdrawn and detailed enquiry at the central level will be initiated.
Mixing of reagents from different kits/ lot numbers	Reagents of each lot are titrated to work optimally as a kit. Therefore, do not mix reagents from different kits.
Damage of kit during shipment and storage leading to deterioration of one or more components.	Do not use contaminated/ deteriorated kits. While receiving a new lot of kits, always make sure that the temperature tracking device attached on the kit box is giving acceptable reading. Store at the optimal temperature and maintain cold chain during transport of kits.

Technologist-dependent Errors	
Error	**Resolution**
Dilution errors	Many kits contain instructions for dilutions, which are based on volumes required per plate (in case of ELISA and some rapid tests). Carefully make calculations and double check the same especially when different volumes are needed.
Carelessness during procedures like not adhering to the test protocol, incorrect pipetting techniques etc.	Retraining of the staff by: Internal teaching program like staff meetings Formal training program like attending workshops Participation in EQAS Competency evaluations like retesting of previous PT samples

Technologist-dependent Errors	
Error	**Resolution**
Improper dropper use (in some rapid tests, a dropper is used for adding reagents) Use and documentation of controls, Improper dropper use (in some rapid tests, a dropper is used for adding reagents)	A dropper should always be kept in the vertical position while adding reagents since the size of the drop is affected by the angle of the bore. Free falling drops should always be used to dispense reagents since allowing the drop to touch the surface when dispensing can lead to variations in actual volume dispensed Always use recommended droppers supplied with the kit and do not interchange droppers between two different kits.
Use and documentation of controls	Always use internal and external control with each run. Record the performance of internal, external and procedural in built (if applicable) controls in the worksheet before interpreting the results. **Internal Controls** If the internal controls fall out of range, consult the run rejection rules in the package insert (sometimes one internal control value is permitted to be rejected without rejecting the run) If controls are out of range, it could be due to technical error or systematic error. Exclude technical errors by having the run repeated by another technologist. If the same results are obtained, this indicates systematic error and all possibilities regarding the equipment and environmental conditions should be investigated. If all trouble shooting measures fail to identify the problem, the most likely reason is kit-dependent error (e.g. contamination of internal controls). **External Control** Detects slight changes in the kit and equipment/ environment performance. (e.g. preparation of Levey-Jennings chart in case of ELISA) Failure of external controls could be due to technical error, equipment and environmental causes and finally due to deterioration of external control/s itself.

Equipment-dependent Errors	
Error	**Resolution**
Pipetting error	Perform regular calibration of pipettes
Improper maintenance and calibration of equipment can be ascertained by use of external controls, which detect trends that suggest equipment variation	Equipment like ELISA readers, washers, refrigerators, deep freezers, incubators, autoclaves and hot air ovens should always be kept under preventive maintenance contract and should be regularly calibrated.

Environment-dependent Errors	
Error	**Resolution**
Most common cause of inaccuracies and imprecision is due to the poor ambient temperature control.	The ambient temperature of the laboratory should be controlled and regularly monitored.
Poor water quality, poor lighting, non-level surfaces and dusty conditions	A laboratory should be properly designed to address these issues.

Key points

The preparation of a flowchart helps determine the source of problems.
Some questions to consider while troubleshooting are:

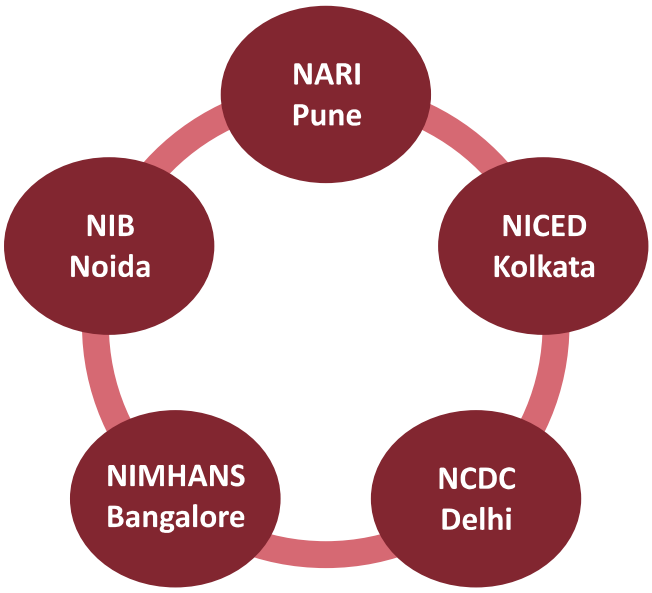
- Is the problem related to a poor sample? Has the sample been collected and stored properly.
- Are factors such as turbidity or coagulation affecting instrument performance?
- Is there a problem with the reagents? Have they been stored properly, and are they still in date? Have new lot numbers been introduced without updating instrument calibration?
- Is there a problem with the water or electrical supply?
- Is there a problem with the equipment?

Make one change at a time based on analysis. If equipment is the problem, review the manufacturer's instructions to verify that all procedures are being followed correctly.

HIV test kit evaluation

The evaluation of the quality of diagnostic kits for HIV and other Transfusion Transmitted Infections (TTIs) procured by NACO for the purpose of distribution in the country is of prime importance. Some of the NRLs provided services earlier for evaluation of these HIV test kits, but the system for assuring quality supply of kits had limitations. There were no uniform procedures followed by these institutes. Therefore, in 2010, a consortium of five NRLs under NACO (Figure 11.1) was formed for the purpose of evaluating the quality of diagnostic kits for TTIs. National AIDS Research Institute - NARI, Pune being an Apex Lab under the NACO, acts as the secretariat of the consortium of the National Reference Laboratories on Quality (NRLonQ).

Figure 11.1: The five member consortium of NRLonQ with NARI as the secretariat



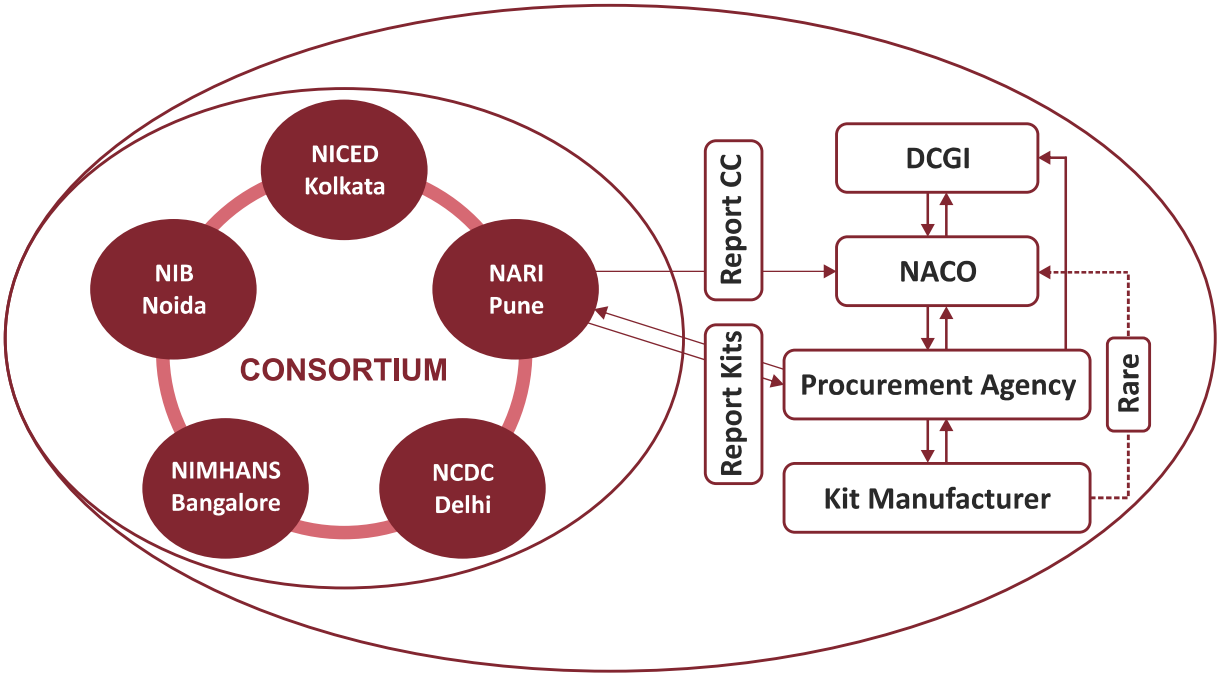
The consortium has developed a national system for assuring the quality of HIV, HBV and HCV ELISA and rapid test kits with uniform approaches and procedures for quality assurance, training and administration. The goal of the consortium is to assure procurement of quality test kits used in laboratory testing of HIV sero-diagnosis and TTIs for better implementation of National AIDS Control Program (NACP).

Process flow for the evaluation of HIV diagnostic kits

Processing the request for a kit evaluation: NARI accepts the requests for kit evaluation from procurement agencies, SACS or the manufacturer/s . NARI then takes a decision on which consortium member will perform the evaluation on the basis of rotation. Based on this decision the request is forwarded to the consortium member and the procurement agency /SACS/manufacturer directed to deliver the kits accordingly (Figure 11.2).

Upon receipt, the consortium member corroborates the documents given by manufacturer and verifies the condition of the kit as per the predetermined acceptance/rejection guidelines. The manufacturer is required to supply a minimum of 1000 tests for each batch of kits to be evaluated. This includes 500 tests for the evaluation and 500 tests for retention with the consortium member for re-testing in case of unsatisfactory performance of the kit in the field.

Figure 11.2: The process for evaluation of a diagnostic test kit



Panel Composition: The consortium has developed a fully characterized panel of positive and negative samples in-house, to be used for the evaluation of HIV, HBV and HCV diagnostic kits. The panel is built using blood bags from blood banks that are not suitable for the purpose of transfusion. These panels are characterized by FDA or CE approved kits based on a well-defined algorithm.

- The HIV kit evaluation panel comprises of 400 true negatives and 100 true HIV positives. The true negative samples are negative for HBsAg, antibodies to HIV and HCV. HIV true positives are reactive for only antibodies to HIV and negative for HBsAg, and anti-HCV. This sample size is adequate to achieve a confidence interval of 95%.
- In addition, interfering samples are included in the evaluation. Interfering samples include those from patients with parasitic infections such as malaria, kala azar and filaria, pulmonary tuberculosis, auto immune diseases such as systemic lupus erythematosis and rheumatoid arthritis and from multiple pregnancies.
- On special request from the manufacturer, sero-conversion panels may be included in the evaluation of the kit. These are commercially available panels and are provided by the manufacturer.

Kit Evaluation Process: The kits are evaluated using the characterized panel and by following the kit literature. The test results are verified independently by a second observer from the same laboratory. The use of quality equipment and good laboratory practices are ensured for quality results. The result obtained with the kit under evaluation using the characterized panel is reviewed and analyzed. Any discordance in results is resolved as per the predetermined guidelines.

Report Generation and Reporting: The reports are generated and dispatched within a maximum turnaround time of two weeks. The reports are signed by the lab in-charge of the respective institute and submitted to the procurement agency with a copy to NACO and the apex laboratory

.

The Consortium of the NRLs on Q, maintain quality standards in their activities in conformance with the requirements of ISO 15189:2012 and NABL accreditation. It serves as a center of excellence for test kit evaluation activities nationwide and is in the process of becoming an autonomous body.

Key points

- National system for assuring test kit quality for HIV testing is established since 2010
- An in house fully characterized panel of samples is used
- The process of request submission, report generation and reporting is standardized

Accreditation for HIV Tests

A laboratory which has a good QMS in place should strive for a formal recognition from an authoritative external body for quality management and technical competence to carry out specific tests based on third party assessment following an International Standard. This formal recognition is known as **accreditation**. The "National Accreditation Board for Testing and Calibration Laboratories (NABL)" is the authoritative body for according accreditation to the laboratories in India. NABL provides accreditation for medical laboratories in accordance with the international standard ISO 15189:2012 'Medical laboratories- Requirements for quality and competence'. NABL is internationally recognized as an accrediting body through Mutual Recognition Arrangement (MRA) through the regional cooperation body "Asia Pacific Laboratory Accreditation Cooperation (APLAC)" to the International Laboratory Accreditation Cooperation (ILAC)".

The international standard ISO 15189:2007 has undergone revision. **The third edition of the ISO 15189:2012 "Medical laboratories — Requirements for quality and competence" cancels and replaces the second edition (ISO 15189:2007)**. From October 2013 onwards NABL would accept applications to be submitted as per the new version of the standard ISO 15189:2012 and all laboratories are required to ensure compliance with the new edition by October 2015.

Benefits of accreditation

- National and international recognition
- Assurance to customers of accurate and reliable test results.
- Improves the credibility of the laboratory
- Provides global equivalence
- Provides comparability in measurements
- Decision makers can rely on test results
- Improves staff motivation
- Ensures better support in the event of legal challenges
- Saves money by getting it right the first time
- Public acceptance

NACO encourages the HIV testing laboratories under NACP to obtain NABL accreditation for the scope of tests performed in NACP and more. In this regard NACO undertakes periodic mentoring and monitoring of its laboratories to facilitate compliance with ISO 15189: 2012 and NABL specific criteria 112.

The ISO 15189:2012 consists of 15 clauses pertaining to management requirements and 10 clauses pertaining to technical requirements (table 12.1). These clauses need to be fulfilled for an effective laboratory QMS.

Table 12.1: Management and Technical QMS Requirements

Management Requirements	Technical Requirements
Organization and Management responsibility	Personnel
Quality Management System	Accommodation and environmental conditions
Document control	Laboratory equipment reagents and consumables
Service agreements	Pre-examination processes
Examination by referral laboratories	Examination processes
External services and supplies	Ensuring the quality of examination results
Advisory services	Post examination processes
Resolution of complaints	Reporting of results
Identification and control of non-conformities	Release of results
Corrective action	Laboratory information management
Preventive action	
Continual improvement	
Control of records	
Internal audit	
Management review	

Preparing for Accreditation

It is important for a laboratory to make a tangible plan for seeking accreditation and then designate, train a responsible person as quality manager to co-ordinate all activities related to accreditation. The tasks to be undertaken by the laboratory for this include

1. Obtain documents available on the NABL website (www.nabl-india.org) to aid the laboratory in preparing for the accreditation process and familiarize staff with all the relevant documents and then undertake a gap analysis
2. Train laboratory personnel on Quality Management System and Internal Audit as per ISO 15189:2012 and NABL 112 and other NABL documents. Procure a copy of the ISO 15189:2012 and enlist in the master document control log
3. Prepare Standard Operating Procedures for each investigation carried out in the laboratory.
4. Prepare a Quality Manual which is a policy document that is supplemented by a set of the next level documents which are the quality system procedures. Ensure that these documents are well prepared
5. Ensure maintenance of effective environmental conditions (temperature, humidity, storage placement) and maintain proper records of the same
6. Ensure calibration of instruments/equipment. If calibration is outsourced, ensure the same through accredited calibration laboratories. NABL document 500 lists the NABL accredited calibration laboratories in the country

7. Ascertain the status of the existing QMS and technical competence and perform a gap analysis
8. Ensure proper implementation of all aspects that have been documented in the Quality Manual and other documents
9. Document and review QC data
10. Participate in PT through an External Quality Assessment Schemes (EQAS). If this is not available for certain analytes, participate in inter-laboratory comparison through exchange of samples with NABL accredited laboratories
11. Perform, review and record corrective actions on QC / EQA outliers
12. All personnel (qualified and competent as per NABL-112) shall be instructed on the use and application of the quality manual and all referenced documents, and of the requirements for their implementation
13. Schedule, conduct and record internal audit followed by management review at least once in a year
14. The laboratory must define the tests for which it wishes to seek accreditation (scope of accreditation)
15. Apply to NABL in the prescribed application form along with appropriate fee (NABL 153)

Process of Application (Table 12.2):

The laboratory must apply to NABL in the prescribed application form (NABL 153) along with applicable application fees and the following documents:

1. Three copies of the application for Medical Testing Laboratories (Signed NABL 153) with 6 annexure each.
2. The duly filled and signed NABL-131 form-Terms and Conditions for maintaining NABL Accreditation
3. Two controlled copies of the Quality Manual
4. A document copy proving legal entity
5. A Demand Draft (amount as applicable) drawn in favour of NABL New Delhi
6. Copy of latest EQAS Report, internal audit report, NC generated with corrective actions and minutes of management review meeting
7. Provide names and signatures of authorised signatories responsible for authenticity and issue of test reports in the prescribed form 71

The NABL secretariat on receipt of laboratory's application, after scrutiny for its completeness in all respects, will issue an acknowledgement and a unique customer registration number to the laboratory. NABL secretariat may seek additional information/clarification (s) from the laboratory, if necessary.

NABL will appoint a lead assessor to study in detail, the information provided by the laboratory in its application and verify the compliance of laboratory's Quality Manual in accordance with ISO 15189: 2012 and NABL Specific Criteria 112. The Lead Assessor sends the "Adequacy