Errors in POCT: When Improbable Situations Become Possible

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Objectives

• Describe common and uncommon sources of error in POCT
• Introduce the key aspects of CLSI EP23: Laboratory Quality Control Based on Risk Management
• Identify ISO guidelines as resources for risk management
Point of Care Testing

• There is no “perfect” POCT device, otherwise we would all be using it!

The iPhone Tricorder App
Point of Care Testing

• Any device can and will fail under the right conditions
• A discussion of risk must start with what can go wrong with a test (errors or nonconformities)
• Lab tests are not fool-proof!
Nothing is foolproof... for a sufficiently talented fool!

(attributed to a distinguished colleague)
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 (a “nonconformity” or “incident” according to ISO 22367)¹

¹ ISO 22367 Technical Report: Medical laboratories, reduction of error through risk management and continual improvement Geneva, Switzerland 2004
What Could Go Wrong?
Identify Potential Hazards

1. Samples
   - Sample Integrity
     - Lipemia
     - Hemolysis
     - Interfering substances
     - Clotted
     - Incorrect tube
   - Sample Presentation
     - Bubbles
     - Inadequate volume

2. Operator
   - Operator Capacity
     - Training
     - Competency
   - Operator staffing
     - Short staffing
     - Correct staffing

3. Reagents
   - Reagent Degradation
     - Shipping
     - Storage
     - Used past expiration
     - Preparation
   - Quality Control Material Degradation
     - Shipping
     - Storage
     - Used past expiration
     - Preparation

4. Laboratory Environment
   - Atmospheric Environment
     - Dust
     - Temperature
     - Humidity
   - Utility Environment
     - Electrical
     - Water quality
     - Pressure

5. Measuring System
   - Calibrator Degradation
     - Shipping
     - Storage
     - Use past expiration
     - Preparation
   - Instrument Failure
     - Software failure
     - Optics drift
     - Electronic instability
   - Inadequate Instrument Maintenance
     - Dirty optics
     - Contamination
     - Scratches

Incorrect Test Result
What Could Possibly Go Wrong?
POCT

• Dozens of sites
• Hundreds of devices
• Thousands of operators!
• Too many cooks…
  spoil the broth!
• The number of sites, devices and operators
  plus the volume of testing creates a
  situation where rare events can become
  probable in every-day operations
Falsely Decreased Glucose Results

- Complaint from an ICU of sporadic falsely decreased glucose results
- Immediate repeat test on same meter, gave significantly higher “clinically sensible” values
- Inspection of unit found nurses taking procedural shortcuts to save time
- Bottles of test strips dumped on counter in spare utility room
- Some strips not making it into trash, falling back on counter and being “REUSED”
Risk of Error from Open Reagents

• Glucose test strips exposed to air for as little as 2 hours have been shown to cause - 26% bias.¹
• Strips left on counters pose risk of reuse, leading to falsely low results.
• Some meters catch reuse and “error” preventing a result. Other meters do not!²

Risk Mitigation

• Liquid quality control is historic means of detecting and preventing errors (nonconformities or incidents)!
  • Liquid controls detect systematic errors that affect every sample the same way (calibration errors, pipette errors, reagent degradation)
  • Liquid controls do a poor job at detecting random errors that affect a single sample uniquely (hemolysis, lipemia, clots, drug interferences)
• Newer devices have built-in electronic controls, and “on-board” chemical and biological controls.
Types of Quality Control

- “On-Board” or Analyzer QC – built in device controls or system checks
- Internal QC – laboratory analyzed liquid surrogate sample controls.
- External QC – blind proficiency survey, samples sent a few times a year to grade an individual laboratory’s performance against other labs
- Other types of QC – Control processes either engineered by manufacturer or enacted by laboratory to ensure result reliability (checking temperature indicator in shipping container on receipt of new reagents)
Quality Control

• No single quality control procedure can cover all devices, since devices may differ in design, technology, function, and intended use.¹

• 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. ¹

¹. ISO 15198:2004 Clinical laboratory medicine: *In vitro* diagnostic medical devices – Validation of user quality control procedures by the manufacturer.
CLSI Project: EP23

• Laboratory Quality Control Based on Risk Management.
• James H. Nichols, Ph.D., Chairholder
• EP23 guideline 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 Manufacturer
  * Obtained by Laboratory
- Information about Healthcare and Test-Site Setting

**Process**

- Risk Assessment

**Output**

- Quality Control Plan

**Continuous Improvement**

- Post Implementation Monitoring
Risk Identification and Mitigation

• Liquid quality control can be effective at detecting and preventing certain errors (nonconformities or incidents)
• Other errors (nonconformities or incidents) may require different control processes
• Newer analyzers have a variety of engineered processes, so laboratory director must find right balance between liquid QC and other control processes
• Need to get to fully automated analyzers that eliminate errors (nonconformities or incidents) upfront, provide assured quality with every sample
• Until that time, need a robust Quality Control Plan to ensure result quality
EP23 Laboratory QC Based on Risk Management

Create a Process Map
(Preanalytic – Analytic – Postanalytic)

Identify Weaknesses in the Process

Define a Process that will Mitigate Risk

Summarize Processes and Actions in a QC Plan
Where is the Risk in Our Process?

Baseball Coach Loans Ferraris to Teenagers. What Could Possibly Go Wrong? April 1, 2009
Identify Potential Hazards

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Incorrect Test Result
Sample Errors: Interferences

• Analytic error
• Maltose (Glucose dehydrogenase PQQ) falsely increased results
• Acetaminophen falsely increased results on glucose dehydrogenase and falsely decreased results on some glucose oxidase meters,
• Vitamin C falsely increases results on some glucose dehydrogenase and falsely decreases results on glucose oxidase meters.
Fatal iatrogenic Hypoglycemia:
Falsely Elevated Blood Glucose Readings with a Point-of-Care Meter
Due to a Maltose-Containing Intravenous Immune Globulin Product

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INTRODUCTION

In July 2005, the Food and Drug Administration (FDA) received a case report of an elderly male diabetic patient who received a 10% maltose-containing intravenous immune globulin product (Octagam®, Octapharma Pharmazeutika Produktionsges m.b.H., Vienna, Austria) and experienced hypoglycemic coma and irreversible neurological damage secondary to excessive insulin administration. His insulin dosing was guided by falsely elevated blood glucose measurements that were obtained from a point-of-care glucose meter (Accu-Chek Inform meter, Accu-Chek Comfort Curve test strips, Roche Diagnostics, Indianapolis, IN, U.S.). The glucose meter test strips used glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) methodology, which may overestimate measurements when blood maltose levels exceed 0.9 mmol/L.

Adverse events have been reported for immune globulin products that contain maltose, which functions as a protein stabilizer and an osmotic agent. Similar adverse events have been reported for Extraneal (Baxter...
Sample Errors: Interferences

• Minimize test interference at the bedside.

• Select technologies not affected by common medication interferences
• Watch for maltose, icodextrin, and other common substances like ascorbic acid known to interfere with glucose meters at elevated levels.
• Assess bias from oxygen and hematocrit effects.
Sample Errors: Interferences

- No current control process for hemolysis
- Problem with whole blood sampling on blood gas and electrolyte analyzers for K+
- We centrifuge all whole blood samples before reporting K+ to detect hemolysis and comment results!
- What about applying too much/too little sample?
Sample Errors: Specimen Volume

- Some glucose meters recommend that operators visually inspect strips for uniform color development after each test (detects underfilling and bubbles).
- Other meters have automate sample detection. (Fill-trigger is designed to prevent short-sampling.)
- Test starts only when enough blood has been applied.
Operator Errors: Training/Competency

- Operator lockout
- Functions through number code or barcoded ID
- List of operators and training/competency dates maintained in data manager system—
- Devices can warn operators of impending certification due dates (in advance of lockout)
- Newer U.S. CLIA Interpretive Guidelines requires 6 elements of competency for moderate complexity tests
  - Includes – 1 observe test performance, 2 result recording, 3 intermediary worksheets (QC, PT, maintenance), 4 observe maintenance, 5 analyze sample of known concentration, 6 problem-solving – Competency documentation not fully automated!
- Infrequent operator competency, need intuitive devices
- Note – operators can share ID numbers to access testing and override lockout!
Managing Risk with a Quality Control Process
Operator Errors: Performing QC

- Devices require periodic liquid QC
- Operators are patient focused and can forget to run QC, or fail QC targets, and proceed with patient testing.
- QC lockout shuts off patient testing if QC not performed or fails target ranges.
- Prevents patient testing unless QC documented
- Operators workaround QC lockout by performing patient testing in QC mode!
- Newer devices distinguish QC samples, prevent patient testing in QC mode and can also warn when operators run a high QC for low range QC and vice-versa.
Operator Errors: Patient Identification

- Incorrect entry of patient identification can
  - Chart results to the wrong patient’s medical record
  - Lead to inappropriate medical decisions and treatment
  - Improper billing and compliance

- Barcoded patient wristbands reduce the chance of misidentification, but patients can be banded with:
  - Another institution’s identification
  - Outdated account numbers
  - A wrong patient’s wristband

- Residual risk of error even with barcoded ID bands
- Barcoded ID entry alone doesn’t satisfy requirement for patient safety - 2 unique identifiers
National Patient Safety Goals

- Joint Commission: “Use at least two ways to identify patients. For example, use the patient’s name and date of birth. This is done to make sure that each patient gets the correct medicine and treatment.”

College of American Pathologists

2. College of American Pathologists. Laboratory Accreditation Program. Laboratory General Checklist. 07.11.2011
Operator Errors: Patient Identification

- Some devices have positive patient ID – ADT feed to device
- Two identifiers plus active confirmation (also satisfies Joint Commission time out)
- Positive patient ID reduced errors from 61.5 errors/month to 3 errors/month.¹ (unregistered patients; 2 ED and 1 non-ED) conducted over 2 months—38,127 bedside glucose tests.

Operator Errors: Data Transfer

- POCT results may not get recorded in patient’s medical record, particular problem for manual tests
- POCT data management ensures capture of data in device (QC and Patient results), but doesn’t guarantee transfer until operators dock device
- Wireless ensures data transmitted to patient record. (Need continuous wireless or operators may forget to push send button)
Reagent Errors: Calibration

- Incorrect entry of calibration code can lead to inaccurate test results
- Devices have automatic calibration via barcode scanning of reagent vials/strips. (no code chips or risk of wrong calibrator codes)
Reagent Errors: Expired Reagents

• **Centers for Disease Control**
  • “Check and record expiration dates of reagents/kits, and discard any reagents or tests that have expired.”¹

• **U.S. Food and Drug Administration**
  • “Check the expiration date on the test strips. As a test strip ages, its chemical coating breaks down. If the strip is used after this time, it may give inaccurate results.”²

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2. Useful Tips to Increase Accuracy and Reduce Errors in Test Results from Glucose Meters, U.S. Food and Drug Administration [http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109519.htm](http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/TipsandArticlesonDeviceSafety/ucm109519.htm)
Strip Wastage When Outdated

- Operator must check manufacturer’s expiration date prior to testing.
- Vials/strips and controls must be manually dated when opened by operator (prematurely expires once opened)
- Undated, opened vials must be discarded. (? expiration)

Discarded strips due to no date

1. Undated vials between September, 2010 and May, 2011, Willis-Knighton Medical Center, Shreveport, Louisiana
Reagent Errors: Expired Reagents

- Serialized vials/strips and controls barcoded for lot number and expiration date (good to stamped expiration date) can recognize individual vials on opening (30, 60 or 90 day open expiration)
- Automatic lockout for expired test strips and controls
- Some devices can also recognize exposure to humidity (few hours), wet or reused strips as additional control measure
Environment Errors: Temperature

- Devices can fail if used under temperature extremes
- Traveling nurses storing devices/strips and controls in cars during summer heat and winter cold
- We experienced increased temperature errors after switching glucose meters in our ambulances
  - Old temp range 0° - 46° C New temp range 15° – 40° C
- Worked with bioengineering student to design a heated carrier

Rust M, Carlson N, Nichols J. A thermo-modulating container for transport and storage of glucose meters in a cold weather environment. Point of Care 2012 in press.
Measuring System Errors: Contamination

- POC devices pose a risk of transmitting infectious organisms.
- POC blood testing devices, such as glucose meters and PT/INR anticoagulation meters, should be used only on one patient and not shared.¹
- If dedicating POC blood testing devices to a single patient is not possible, the devices should be properly cleaned and disinfected after every use as described in the device labeling.¹
- POC devices need more durable plastics, fewer crevices and seams, and a design that prevents liquid egress into ports.

Measuring System Errors: Contamination

- Reagents and carriers besides the devices can also transmit infectious organisms.\textsuperscript{1,2}

- Recommendation to dedicate vials of strips to individual patients. Manufacturers should further consider single-use packaging.\textsuperscript{1}

- We estimated cost of dedicating strips based on survey of glucose monitoring in 100 inpatients.
  - Average number of 3.4 tests/day (1 – 7.2)
  - Average of 8.4 day length of stay (1 – 81 days)
  - 278 patients per day requiring glucose monitoring

- Annual cost of test strip waste ranged from $>80,000 for 25 count vials to $>170,000 for 50 count vials compared to single-use packaging. (submitted to Clinica Chimica Acta)


Where is the Risk in the Process?

What Could Possibly Go Wrong?
Falsely Increased Hgb Results

• Spurious increased Hgb results 18 – 23 g/dL (55 – 70% Hct) on ICU patients
• Meter, QC and reagents examined and fine, no single operator tied to trend
• Continue to experience spuriously high results, trend went on for several weeks
• One day, POC coordinator watching operator perform Hgb test in spare utility room. Operator took shortcut (procedure is to load cuvette from fresh drop of well mixed sample)
• Instead, operator was filling cuvette from drop of blood remaining from glucose test. Test strip was absorbing plasma portion of sample and artificially increasing Hgb/Hct in remaining drop!
• Remedial action to retrain entire unit staff!
Summary

• Understand your laboratory workflow and processes to identify weak points in those processes where errors, nonconformities or incidents may occur
• Prioritize those weaknesses, address those of greatest risk 1st
• Work with your manufacturers to identify ways to improve error detection and prevention - Automation reduces error
• Utilize CLSI and ISO guidelines as resources for managing risk in your POCT program and laboratory
• A quality control plan simply summarizes the potential errors for a device and how the lab intends to address those errors.
• Once implemented, the quality control plan is monitored for effectiveness and modified as needed to maintain risk to an acceptable level.
Don’t Be Discouraged – Risk Management is Documenting Much of What We Already Do!