Quality Control of the Future: Risk Management and Individual Quality Control Plans (IQCPs)

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Overview

• Define Quality Control
• Define risk management and its application to clinical laboratory testing
• Understand common sources of error in the laboratory and mechanisms to reduce risk.
• Use the CLSI EP23 document as a resource for developing a quality control plan
Audience Poll

- Physician calls questioning a positive ethanol result of 135 mg/dL in a patient on the liver transplant list. A positive result would remove the patient as a candidate. This was first occurrence and patient is an adamant teetotaler! Repeat analysis of the specimen was negative (<10 mg/dL). Further investigation revealed that the technologist calibrated the assay backwards by switching positive and negative calibrators (Hi cal labeled #1 and Low cal labeled #2). Controls did not pick up, as they were switched as well. What should you do?

A. Chastise the technologist
B. Contact manufacturer to determine how the assay calibrated without error
C. Seek better quality control
D. Run for cover under risk management umbrella
Quality in Laboratory Results

• Clinicians rely on laboratory results for medical decision-making.
• Quality is an essential component of laboratory testing.
• Errors in laboratory results can lead to missed diagnosis, medical mismanagement and increased cost of care.
Definitions

• **Quality assurance** in pathology and laboratory medicine is the practice of assessing performance in all steps of the laboratory testing cycle including pre-analytic, analytic, and post-analytic phases to promote excellent outcomes in medical care.

• **Quality control** is an integral component of quality assurance and is the aggregate of processes and techniques to detect, reduce, and correct deficiencies in an analytical process.

• **Quality improvement** is the practice of continuously assessing and adjusting performance using statistically and scientifically accepted procedures.

College of American Pathologists
Historical Quality Control

• Quality control historically used to document stability of an analytical system (environment, operator, and analyzer).
• Born from the 1950’s industrial model of quality in analytical process
• Quality control is a stabilized surrogate sample analyzed like a patient sample containing known amount of measured analyte.
• If the analytical system can achieve the desired result using the QC sample, then the system is stable and quality patient results are being produced.
ISO QC Recommendations

• ISO 15189 – 5.6.1 The laboratory shall design internal control systems that verify the attainment of the intended quality of results. Special attention should be paid to elimination of mistakes in the process of handling samples, requests, examinations, reports, etc.
• Documentation should include quality control procedures based on manufacturer instructions for use.
• Internal Quality Control (internal to the laboratory) is defined as a set of procedures undertaken by laboratory staff for the continuous monitoring of operation and the results of measurements in order to decide whether results are reliable enough to be released.
• The regular analysis of QC materials can serve as an essential component of a laboratory’s internal control system.
Cape Clinic Laboratory
L-J Chart for XYZ Chemistry Analyzer

<table>
<thead>
<tr>
<th>Analyte: Glucose</th>
<th>Control Material: Level 1</th>
<th>Units: mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lot #: 3-123</td>
<td>Exp Date: 19/4/20XX</td>
<td>Target Value: 3.39</td>
</tr>
<tr>
<td>From: June 1, 20XX</td>
<td>Through: June 30, 20XX</td>
<td>TEa: 6.90%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SD assign</th>
<th>SD assign</th>
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<tbody>
<tr>
<td>0.05</td>
<td></td>
</tr>
</tbody>
</table>

Control Value: 3.48

Run | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 |
---|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
3.43|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
3.38|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
3.33|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
3.48|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
3.53|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
3.58|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
3.63|   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |

From: June 1, 20XX
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Quality Control

• A stabilized surrogate sample of known concentration analyzed like a patient sample to determine assay recovery and result stability over time

• Advantages
  – QC has target values, if assay recovers target, then everything is assumed stable (instrument, reagent, operator, sample)
  – QC monitors the end product (result) of the entire test system

• Disadvantages
  – Failure to analyze QC periodically or take action when QC fails
  – Possible to release patient results before a problem is detected particularly with autoverification or continuous release automated tests
  – With autoverification or continuous release of results - When problem detected must go back and reanalyze patients since last “good” QC and possibly send out corrected results.
  – Clinical action could be taken on erroneous results in the interim of correcting an unrecognized issue!
QC and Error Detection

- Systematic errors affect every test in a constant and predictable manner
- Can occur from one point forward or for a limited period of time
- QC samples do a good job at detecting systematic errors, like:
  - Reagent deterioration or preparation
  - Improper storage or shipment conditions
  - Incorrect operator technique (dilution, pipette setting)
  - Calibration errors – wrong setpoint, factors
- Random errors can also be detected by increased QC variability, but QC does a poor job overall at detecting random errors!
Audience Poll

• Oncology clinic calls to question 6 patients from earlier this day. Patients showed low sodiums (118 – 128 mmol/L) when repeated later in day, sodiums were higher by at least 10 mmol/L (128 – 138 mmol/L) [reference range 135 – 145 mmol/L]. Quality control showed a low trend earlier that day after morning calibration, but QC was acceptable. Medical director review noted QC ranges (120 +/- 3 mmol/L) were wider than CAP PT acceptability limits of +/- 3 mmol/L. This allowed for a 4 SD shift of nearly 12 mmol/L and still be acceptable! Analyzer had been in use for past 6 months without issue, and had adopted QC ranges from previous analyzer. What should you do as laboratory director?

A. Resign
B. Contact risk management
C. Rerun all patient samples from period of low QC trend and correct any results outside CAP limits of +/- 4 mmol/L
D. Revise the QC ranges
Quality Control

• Laboratory QC has limitations:
  – Range for QC must be established by laboratory
  – Setting ranges too wide can allow imprecision or too much method variability
  – Incorrect establishment of control means can allow test result biases
  – Biases in a single laboratory would go undetected without inter-laboratory comparison (PT or External Quality Assessment Schemes – EQAS)
New CMS QC Recommendations

• Analyze at least 2 levels of QC (different concentrations) with each batch of patient samples
• Minimum of 2 levels of QC each day of testing
• Hold patient results and troubleshoot test performance when QC fails to recover expected range of results.

• OR

• Develop an Individualized QC Plan (IQCP) based on risk management (US Centers for Medicaid and Medicare Services recommendations starting in 2014)
History

• CLSI EP23 document introduces industrial and ISO risk management principles to the clinical laboratory
• CMS adopted key risk management concepts to develop the IQCP option for quality control
• IQCP allows laboratories to develop a plan that optimizes the use of engineered, internal control processes on a device and the performance of external liquid QC
Why Should Labs Care About CLSI EP23?

• New generation of laboratory devices contain a variety of internal control processes.
• Labs are challenged with deciding appropriate liquid QC interval given QC engineered into newer devices.
• Package inserts provide little help from the manufacturer.
Package Inserts

• Current Good Laboratory Practice includes the daily use and documentation of either liquid controls or electronic internal controls to assure that the calibration of the diagnostic device is maintained within acceptable limits. (fFN test)
• Good Laboratory Practice suggest that external controls should be tested with each new lot or shipment of test materials, and as otherwise required by your laboratory’s standard quality control procedures. (hCG test)
Package Inserts

• For quality control use the control materials listed. Other suitable control material can also be used in addition. The control intervals and limits should be adapted to each laboratory’s individual requirements. (CO2 reagent)
• For best results, performance of reagent strips should be confirmed by testing known negative and positive samples, or controls whenever a new bottle is opened. Each laboratory should establish its own goals for adequate standards of performance and should question handling and testing procedures if these standards are not met. (Urine dipsticks)
Definitions

• Risk management is a way for labs to develop an individualized QC plan for their tests.

• A “Quality Control Plan” – from CLSI EP23 – a document that describes the practices, resources, and sequences of specified activities to control the quality of a particular measuring system or test process to ensure requirements for its intended purpose are met.

• An “Individualized Quality Control Plan (IQCP)” – from CMS CLIA Interpretive Guidelines – a new quality control option based on risk management for CLIA laboratories performing nonwaived testing.
Risk Management Definition

• Systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, controlling, and monitoring risk (ISO 14971)
Risk Definition

• Risk – the chance of suffering or encountering harm or loss (Webster’s Dictionary and Thesaurus, 1993 Landoll, Ashland, Ohio)

• Risk can be estimated through a combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51)

• Risk essentially is the potential for an error to occur
Quality

• There is no “perfect” device, otherwise we would all be using it!
• Any device can and will fail under the right conditions
• Any discussion of risk must start with what can go wrong with a test (errors)
• Lab tests are not fool-proof!
What Could Go Wrong?
Sources of Laboratory Error

- **Test System:**
  - Reagent contamination, deterioration, lot variation
  - Reaction fluctuations
  - Inadequate sampling
  - Improper or loss of calibration
  - Electronic or mechanical failure
  - Power supply

- **Environment:**
  - Temperature and airflow
  - Humidity
  - Light intensity
  - Altitude

- **Operator:**
  - Improper specimen prep, handling
  - Incorrect test interpretation
  - Failure to follow test system instructions

Fishbone Diagram from CLSI EP23…Refer to Appendix A in CLSI EP18 for more comprehensive list of error sources
Managing Risk with a Control Process

• Once we identify the risks, we need to detect and prevent those errors from harming the patient.

• Control processes reduce risk by enhancing detection of errors or limiting harm if errors go undetected.

• Control processes can take many forms from liquid quality control to engineered checks within a device
Types of Quality Control

- “On-Board” or Analyzer QC – built in device controls or system checks (IL GEM, Radiometer ABL80, i-stat)
- Internal QC – laboratory analyzed surrogate sample controls. (Manufacturer controls performed on kit)
- External QC – blind proficiency survey, samples sent a few times a year to grade an individual laboratory’s performance against other labs (CAP or Wisconsin State)
- Other types of QC – Control processes either engineered by manufacturer or enacted by laboratory to ensure result reliability (reagent barcoding to prevent use of expired reagent)
Quality Control

• No single quality control procedure can cover all devices, since devices may differ in design, technology, function, and intended use.
• QC practices developed over the years have provided labs with some degree of assurance that results are valid.
• Newer devices have built-in electronic controls, and “on-board” chemical and biological controls.
• Quality control information from the manufacturer increases the user’s understanding of device overall quality assurance requirements so that informed decisions can be made regarding suitable control procedures.

CLSI Project: EP23

• Laboratory Quality Control Based on Risk Management.
• James H. Nichols, Ph.D., Chairholder
• EP23 describes good laboratory practice for developing a quality control plan based on manufacturer’s information, applicable regulatory and accreditation requirements, and the individual healthcare and laboratory setting
EP23 Laboratory QC Based on Risk Management

Input Information

- Medical Requirements for Test Results
- Regulatory and Accreditation Requirements
- Test System Information: Provided by the manufacturer Obtained by the Laboratory
- Information about Health Care and Test-Site Setting

Process
- Risk Assessment

Output
- Laboratory Director’s QC Plan
- Post Implementation Monitoring

Continuous Improvement

CLSI EP23 Table
Individualized Quality Control Plan

- Risk Assessment
- Quality Control Plan
- Quality Assessment

Individualized Quality Control Plan
Benefits of IQCP to Lab

• Single-use cartridge based methods – use engineered controls in lieu of 2 levels QC/day
• POCT analyzers – perform QC by lot of cartridge (using subset of devices) rather than every lot and each device.
• Core lab analyzers higher complexity tests – helps labs identify weaknesses and appropriate actions to reduce risk of error (may need >2 levels QC/day)
Audience Poll

- As laboratory director, you are reviewing monthly temperature logs and notice a problem. The -20°C freezer logs showed temperatures out of range for past several days (ranging -16 °C to -19°C for expected temps of < -20°C), with no corrective actions. Lead signed off the monthly log. When approached, the lead tech looks baffled and indicates that -16 °C is colder than -20 °C so no corrective action. You explain this problem to the manager who approaches the other techs involved with similar amazement. What do you do?
  
  A. Fire the techs involved and hire more competent staff
  B. Retrain the techs on negative numbers, put a number line as reminder on the freezer door, and change <-20°C to a range.
  C. Discard all the controls and calibrators stored in the freezer and call for maintenance
  D. Move the controls and calibrators to a working freezer and continue to use them. If controls are in, they are still good.
Summary

- Anything can and will go wrong without robust control plans!
- A quality control plan simply summarizes the risk for potential errors with a device and how the lab intends to address those risks.
- A quality control plan can be high level or very detailed depending on the device, the laboratory, and clinical application of the test result and may vary from one lab to next.
- Risk management and developing QC plans are generally accepted by the industry and required for FDA test approval
- Once implemented, the quality control plan is monitored for effectiveness and modified as needed to maintain risk to an acceptable level.
Where’s the Quality Control?
Review Questions

• Which device would best benefit from an individualized quality control plan?
  A – A glucose meter where manufacturer recommends daily QC
  B – A high volume chemistry analyzer requiring QC 3 times daily
  C – A molecular test with 500 reactions occurring on a single use cartridge
  D – A batch analyzer for infrequent therapeutic drug testing

• Which errors would most likely be detected by traditional liquid QC?
  A – A mistake where the assay pipette is set to the incorrect volume
  B – Drug interference in a patient’s sample
  C – Hemolysis in a neonatal specimen
  D – A clot in a dialysis patient sample

• Staff approach the medical laboratory director with a problem. During maintenance on Monday morning, a brown precipitate was found in the acid wash buffer which cleans all the cuvettes. It appears sometime over the weekend, staff poured an assay reagent into the wash buffer. What is the best course of action?
  A – Fire the weekend staff
  B – Call the manufacturer to determine how to flush the analyzer
  C – Verify the validity of the weekend quality controls and reanalyze all the samples, correcting results as necessary
  D – Contact risk management