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REVIEW ARTICLE

Quality Management System in the Microbiology Laboratory…Step by Step Approach

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ABSTRACT

Quality management system implementation in clinical laboratories is becoming mandatory. A reasonable easy to practice approach is a key element for success. Clinical and Laboratory Standards Institute (CLSI) QMS01-A4 has provided a detailed practical approach that focuses on twelve main items; named quality essentials. Incorporating these essentials in daily practice in the microbiology laboratory mandates creating an environment that practices 'quality' by default. This review provides a step-by-step approach to facilitate the implementation of the twelve essentials of the CLSI QMS while keeping an eye on the ISO 15189 requirements. The twelve quality essentials delineated namely are: Organization, Customer focus, Facilities and Safety Management, Personnel Management, Purchasing and Inventory Management, Equipment, Process Management, Documents and Records, Information Management, Nonconforming events Management, Assessments and Continual Improvement. These essentials are designed to cover the whole testing process. Whenever applicable, real-life examples from the daily practice are added to make the picture clearer.

INTRODUCTION

The healthcare system counts upon the clinical laboratory and reports it generates in making clinical decisions that impact patients and their lives. Increased awareness of the potential adverse effects of laboratory errors on patient outcomes together with the eagerness for continual improvement of laboratory services have added challenges to the medical laboratories and their staff[1]. The ongoing era of standardization and accreditation from national and international organizations has created the motive to follow stringent quality measures in the laboratories.

Quality in medical laboratories can be defined according to WHO as generating accurate, reliable, and timeliness reports while quality management system (QMS) encompasses description of an approach to reach these objectives[2,3].

Clinical microbiology laboratories and their role in diagnosis of infectious agents that represent a threat to the whole globe owing to the records of related morbidity and mortality, are not away from this system. The antimicrobial resistance crisis has underscored the role microbiologists play to combat the deadly bugs throughout their daily activities. Not surprisingly, microbiology laboratories particularly are less docile to follow stringent quality control programs owing to workflow nature. This starts from the difficulty to automate, the dependance upon the expertise of the human factor in every single step and does not end by the art of reporting the results that require to be tailored case by case[4].

QMS for medical laboratories including microbiology laboratories have been described in many international standards; among which Clinical and Laboratory Standards Institute (CLSI) QMS01-A4[3] and International Organization for Standardization (ISO) 15189[5].

QMS at a glance

QMS can be defined as integrated group of activities applied to control the work from preanalytical till reaching postanalytical stages, handle resources, perform evaluations, adopt the ideology of continuous improvement to ensure the quality of reports released from the laboratory. The Clinical microbiology laboratories perform quality control (QC), which is the first level of controlling a procedure. The next step is applying quality assurance (QA), where QCs and quality indicators (QI) are monitored, and results are analyzed. QA is a detailed process that digs deeply in all details related as monitoring supplies, equipment calibration, personnel competency, proficiency testing (PT), as well as all steps related to the laboratory testing starting from specimen collection till releasing timely reports. QMS integrates all the quality elements into the work process and defines deviations from the expected performance as nonconforming events (NCEs) that should be reviewed and resolved while taking corrective actions to prevent recurrence[6].

CLSI Quality Essentials

As per CLSI, QMS is composed of 12 quality essentials that represent a road map to construct the laboratory workflow and operate under sound quality umbrella (3). These essentials are:

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

1. Organization

Management should be supporting establishing the QMS. Success in implementation will be ruled by commitment to provide all system logistics. In addition, support is required to establish a quality manual that comprises quality objectives, policies, procedures, standards, and regulations followed by imposing culture change among all laboratorians to adopt behaviors coinciding with these items. Clear definition for quality objectives for the laboratory should be present. Communications and regular meetings with all stakeholders are mandatory for system implementation. To ensure both transparency and coordination, the documentation of meeting minutes in any form, whether electronic or in paper form. [6].

The laboratory director is fully responsible for such elements. However, he has the right to practice delegation of responsibilities for certain specialty areas. A quality manager whose job is ensuring correct implementation of the system should always exist. Like infection control, quality is the role of everyone in the laboratory. The organization hierarchy should always be clear and available for all employees with a well-defined job description for everyone in the laboratory.

While chemist's and technician's jobs should always be clear, the doctors will be directly responsible for doing sophisticated work that requires their talent and experience. The whole team should perform their job in line with quality objectives and it is now the microbiology laboratory manager's job to ensure that the team is knowledgeable about the essential related quality items linked to the job they perform. Similarly, the latter would be allied to edit and approve procedures required, review documents, and determine turnaround time (TAT) for reporting results with special concentration on tests deemed critical like blood cultures, CSF examination and acid- fast bacilli smear examination. Reviewing the whole process is an integral part of the manager's job to allow for corrections and improvement all the time[6].

A review committee with higher level leadership may exist in certain institutions and in such conditions rules for data filtration should apply to ensure optimization of functions of such committees. As an example, a wrong result released due to faulty interpretation of an antibiotic disc when discussed from the technical aspect would require too many details; including the product name, its lot number, the vendor, revision of the storage conditions of the discs, competencies of the personnel involved in the process of reading & reporting of the results and even other details. However, on higher administration levels data reporting would be summarized to convey the incidence and its impact. Corrective actions would be taken as changing the supplier or revising technical competencies of the personnel or whatever according to the detailed investigation of the incident.

Similarly, highlighting spots of innovation and improvement need be addressed in the same maneuver. In return, the higher leadership's support to complement these reviews would need recording, implementation, follow- up and staff orientation to ensure enhancement and improvement. As seen, the process resembles a cycle rather than a stepladder approach.

In ISO 15189 this item is discussed under three standards: organization & management responsibility, quality management system and management review[5,6].

2. Customer focus

Customer focus represents an integral element of any quality program. Microbiologists offer services related to diagnosis of microbial illnesses, antibiotic sensitivity, antibiogram reporting, biosafety and biosecurity issues. The microbiology laboratory is responsible for applying a laboratory system with its three main basics; preanalytical, analytical and postanalytical processes. Effective communication with patients and healthcare providers would resolve too much trouble and provide information essential for results reporting. As with all elements , the way and time of communication should be clearly explained to all stakeholders and documented[6].

Communication must always be regarded as a multi-directional process where patients, pharmacists, infection preventionists, clinicians and antimicrobial stewardship committees should know how and when to ask to communicate. A notification system for communicating critical results should exist and be implemented.

Communication will always be very important when a modification of a laboratory methodology has been applied or a new test has been introduced, an alarming pathogen is circulating in a particular zone or hospital[6].

Failure of establishment of successful communication system can result in not only affection of the patients' health and safety but also may be directly related to declines in the laboratory revenues.

While many laboratories have introduced PCR technology to determine specific genes of resistance prevalent among bacteria especially Gram-negative bacteria, only few will adopt a reporting system that adds a commentary paragraph explaining the findings in

terms of definition made palatable to clinician. Questions will keep circulating about the significance of detection of CTX-M gene or the difference between NDM and KPC carbapenemases. Mainly through communication, such issues could be handled.

This QMS essential is discussed in ISO 15189 under the title of advisory services[5,6].

3. Facilities and safety Management

The laboratory design should support space dedication for all activities including sample collection, testing sites, equipment, staff resting zones and others. Design should ensure safety for both staff and visitors. Safety should be a crucial part of a sound QMS. An authority matrix should exist to define access control for different laboratory areas. Control in restricted areas where microbiological testing is done should comply with requirements of biosafety level-2 laboratories (BSL-2)[6]. Areas where mycobacteria cultures are performed should be escalated to BSL-3 practices; especially properly designed ventilation system and appropriate class of biological safety cabinet (BSC), namely Class IIA2 BSC with strict adherence to proper utilization of N-95 respirators[7]. Similarly, construction of areas for molecular testing should include demarcation between areas for extraction and amplification steps[8]. Signs and posters describing biohazardous areas, personal protective equipment (PPE) and contact data of assigned persons in cases of emergency should be present. All work spaces including storage areas should have a designation that prevents cross-contamination[6].

Benchtop surfaces in laboratories are very eligible to carry risks of transmission of infection to staff and thus being of non-porous material readily disinfected is very important.

Since microbiologists spend long hours in examination of films, culture plates and writing reports, avoiding musculoskeletal stress is inevitable unless considered in the design and education about the correct way of sitting through posters and on- job training. In addition, sinks dedicated for hand hygiene and sinks designed for kits preparation or biological fluids spilling should be sharply demarcated and located. Even other environmental conditions that may affect the quality of the results as noise, dust and electrical supply including emergency back-ups for precious devices as thermal cyclers or automated systems, must be considered in the design. Ventilation systems with paying interest in temperature and humidity should be rigorously monitored as they affect workers abilities and concentration and impacts efficiency & durability of instruments as BSCs and incubators in the laboratory[6].

In addition, safety programs should typically cover all safety issues including biosafety, biosecurity, chemical hygiene, radiation, first-aid training, and infectious waste handling. To ensure compliance, physical training, on-job training and competency assessment should be applied for all staff including secretary, office boys and workers handling wastes and any other employees[9,10].

Safety supplies vary according to the biosafety level of the laboratory. Microbiology laboratories' requirements performing sampling and providing lab-to-lab services will be handled in a different way from labs performing TB cultures. Spill kits and spill drills should always be available in all laboratories. Finally, occupational health safety office providing services like conduction of risk assessment tools for risk mitigation of laboratory acquired infections and offering vaccination programs as HBV vaccine to staff should be acknowledged in any safety program[6].

This QMS is included in item entitled facilities and environmental conditions in ISO 15189[5,6]. However, specific safety standards are discussed in ISO 15190 document[14].

4. Personnel Management

In microbiology laboratories, no matter the level of automation present, microbiologists will always be the maestros that guide the symphony of testing till reaching the reporting stage. Interpretation of cultures, linking direct examination films with culture findings and selective reporting of antimicrobials guided by clinical condition of cases will always mandate the opinion of the human microbiologist.

Hiring tasks, orienting, and training the staff are essential for obtaining the best results. Job descriptions, hiring prerequisites qualifications and licensures of staff is the main drive to success and is especially important to show compliance with governmental laws.

The process usually starts by giving information to the new staff members about the laboratory policies as safety issues, ethics, number of shifts and working hours and vacation. Similarly, training of the new staff to provide them with capabilities and knowledge required for their jobs should be done[6].

Training should also comprise detailed information about troubleshooting, complaints forms and the degree of reporting to avoid conflicts.

Meanwhile, training and competency assessment of the old staff should always be figured out in any comprehensive training program to accomplish the laboratory aspiration[6].

Direct observation of the training programs outcomes should be under the supervision of senior staff and laboratory manager or his designee. The complexity of the job to be performed must be reflected in the level of assessment and who does this assessment. As an example, the process of plating out samples will not need as comprehensive monitoring as reading of a sensitivity plate. The technical expertise required for preparation of culture media will require close monitoring if compared to the process of receiving kits and reagents.

Similar to all activities done documentation and reviewing as well as evaluation is required. Evaluations should be transparent and unambiguous and most importantly measurable to apply continuous enhancement to the process. Determination of time needed for initial evaluation, schedules for on-the-job training &monitoring, and frequency of assessment should be done and should comply with the accreditation requirements of local or international agencies[6].

While the training department is usually responsible for conduction and evaluation of the training, creating a fruitful working environment will be a collaborative outcome of all the staff. Open discussions and insights from the staff should be inspired. On the managerial level, every single effort to provide opportunities for staff enhancement should be made[6].

Success and revenue maintenance in this ever-changing field will require efficient indulgence in attending continuous education programs, participation in scientific events and updating documents used in daily work like CLSI M100 with its annual updates on antibiotics testing and breakpoints determination.

Successful organizations are in a part, those that maintain high stability of retention and low turnover among workers thus keeping and preserving experienced talented staff[6].

This QMS is discussed similarly under the title Personnel in ISO 15189[5,6].

5. Purchasing and Inventory Management

Purchasing of high-quality supplies and services represent the cornerstone of the laboratory work and the main drive for correct reporting. This section will briefly discuss the essentials of purchasing supplies and services required by the microbiology laboratory.

a) Supplies and Inventory:

The general specifications of materials whether reagents or supplies required for testing should be detailed. The collaboration between the microbiology laboratory manager, the supply chain, and the quality department should lead to accomplishment of the task of keeping supply of quality approved supplies and alternatives when shortage occurs.

Purchasing supplies is a multi-step process that includes the **pre-purchase process**, in which determination of the requirements is done after revising records for NCEs, vendors former performance, results of QCs, results of proficiency testing (PT) and other factors to ensure convenience and quality of reports[6]. For example, vials of antibiotic discs non-compatible with disc dispensers will not suit laboratories which perform large number of antibiotic sensitivity tests manually. Similarly, shelf-life of kits and reagents required for non-common requested tests should be considered when ordering such agents.

The second step of the purchasing process is the **actual purchase** where the supply chain of the institution finalizes pricing issues, places orders, and proceeds with payment. In the third step of the **post-purchase**, verification that items received are performing well according to the predetermined standards is done. In case of any violation to quality standards of the laboratory, the microbiology laboratory manager should notify the responsible parties to take suitable corrective actions that may include arrangement for back orders or replacement to the laboratory. Throughout the whole process, all items have to be stored as per manufacturer recommendation[6].

A common method to ensure consistency while using reagents shipped to the laboratory with different lot numbers is performing 'cross lot validation' that tests new shipments versus old ones using retained patient samples.

Inventory is an important part of this process and whether manually or electronic managed, this should ensure organized used of supplies including 'first in, first out' policy and systematic ordering of supplies according to rates of utilization to prevent delay or interruption of the workflow.

b) External Services:

Purchasing is not limited to laboratory supplies but extends to external services needed as referral laboratories, external consultants, equipment maintenance, security services, housekeeping services, and final waste disposal facilities. For each of these, a service-level agreement should be present which is a contract between the provider of the service and the laboratory that determines the conditions of service expected and demarcates the exact responsibilities of all parties involved[6].

Among these mentioned external services, referral laboratory appears to be of utmost importance. A referral laboratory is usually a laboratory that offers services not ordinarily performed in a clinical laboratory. Selection of such service is usually a coordinated effort between the microbiology laboratory manager who should check for the technical related and the quality assurance department which will ensure that level of accreditation of the referral laboratory meets the minimal requirement for the organization and officially keeping these documents for any inspection or audit.

All sophisticated steps of testing that starts from packing the specimens and sending them to referral laboratory till the time of receiving the reports while considering the result form, the added comments, the responsibility of notifying health authorities in case of an alarming pathogen for example, and all other details should be clearly delineated in the service level agreement. Stringent

checking of the performance parameters of the referral laboratory is a mandatory continuous step as long as this referral laboratory generates reports for the original organization[6].

This section is discussed in ISO 15189 under the titles: Reagents and consumables, Service agreements and Externally provided products and services[5,6].

6. Equipment

Equipment in the microbiology laboratory ranges between those that provide testing, computer systems, and the Laboratory Information System (LIS). Qualifying new equipment is a multistep procedure that includes selection, installation, operation, and performance. All of which should be performed before being involved in testing patients' sample[6].

The process starts with a step known as **"Selection Qualification" (SQ)** through which the laboratory documents the purposes required from the new equipment and identifies qualified suppliers for this equipment. An eye should be kept upon the functional specifications, environmental hazards caused by this equipment and the supplier's capability to offer preventive maintenance to the equipment. A comparative exercise should be done among available vendors to widen the options and meanwhile discussing alternative acquisition as renting. Finaly, comparing quotations and justifying selection of any is done and documented[12].

Following purchasing of the new equipment, the next step comes and is designated **"Installation Qualification" (IQ).** This simply ensures new equipment has been installed as per the manufacturer's instruction. This step is to be followed by operating the new equipment again in accordance with the manufacturer's specifications, a process known as "**Operational Qualification" (OQ)**. The final step would be the **"Performance qualification" (PQ)** which should be performed by the laboratory staff performing the testing to ensure that the equipment performs effectively[12].

A detailed master list for all equipment in the laboratory should be always present and serves as a checklist for assessments and audits[6].

Every detail of concern about each equipment is present in this file starting from the first day of installation, certifications, scheduled calibration plan and routine preventive maintenance documents. This data is to be kept till the time of retirement, refurbishment, or any other way of terminating functionality of any equipment in the laboratory.

Finally, in case of equipment retirement it is the laboratory responsibility to ensure its proper decontamination plus keeping patients' data confidential[6].

This section is discussed in ISO 15189 under the section entitled Equipment[5,6].

7. Process Management

This section discusses the whole testing process which is covered by three main steps: preanalytical, analytical and postanalytical processes.

a) Preanalytical process:

It is the process that encompasses steps occurring before the specimen reaches the laboratory. Although these steps occur outside the microbiology laboratory, they are a great source of errors, and this is why ensuring consistency and correctness is required.

Examples for preanalytical errors in microbiology laboratory are endless given the nature of tests handled that deal with areas colonized with opportunistic pathogens or inhabited with normal flora. Examples include sending single blood culture bottles for a case of sepsis or incorrect blood volume, failure of cleaning external genitalia before voiding a urine sample for culture, mislabeling a specimen, expectorating saliva rather than true sputum, CSF samples stored in refrigerators, failure of transportation of specimens in the correct time, dried swabs for wound culture.

The main aspect that should be always laid upon in microbiology is the rule "junk in, junk out"[6]. For this reason, the microbiology laboratory should be responsible to provide comprehensive description of all specimens' collection instructions in details while providing enough training and testing competencies of all those involved in this process. Details should include supplies required, correct labeling, revising of clinicians' requests, obtaining patient's consent, adherence to aseptic techniques, proper transportation, and delivery to the laboratory. Comprehensive detailed instructions on proper sample collection are present in many guidelines and references [13].

b) Analytical process:

This step starts when the diagnostic procedure starts. Appropriate testing methodology should be adopted by the microbiology team. Under this section four main aspects are needed to be outlined; verification, validation, writing standard operating procedures (SOPs), and measurement of uncertainty for tests with quantitative results[3].

- **Verification and Validation:**

Although both terms are used interchangeably, they are different. Whilst **verification** is defined as a process applied to Food and Drug Administration (FDA) approved tests to ensure that predetermined performance standards are met after setting the new test in use in the new laboratory environment, **validation** is another very different process. It is a comprehensive plan designed and implemented to challenge and record the result of a new or modified process to ensure the

process works up to standards predetermined before implementation. In this context, **validation** is needed for any non-FDA approved testing methodology or equipment[3].

An automated identification (ID) and susceptibility testing (AST) that is FDA approved for use on colonies growing on a culture plate will need only verification when set in a new laboratory to use for this purpose. If the microbiology laboratory decided to utilize this equipment to directly determine the ID and AST of a bacteria directly from positive blood culture bottle, a process called an in-house or laboratory developed test, the methodology and the whole process will need validation.

Verification questions the performance characteristics of **accuracy** (acceptable agreement of results between the new method and a comparative method), **precision/reproducibility (**acceptable within-run, between-run and operator variance). Moreover, **reference interval of normal values** (normal result for the tested patient population) and **reportable range** (the acceptable upper and lower ranges). These last two parameters apply mainly to quantitative tests[6].

Validation is a process that usually requires testing performance standards included in verification plus sensitivity, specificity, measurement of uncertainty and comparison with the old method or old equipment[3]. In addition, data on inhibitors of testing, the frequency of these inhibitions and the detection limit is required[6]. Validation studies should be properly planned for, executed by professional authorized laboratorians, and approved by the laboratory director. Verification and validation clinical microbiology laboratory procedures have been extensively elucidated[14,15].

- **Writing standard operating procedures (SOPs)**

Having all detailed procedures for laboratory performed tests in the laboratory is a crucial step in any QMS. The details describing the test purpose, sample requirements, and detailed instructions performance are the usual items included. SOPs have a steady clear format to ensure consistency and compliance. A hard and/or soft copy should be available to the staff who perform the test. Package inserts should not be used as a surrogate for SOPs but may be kept as a reference . Periodic review of SOPs for modification or change should be done according to a predetermined schedule. Summary of changes and revision history should always be clearly inscribed[6].

- **Measurement of uncertainty**

Uncertainty measurement estimates should be established to eliminate the effect of elements which lead to variability of patients' results. A measured value is a real value of the element measured regardless of imprecision, imperfect bias correction, and imperfect specificity. Such elements may exist in the preanalytical or analytical or even postanalytical phases. However, following SOPs can minimize uncertainty in pre- and post-analytical phases. In analytical phase, running a sample many times and taking the average of the result, would ensure a more true value[6].

In microbiology laboratory tests that have quantitative values, such as urine colony counts, or quantitative viral loads, this item applies. Microbiologists can perform multiple cultures on the same urine sample to declare that a urine culture result of 60,000 CFU/ml may lie between 50,000 and 75,000 CFU/ml (6). Similarly, a titer of Widal test of 1/320 after repeating many times may appear to fall in the range of 1/160 and 1/640.

Guaranteeing results quality generated in the analytical step requires a comprehensive program which starts by monitoring tests with quality controls (QC), followed by tracking trends of QC results by quality assurance (QA). When determining frequency of QC testing, two main points should be considered: risk assessment of the test itself and the manufacturers' recommendation[6].

Providing an external assessment of the laboratory performance using proficiency testing (PT) is deemed mandatory and is considered an essential part of performance enhancement.

Commercially available PT programs usually meet the scope of the laboratory for most of its diagnostic assays. When working with PT samples, the same testing protocol is applied with the same staff member who perform the test on the patients' samples. No interlaboratory communication is allowed till releasing results. When innovative testing methods are performed for which participating in a PT program is not available, an alternative assessment plan can be performed. Generation of an "unknown" sample using QC material or retained patient samples that were evaluated by another test methodology that has a PT program or using interlaboratory comparison or inter-personnel comparison are options when no PT exists. When designing alternative assessment plans, the acceptable criteria should be settled and compliance with accreditation agencies should be ensured[6].

For both PTs and alternative assessments results should be evaluated through grading and any deviation would be tackled as a non-conformity (NCE) that needs corrective and preventive action (CAPA).

c) Postanalytical process

This phase includes two main activities: result reporting and samples management.

- **Results reporting**

The result report is the only document the patient and the healthcare provider view after a long journey the sample goes through starting from the specimen collection passing through the analytical phase and ending by report review before releasing. If for any reason, any of these steps is compromised the report credibility will be questionable and this is why under certain conditions and in certain specimens, suspecting the sample integrity should be declared in the generated report. For the same reason some laboratories document

that "specimens have been delivered to the laboratory under the responsibility of…..''.

Throughout the whole testing process and especially the reporting step, patient confidentiality should be guaranteed. For this reason, adequate security training should be conducted for all the staff to guarantee this[6].

The review of results in the microbiology laboratory is a crucial step. While the normal data including demographic data of the patient, specimen type, previous results for same test and layout result format review is done in all laboratory units, the microbiologists will have other many items to be reviewed as well. The culture result for example should be correlated with direct film examination, the finding of abnormal pathogens in relation to sites should be elucidated. The abnormal sensitivity patterns must be double checked before releasing. Ensuring compliance with antimicrobial reporting policy, if present, also should be done. Reviewing of antibiotic options for special cases like children and pregnant females is very important. Such items and others make report reviewing of microbiology reports a very sophisticated process that is usually carried out by experienced consultants.

Adding comments whether clarifying or interpretive comments in the reports, like defining certain pattern of resistance or recommending combination of antibiotics for treatment of multi-drug resistant bacteria (MDR) bacteria is sometimes very helpful and appreciated.

Determination of the reference range, mentioning methodology of testing or test limitations are all helpful tools and augment the clinical role of the microbiologists as partners in decision making.

A crucial part of the reporting system in the microbiology laboratory is communicating critical results as a positive film for acid-fast bacilli or positive blood culture result. Documentation of this reporting is relevant for quality and legal reasons. Failure to notify a critical result is a serious failure of the QMS as a whole. A policy for releasing amended or even corrected reports should exist to ensure patients will, under all conditions, receive a meaningful correct result[6].

Turnaround time determination (TAT) for every test should be documented with every effort to ensure timely release of results. Culture and sensitivity is a cumbersome lengthy process. Critically ill patients therefore may benefit from releasing preliminary reports like results of Gram-stained direct examination of tracheal aspirate from a patient suffering from ventilator associated pneumonia (VAP) or Gram-stained film from a flagged blood culture bottle of a septicemic patient.

In the era of automation, linking automated ID and AST devices have enabled linking these systems to the LIS and subsequently automatic release of reports. In such conditions, proper monitoring and control on release is compulsory to prevent release of any result that may require modification or further confirmation[6].

- **Samples management**

Having a clear policy and inventory system to keep specimens for predetermined periods for many purposes is a must. Purposes include further testing, sending to a referral laboratory, molecular typing for epidemiological purposes and others. Storage conditions and length of retention periods should comply with biosecurity and regularity rules of the institute and the country (3).

Final safe disposal of microbiological wastes should be carried out in agreement with regulatory laws. A waste management policy in the microbiology laboratory should be available and followed starting from initial discarding till final steps of management that are usually carried out in off-site agencies.

This quality essential is detailed in ISO 15189 under the section entitled Process requirements (Pre-examination processes, Examination processes and Post-examination processes)[5,6].

8. Documents and Records

Documentation and keeping of all data of the laboratory is a fundamental element of any QMS. A document control strategy should apply to electronic or paper form. Any laboratory documents ought to be approved by an authorized body before being put into use[3].

Documents being un use in the laboratory are many. Examples include policies, processes, procedures, forms, job aids, records and others. A **policy** is a structured statement of directions to provide consistency and efficiency to the work done. Policies may be technical as a policy entitled ''Waste Management Policy" or related to the institute administration like "Delegation Matrix Policy". A **process** is a group of actions that transfer givens into outputs. **A procedure** is a set of instructions for completing a single task or activity within a process. While antimicrobial sensitivity testing is a process, steps of preparing of the inoculum, spreading the inoculum and applying antibiotic discs is the procedure. Displaying of the processes can be done in different formats including flowcharts and process maps and SOPs. A **form** is a document used to register data. An example is a registration log for complaints or a template to record zones of inhibition for QC organisms used in a Kirby-Bauer antibiotic susceptibility test. **A job aid** is a summarized group of instructions to accomplish a task, it may be a flowchart or a simple diagram. For example, a job aid showing the steps for performing Gram stain or acid-fast staining. This is neither an SOP nor a surrogate for SOP but could be linked to an existing SOP[6].

All documents should be eligible for periodic review for relevance and for other reasons. This is mandatory regardless of the document type. To begin a change in a document and to help keep modifications, "document change request" (DCR) should be available. Neither correction fluid nor deletion of the original information. In all cases, the person in charge should sign and mark

the date of the change. Next, revision history has to be updated, assigned a new revision number and approved. Old documents or even retired documents should be archived for a predetermined time interval before secure disposal[3].

A **record** in the laboratory is defined as a document that provides evidence that a result has been achieved or an activity has been accomplished. All SOPs, procedures, patients' worksheets, instruments print out data, QC readings, maintenance sheets, verification & validation documents, audits, meeting minutes, patients' complaints are important records. To avoid mess that might result from keeping all such records there must be an organized master list for all records, a clear process to index them and a predetermined period to keep them before discarding with an appropriate previously determined process to keep confidentiality and security[6].

This part is delineated in ISO 15189 under two subheadings: Document control and Record control[5,6].

9. Information Management

Information system of the laboratory which is known as the laboratory information system (LIS) is managed manually or electronically according to the laboratory style and workflow. Under all conditions, **data security** (protection of data from accidental unintended or intended malicious access), **data integrity** (ensuring accuracy and steadiness of the data), and **data traceability** (tracking data flow throughout the whole work path) must be guaranteed. Data could be raw as all examples of documents mentioned in the previous heading or maybe information that result from the process of data mining[6].

Antibiotic susceptibility reports released are data, while the cumulative antibiogram report prepared either manually or by specialized software is a result of data mining. Both are subjects of information management.

Verification is done to ensure the accuracy of data transfer or manipulation. For example, mathematical calculations done by LIS should be verified at regular time intervals and after software updates to ensure that they are properly working.

To comply with this quality essential, installation of new computer systems is mandatory. The LIS has to fulfill the needs of staff and customers. As a part of the data security plan, the level of access should match every job title and should be clearly defined. Personnel who enter patients' data will not have access to write a susceptibility report and in turn those will not have authority to review and authenticate results. All staff should obtain enough technical training to ensure their competency in performing assigned tasks. Data retrieval and backup maintenance is a crucial part of information management. It is essential to accomplish this goal under all conditions or even catastrophic events like natural disasters (3).

This part is delineated in ISO 15189 under the headings: Control of data and Information Management[5,6].

10. Nonconforming events management

Nonconforming event (NCE) is simply defined as non-fulfillment of a requirement. Reasons may be failure to practice the procedures correctly or using procedures that are not suitable for the requested purpose (16). Examples are many, they include QC falling outside acceptable limits, unacceptable performance in PT, amended reports, clerical error and results of audits. An NCE may range from being an incident (an event that reached the patient), a near miss (an event occurred but failed to reach the patient) or a just unsafe condition[6].

A comprehensive program for nonconforming event management should exist in any QMS to track, document, and correct NCEs. The identification of NCEs can be through analysis of the customers' complaints, the staff feedback or an event-tracking system. Several classification systems can be used to facilitate grouping and analysis of NCEs. Examples include classification as per the workflow; preanalytical, analytical or postanalytical. Another classification identifies the NCE as being a random error or a systematic error that occurs in a cluster of cases as a result of reagent problem for example.[6].

To be successful, the NCE management program has to focus on elimination of the likelihood of reoccurrence. A shift of culture is needed to make the old quote of the Irish poet Oscar Wilde: "*Experience is the name we give our mistakes*" the spirit of the program.

The NCE management program must assign authorized personnel to evaluate the degree and impact of the NCE and hence decide and implement the corrective action & preventive action (CAPA).

An NCE that resulted in a wrong antimicrobial sensitivity report release (sentinel event) should be communicated with the healthcare provider whereas a clerical error in typing non-medical data in the patient's report may need less stringent intervention.

Similarly reporting *Staphylococcus aureus* as being MSSA rather than MRSA (sentinel event) is not managed as misreporting of *Staphylococcus hominis* as *Staphylococcus capitis*[6].

Investigation of an NCE should be documented in a form dedicated to this purpose and should start from the point of occurrence and comprise all related investigation and analysis. Based on this, root cause analysis may be essential for events that cause high cost or serious consequences. Following the investigations comes remedial action, corrective action, and preventive action[3].

An example is the release of a faulty report in the night shift. The remedial action is to release an amended report with notification to the healthcare provider. Analysis revealed that this incident occurred due to the absence of a senior staff in the night shifts to review and authenticate results. A corrective action will be calling for hiring a consultant for the night shifts. A preventive action will be reviewing job descriptions of all titles and

defining the authority matrix to prevent re-occurrence of this NCE.

These corrective and preventive actions should be evaluated to ensure effectiveness. All data should be documented, reported to the suitable managerial level, kept for analysis and identification of trends (6).

This part is delineated in ISO 15189 under the headings: Nonconformities and Corrective actions (5,6).

11. Assessments

This item will focus on three entities for performing assessments of the system. These are audits, encouraging feedback and quality indicators[6].

a) Audits:

Audits are procedures performed to assess the workflow in the laboratory and ensure that policies are placed effectively and achieve desired goals. It is a sentinel item in any accreditation program and has always been regarded as the main drive to implement QMS.

Audits can be conducted internally or externally by using an established checklist to test for various laboratory activities. External auditors usually perform their audit within a predetermined frequency that is usually calculated according to the type of processes performed and the risks associated. Internal audits in microbiology laboratory can be performed by supervisors, infectious diseases doctors or postdoctoral medical microbiologists, after they complete audit training. They should assess laboratory QMS against a well-defined set of standards that applies to the quality system described[6].

At the end of the audit, a conference is usually called for to clarify and document NCEs found, if any and provide a chance for questions and experience sharing. Following this, the laboratory should address NCEs for implementing the whole process of investigation and correction discussed under the previous section. Documenting the whole experience and the outputs is essential[3].

b) Feedback

Feedbacks collected proactively from both customers and employees is another smart and easy way to provide enhancement and improvement. Microbiology laboratories provide services to many partners who have to be continuously questioned for their feedback. Apart from patients and healthcare providers, the antimicrobial stewardship committees, the infection control teams, and the clinical pharmacists will always keep having thrills and inputs to drive improvement. Their input in testing methodologies to decrease TATs, their opinion on the way of communication, their requests to increase the frequencies of performing point of care testing (POC) related to screening for MDR bacteria and many issues ought to be regarded as valuable tools to manipulate laboratory procedures and policies.

Even valid complaints from aforementioned parties should always be communicated and discussed to provide enhancement[6].

The staff members should feel free to speak out and give feedback and opinions to their direct managers. Successful management would regard the staff members as the most valuable assets it has, especially those with technical expertise. Feedback regarding the SOPs, the kits used, the problems they face in the night shifts, the difficulties they might have with LIS, the workflow in the vacations and other issues should be tackled when looking for improvement[6].

c) Quality indicators

These are defined as systematically measured data collected to monitor laboratory performance. Quality indicators should be designed to cover technical as well as non-technical activities.

Quality indicators targeting technical aspects should monitor essential elements in the total test process and are ideally divided to cover pre-analytical, analytical and post-analytical processes. Common indicators include blood culture contamination rates, percentages of rejected samples, number of out of range QC results in AST, number of wrong or amended reports, critical results notification, and others. Whereas quality indicators targeting non-technical aspects may include number of laboratory-acquired infections, number of service calls for blood culture analyzer or media preparator device, no. of episodes where incubator temp exceeded acceptable range, number of customer complaints and others[6].

Monitoring and tracking quality indicators patterns should help enhancement and improvement as well as be regarded as a part of evaluating employees for salary rise and bonus rewards.

This part is discussed in ISO 15189 under the headings: Evaluations[5,6].

12. Continual Improvement

Continual improvement (CI) is the last but not the least item in the QMS proposed by the CLSI. As the name implies, it is a dynamic process that continuously change that involves risk assessment followed by risk mitigation and identifies opportunities for improvement from assessments, NCEs, valid complaints and staff feedback. It is a process that tells the old quote *"The race for excellence has no finish line"*. All team members are supposed to share in this process while the management has the final decision to prioritize opportunities through well-defined strategic plan and allocate resources required. Even small improvements are well appreciated and of course so is strategic innovations. Such small improvements give tangible outcomes and inspire employees to add more[6].

Tools used in continual analysis are many, among which strength, weakness, opportunity, threat (SWOT) analysis is widely used (6). Improvement models also

are many. Among the most used is plan-do-check-act PDCA[17].

Regardless of the tools or models employed, a way to monitor the solution reached out is mandatory to examine if collateral damage occurred and to incorporate the new model in the conduct of employees permanently. Throughout the whole process, effective communication is the key to success[6].

This QE is discussed in ISO 15189 under the heading: Improvement[5,6].

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