Internal Quality Control and External Quality Assurance Program

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What is Quality Management Systems

- QMS is a framework to identify, fix, and prevent recurrence of issues in all phases of laboratory operations
- QMS has to cover all phases of the laboratory's operations
  - Pre-analytical
  - Analytical
  - Post Analytical

Importance of QMS

In order to provide and **maintain consistent quality** testing, labs must have a system in place that

- Identifies errors that have occurred and their causes
- Provides an effective process to resolve errors when they occur
- Most importantly, has a process in place that provides on-going surveillance of all lab areas to identify potential sources of error before an error can occur

QMS-2

- The laboratory has to have written Policies and Procedures for every aspect of laboratory testing
  - ***The Elements of a QMS Are:***
    - Communications
    - Complaints
    - QA review with laboratory staff
    - Document Control and Information Technology (IT)
    - QA records
    - QC
    - ***Proficiency Testing***
    - Safety
    - Validation

Quality Control and Proficiency Testing

- QC: Internal verification of accurate and reliable results
  - The only way you know that your systems are working at the moment you are doing testing
- PT: External verification of accurate and reliable results
  - Laboratories getting the same results on the same samples verifies that the labs are producing accurate and precise results

What is control

- It is analytical part of QMS
- Used to check calibration of a test system
- Manufacturers make pools of serum or plasma by assaying & adding analytes to get “normal” and abnormal controls
- Less expensive than standards
- Patient’s serum/plasma can be used as a “control”

Why testing Internal Controls?

- They Monitor
  - Instrument
    - Environment (lab too warm, dusty,…)
    - Reagent (stability, new, old,…)
    - Calibration curve (deterioration, lot change,…)
    - Alignment (bulb, cuvettes,…)
  - Monitors CLS
    - Performance (pipetting, mishandling QC, standard, competency,…)

Controls Are An Investment In Time and Money!

- Paperwork (old and new lots must be documented):
  - Old lot out of service (date, copy of the ranges,…)
  - New lot statistics established
    - For all tests in an instrument (starting date, copy of the range,…)
- Reagents
- CLS time and effort

QMS Elements
General Lab Systems

- Facilities, Safety, Document control/IT
- Confidentiality of Patient Information/Communication
- Proficiency Testing (external quality control)
- Complaint Investigations
- Personnel competency assessments and review
- Records Retention
- Complaints

The Role of Proficiency Testing (PT) in Laboratory Quality

- Laboratory results play a major role in guiding clinical decisions
- Proficiency testing (PT) is a basic component of quality-management systems (QMS)

The Role of Proficiency Testing (PT) in Laboratory Quality-2

- PT or external quality control is the testing of unknown samples sent to a laboratory by an approved PT programs (such as CAP, AAB,…)
- Most sets of PT samples are sent to participating laboratories three times per year
- After testing the PT samples in the same manner as its patient samples, the laboratory reports the results back to their PT program
- PT program grades the results and sends the laboratory scores showing how accurately the lab performed

Proficiency Testing (PT)

What is PT?

- PT is a tool to monitor laboratories' quality of performance
- PT determines the performance of individual laboratories for specific tests
- PT is an inter-laboratory comparison
- It is a way to verify that all aspects of the laboratory measurement system is working (pre-analytical, analytical, post-analytical)

Proficiency Testing (PT)

- ***CAP/ISO Requirements***

- Lab must enroll in a proficiency testing program such as:
  - CAP
  - AABB
- Lab must develop PT with another lab if there is no PT available
  - At least every 6 months
  - Lab must have a written P&P for this, including acceptability criteria
  - Lab must document and keep records (2 years in US)
- The lab must assess the effectiveness of corrective action taken to address any unacceptable, unsatisfactory, or unsuccessful PT results

List of Approved PT Program in USA

- Accutest, INC.
- American Academy of Family Physicians (AAFP)
- American Association of Bioanalysts (AAB)
- American Proficiency Institute (API)
- The college of American Pathologists (CAP)
- Medical Laboratory Evaluation (MLE)
- Commonwealth of Pennsylvania (only Toxicology)
- Puerto Rico Proficiency Testing Services
- Wisconsin State Laboratory Hygiene (WSLH)
- American Society for Clinical Pathology (only Cytology)
  - **Note:** *CAP is the largest PT provider in the world*

Why is PT Important?

- PT is important because it is a tool for the laboratory to verify the accuracy and reliability of its testing
- Routine reviews of PT results reports will alert the lab to areas of testing that are not performing as expected
- It also indicate shifts and trends that, over time, would affect their patient results

PT and Accreditation Process

- It is required by CLIA and all Accrediting agencies such as: CAP, TJC, COLA, …
  - Section 42 CFR, part 493, laboratory requirements, subpart H, requires all lab enroll in PT program
- It is required by ISO
  - Section 5.9, requires all laboratories to have a procedure to monitor the validity of testing

What if PT samples are not available?

- If PT materials is not available for some tests, OR, if a laboratory has more than one method of performing the same test. OR, the if a laboratory has more than one instrument performing tests, then they must (at least twice a year) compare results by both methods
  - Must have written P&P on how to do it
  - Must maintain the records (for at least 2 years in US)

PT Requirements

- It has to be designed to meet the laboratory's need
- It has to be approved
- Usually, PT is performed three times per year (5 specimens) per analyte

Monitoring PT

- After testing the PT samples (in the same manner) as patient's specimens, the lab reports the results back to their PT program
- The PT program grades the results and sends the scores reflecting how accurately the lab performed the testing
- PT programs routinely monitor their laboratories' performance

Other Issues

- If the lab have 2 or more sites, they need to be enrolled in PT for each site
- They **can not** share their PT samples or results
- If the lab have 2 or more instrument for testing, they can report only the instrument that was used that day
- Document and keep all records of PT(2 years in US)

What is Bio-Rad Unity Real Time?

- Unity Real Time® is a quality control data management software package
- It provides data access, analysis, review, management, storage, and reporting
- The laboratory submits their QC results to Bio-Rad and in return receives reports of analytical performance
- The peer comparison reports are available will be available online
  - **Note:** *It is a daily PT testing*

Advantage of Participation in Unity Program

- Detection and identification of analytical errors
- Supplemental proficiency testing program (daily)
- Assurance of success in PT
- Getting immediate analysis for trouble shooting
- Instant QC Report / Monthly Evaluation Report
- Laboratory Comparison Report
- Worldwide Report

Questions & Answers

How to be a PT Program Provider

- Congress of US, passed the Clinical Laboratory Improvement Amendments (CLIA) in 1988 establishing quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results
- The requirements are based on the complexity of the test

How to be a PT provider-2

- In order to receive an approval from the HHS, the organization must:
  - Be a non-profit
  - Be a Federal or State agency
  - Complete the application
  - Provide Technical assistance, AND:

How to be a PT provider-3

- For each specialty the organization must:
  - Assure the quality of the samples appropriately evaluate and score the test
  - Sufficient annual challenge and frequency
  - Report the result to the lab and the agency
  - Provide the forms needed having MD/TP signed
  - Provide schedule and comply with shipment rules
  - Have a process to resolve technical problems

How to be a PT provider- 4

- PT program by specialty / subspecialty
  - Microbiology
    - Bacteriology (gram stains, identifications)
    - Mycobacteriology (acid-fast stains, identifications)
    - Mycology
    - Parasitology
    - Virology
  - Diagnostic Immunology
    - Syphilis serology
    - General immunology

How to be a PT provider- 5

- Chemistry
  - Routine chemistry
  - Endocrinology
  - Toxicology
- Hematology
- Cytology
- Immunohematology

Questions & Answers

Validation

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Test System Validation: Why and How

By the end of this session, participants will:

- Understand the laboratory test systems validations ***process***
- Understand ***how*** and ***when*** to validate lab test systems
- Understand how to do test systems validations in their own labs
- Have a basic understanding of CAP/ISO 15189:2012 (“ISO”) validation requirements

What is Validation?

- Validation involves scientifically documenting that patient test results from a clinical laboratory test system are accurate, precise, and reliable
- Validation ≡ verification of performance characteristics of a test system
- Physicians make medical decisions based on the patient test results we provide – they MUST be as near perfect as possible

When Do We Perform Validation?

- Validation is required any time you make a "significant change" to any test system
  - Install a new lab instrument in your lab
  - Move an instrument in your lab
  - New reagent lot for a test system
  - Major repair or servicing of an instrument
- Always *document* validations, keep records for a minimum of 2 years

System Validations

- The reason for any analytical measurement validation is to get consistent, reliable and accurate data
- Instrument validation is done first.
- Proper functioning and performance of analytical instruments and computer systems plays a major role in achieving this goal. There are a few steps to validation:
  - Analytical instrument qualification (AIQ)
  - Computer system validation (CSV)

System Validations…cont'd

- Each instrument in the lab and its software used for testing and calibration shall be uniquely identified
- Equipment that has been subjected to overloading, mishandling, gives suspect results, or has been shown to be defective or outside specified limits, must be taken out of service until re-validated

System Validations…Cont'd

- After the instrument is installed and functioning according to vendor's recommendations:
- Operational qualification (OQ) checks verify the instrument conforms to the manufacturer's functional specifications
- Performance qualification (PQ) verifies that the complete system works for selected applications (i.e., testing patient specimens)

Methods Validation

- After the *instrument* has been *qualified* (meets the manufacturer's specifications and is functioning properly), the scientist validates the analytical methods
- The scientist must qualify every new instrument
- The scientist must validate every test system, i.e., each assay run on the instrument.

Method Validation - Calibration Verification

- Calibration verification is necessary to verify that an analyte's calibration is still valid
- It confirms that testing provides continued accurate results throughout the previously established reportable range
- By regulations, the lab must perform it every 6 months in the USA unless test is calibrated more often than 6 mos.
- CV consists of running calibrators as patients

Method Validation - Control Validation

- Test your current lot multiple times (20 x)
- Establish QC ranges (mean and sd)
- Test your old lot if you still have some
- Test old proficiency testing (PT) samples if you have them
- Begin testing patients
  - Between instruments in your lab
  - Obtain patient samples from other labs

New Reagent Validation

- For all quantitative test systems, reagent validation must address:
  - Accuracy
  - Precision
  - Reportable range (AMR)
  - Analytical sensitivity
  - Analytical specificity
  - Reference intervals (normal values)
- Running CV and QC vs. old reagents is a good way to validate new reagents

Linearity

- AMR (= “linearity”)
- You must document (**prove**) how low and how high you can accurately report results
  - Test samples at the high end of your reportable range. Do they meet your defined criteria?
  - Test samples at the low end of your reportable range. Do they meet your defined criteria?
  - “Defined criteria” = ***before*** doing the AMR study, your lab director has to decide limits (% deviation) that are acceptable

Reportable Range (AMR)

- “Analytical Measurement Range”
- In order to determine patient’s reportable range, the laboratory needs to perform a “Linearity study”
- The linearity for each analyte is assessed by checking the performance of recovery throughout the manufacturer’s stated range of the testing system

When to Run AMR

- Linearities must ***always*** be performed when a new analyzer, analyte, or method is introduced into the laboratory
- When an analyzer is replaced
- For troubleshooting purposes
- Major analyzer repair or replacement of a major part

How to run Linearity

- By using a set of standards containing varying levels of an analyte; high and low concentrations that cover the entire range of the test system

- Testing should be performed in triplicate, or at a minimum in duplicates so that if one value deviates greatly from the others due to random error, it can be removed

New Reagent Validation

- Sensitivity & Specificity
  - ***Sensitivity*** = how low you can *accurately* and *reliably* measure an analyte
  - ***Specificity*** = freedom from interferences, you are only detecting the analyte of interest
- Sensitivity and Specificity must be defined by the lab director!!!
- May vary by assay – the LD decides what is acceptable before the studies are done and patients are reported

Analytical Sensitivity

- Analytical sensitivity represents the smallest amount of substance in a sample that can accurately be measured

- False-negative: test result that indicates a person does not have a *clinically significant level* of analyte, when the patient actually does have a clinically significant level.

- False positive: a false-positive test result indicates that a person has a *clinically significant level* of an analyte when the patient actually does not have it

Analytical specificity

- Analytical specificity, refers to the ability of an assay to accurately identify and measure a particular specific substance (rather than others), in a patient sample
- It is usually expressed as the minimum detectable concentration of the analyte
- False Positives
- False Negatives

Reference Intervals

- Reference intervals are the most common decision support tool used for interpretation of numerical lab reports
- It may be impossible for a laboratory to perform the study for normal range for each test, then consult data from the literature, manufacturers, other labs in the area
- Document how you determine your RI's in case inspectors ask for them…

Validation References

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