Quality Control Procedures: one lab director’s perspective

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Integrated Quality System

Statistical Process Control (QC)

SAMPLE THE MEASUREMENT PROCESS

- REPEAT PATIENTS
- CORRECTIVE ACTION

STABLE?

- NO
- YES

REPORT PATIENT RESULTS

QM System
- Personnel
- Written SOP
- Pre-analytical
- Analytical
  - Calibration
  - Maintenance
- QC
  - PT/EQA
- Post-analytical
- Documentation
- Review; CQI
What the lab director needs to know

• Result has a high probability to be correct

• Information needed:
  • What can go wrong (risk assessment)
  • How to monitor the measurement process
  • Data to support the result is correct
What can go wrong

• Manufacturing
• Transportation
• Storage
• SOP by user
• Measurement process
What can go wrong: transportation and storage

• Temperature and humidity
• Stability after opening
What can go wrong:
SOP by user

- Sample handling
  - Incorrect volume
  - Incorrect fluid, anticoagulant, preservative
  - Evaporation, storage, mixing
  - Pretreatment
- Reagent lot with incorrect calibrator
- Procedural errors
What can go wrong: measurement process

- Calibration drift or shift
  - Reagent stability (esp. after opening)
  - Calibrator stability (esp. after opening)
  - Dirt (e.g. spilled reagent or sample)

- Imprecision deterioration

- Component failure
  - Fluid handling
  - Temperature and humidity control
  - Electronics
How to monitor the measurement process

- Traditional QC
  - Assess overall performance with surrogate samples
- Measurement system monitors, e.g.:
  - Volumetric parameters
  - Signal magnitude and stability
  - Electronic simulator
- Equivalent QC
  - Internal controls
Essential components of QC

• Know method performance characteristics when it is working correctly (i.e. is stable)

• Have stable monitoring processes

• Define acceptance criteria for the monitoring results that can verify stable method performance

• Document the process
Statistical Process Control

Verify that a measurement system is performing as expected

1. Calibration has not changed

2. Imprecision is within the expected variability
   • Must include all sources of variability over an extended time period
Sources of variability; normal operation

- Gaussian error distribution
  - Pipet system
  - Temperature control
  - Electronic noise, detector response
- Non-Gaussian error distribution
  - Reagent, calibrator or QC deterioration (esp. after opening)
  - Calibration cycles
  - Reagent lot changes
  - Calibrator lot changes
  - Instrument maintenance, component replacement
  - Environmental control (temp., humidity)
Variability must include all sources

Reagent lot change 1
No method changes
Reagent lot change 2

Glucose, mg/dL

Reagent lot change 1
No method changes
Reagent lot change 2

+3 SD
+2 SD
Mean
-2 SD
-3 SD

No method changes
Variability must include all sources

Reagent lot change 1

Calcium, mg/dL

Reagent lot change 1

N = 1276

+3 SD

+2 SD

Mean

-2 SD

-3 SD
Important limitation of QC materials

- Frequently, QC materials are **NOT** commutable with native clinical samples

- Commutable means a QC material has the same numeric relationship between two methods, or reagent lots, as observed for native clinical samples
Reagent lot change: patient samples comparison

Glucose

NEW LOT (mg/dL) vs NEW LOT (mg/dL) vs

OLD LOT (mg/dL)

y = 1.00x – 3 mg/dL
Reagent lot change: QC samples

Glucose, mg/dL

Reagent lot change

High QC

Days

Low QC
QC Acceptance Criteria

• Method stability
• Clinical requirements

Interpretive rules are based on:

• Probability to detect an error of magnitude that can impact clinical care
• Low false alert rate
Most common causes of QC alert

1. QC material has deteriorated
   • Mishandled after opening or reconstituting
   • Analyte stability less than desired

2. False alert due to inappropriate acceptance criteria
   • Reagent lot change causes change in target value
   • The inherent variability in the measurement procedure was underestimated
   • 1-2S rule was used

3. Measurement procedure problem
QC Fault Response

1. Identify and correct the problem.
   - Do not assume an “outlier”

2. Repeat patient samples.
   - Sample patients over affected time interval to determine if/when clinically significant changes occurred
   - Written acceptance criteria
   - Correct reported results if a clinically significant analytical problem occurred

Assay new control

OK → YES → Continue testing

TREND ?

NO → Check instrument and reagents; Repeat controls

OK → YES → Repeat patient samples

NO → Recalibrate or verify calibration; Repeat controls

OK → YES → Repeat patient samples

NO → Further technical investigation
QC alerts requiring intervention
(Does not include QC material degradation, nor new lot mean adjustment issues)
Most common causes of variability in patient results

- Calibrator lot to lot variability
- Reagent lot to lot variability
  - which always requires a re-calibration
Lot to lot variability: T4

Patient samples comparison

Slope, new lot vs. old

Lot number
Lot to lot variability: TSH

Patient samples comparison

Lot number

Slope, new lot vs. old
Lot to lot variability: Troponin I

Patient samples comparison

Slope, new lot vs. old

Lot number
Point of Care / Near Patient Testing

- MD expects same reliability as main lab
  - Typically less precise
  - May have different measuring range
  - May have different specificity (interferences)
  - Need sophisticated internal controls
## B-type Natriuretic Peptide

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<th>Lab</th>
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### Hemoglobin A1c

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<td>CV</td>
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<td>4%</td>
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Key information needed from mfr.

To define QC monitoring procedures:

- Precision near limits (esp. lower) of AMR
- Expected variability between lots of reagent and/or calibrator
- Results of risk assessment
  - What needs to be monitored
  - Additional risk factors at laboratory level (out of manufacturer’s control, but not responsibility)
- Maintenance; what to do, and at what frequency, to prevent problems
Internal controls

- Control for all likely risks, e.g.:
  - Sample volume and type
  - Reagent volume(s)
  - Reagent stability
  - Calibrator integrity, and matched to reagent lot
  - Calibration stability
  - Measurement system integrity
  - User errors

- Disable result if a defect is identified
QC: sampling frequency

• Method stability
  ➔ Consider all sources of error

• Clinical requirement
  ➔ Patient impact of incorrect results
  ➔ Value of documenting that no error condition was present when result was reported
QC frequency: cost considerations

- Cost of QC materials and reagents to perform the assays

Balanced by:

- Cost of erroneous medical procedure(s)
- Cost of repeating previously reported patient results
- Cost of recollecting samples for those QNS to repeat
Thank you for your attention

Questions?

Comments

Discussion