Quality Control Procedures: one lab director's perspective

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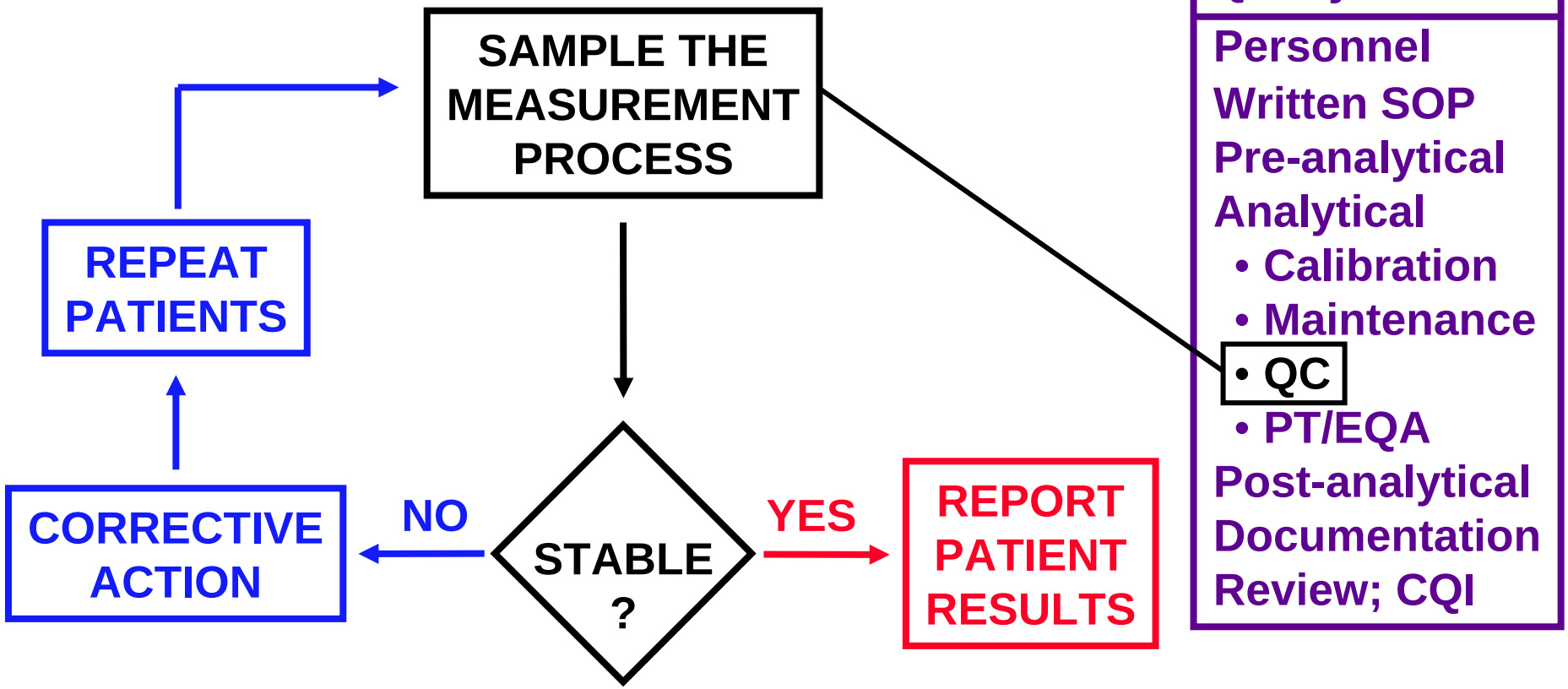
Integrated Quality System

Statistical Process Control (QC)



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

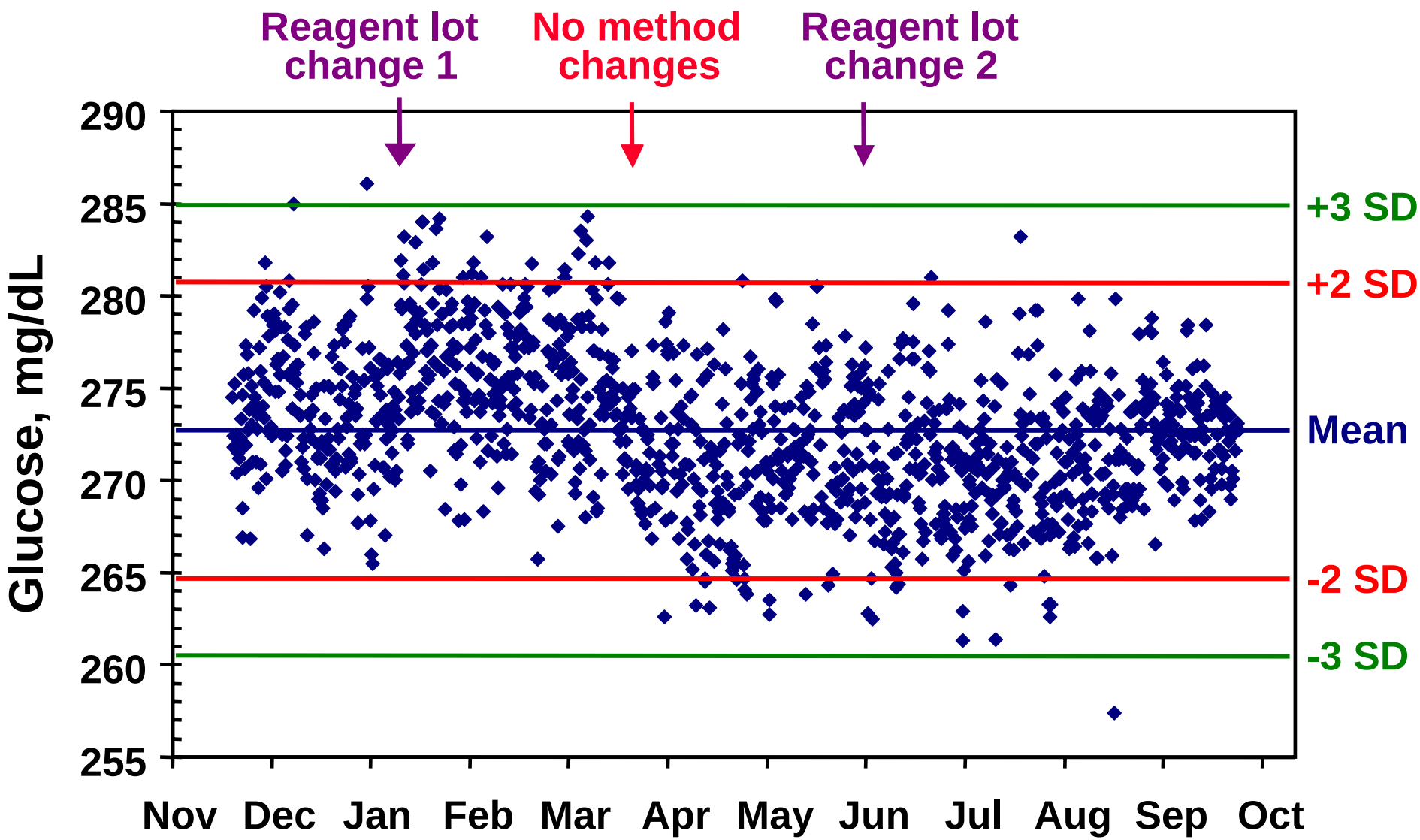
Verify that a measurement system is performing as expected

1. **Calibration has not changed**
2. **Imprecision is within the expected variability**
   - **Must include all sources of variability over an extended time period**

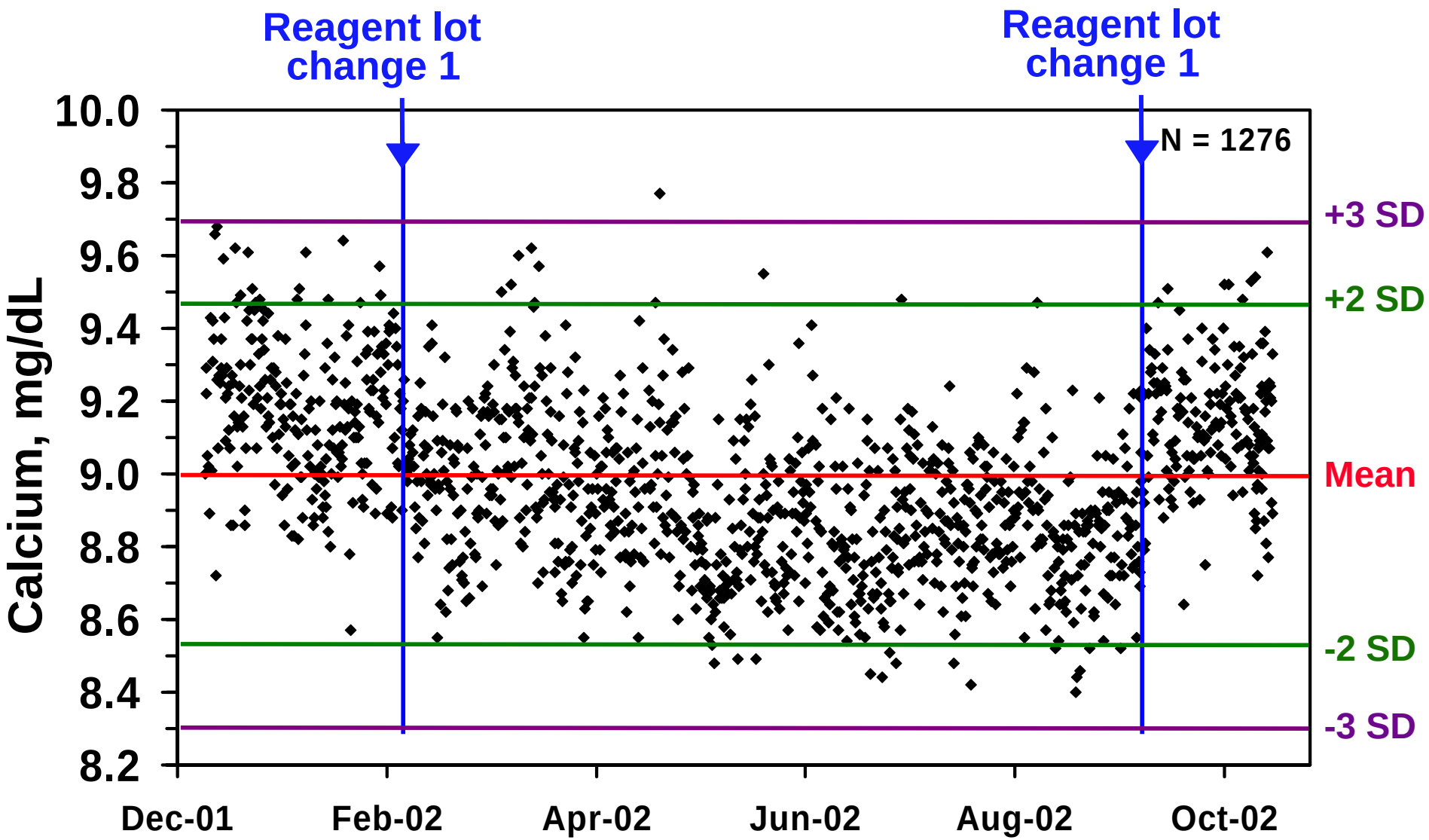
Sources of variability; normal operation

- **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



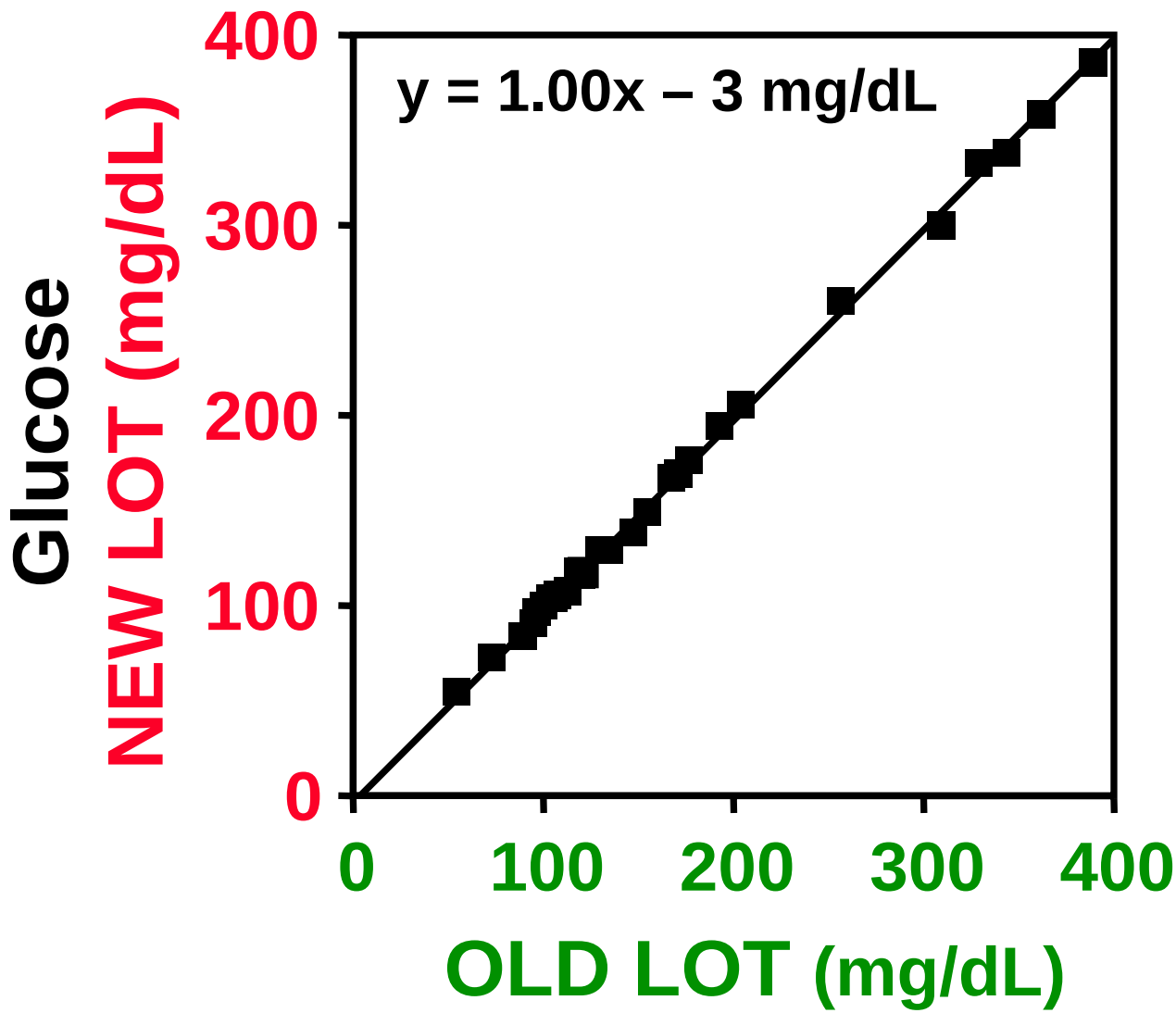
Variability must include all sources



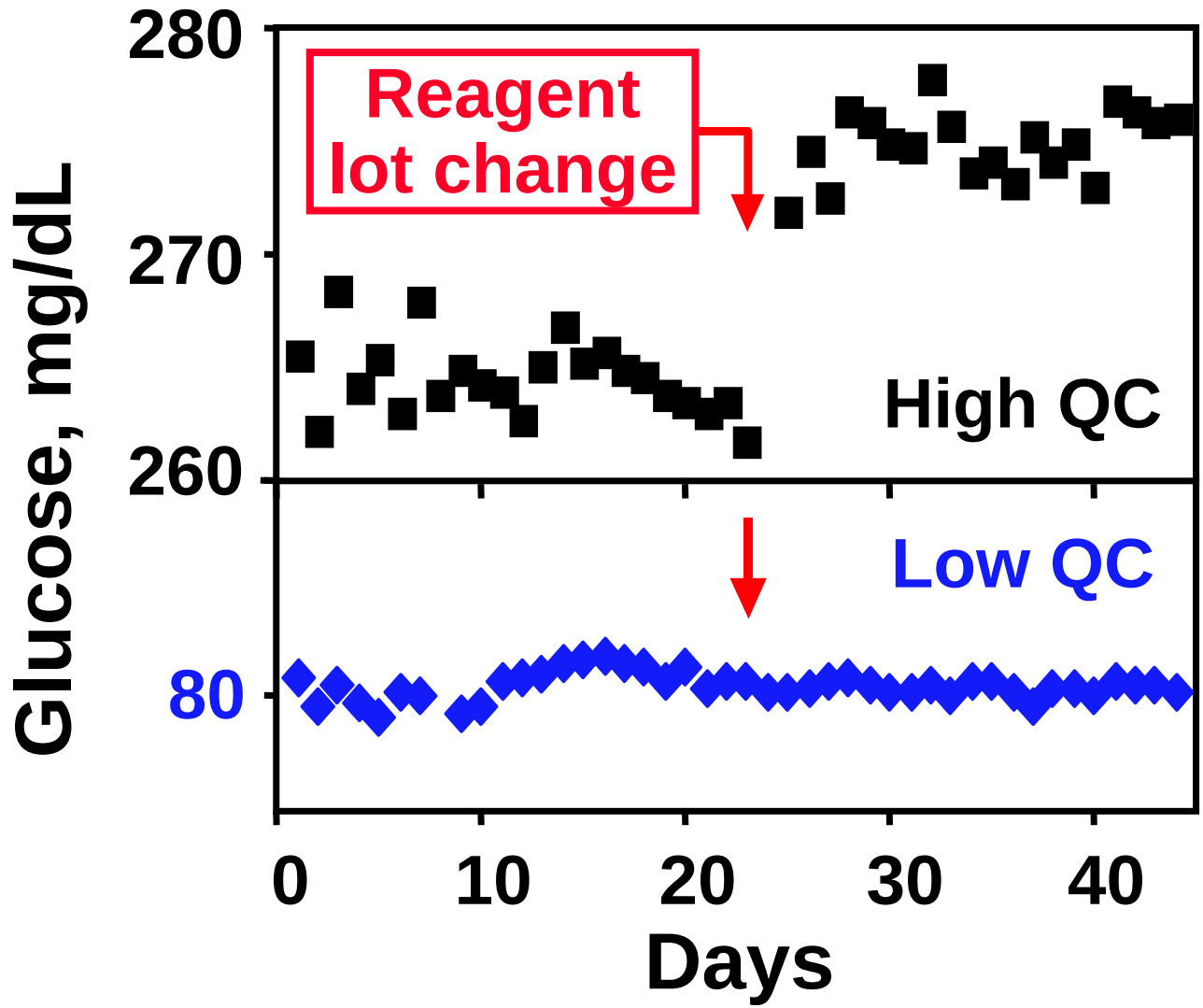
Important limitation of QC materials

- **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



Reagent lot change: QC samples



QC Acceptance Criteria

- **Method stability**
- **Clinical requirements**

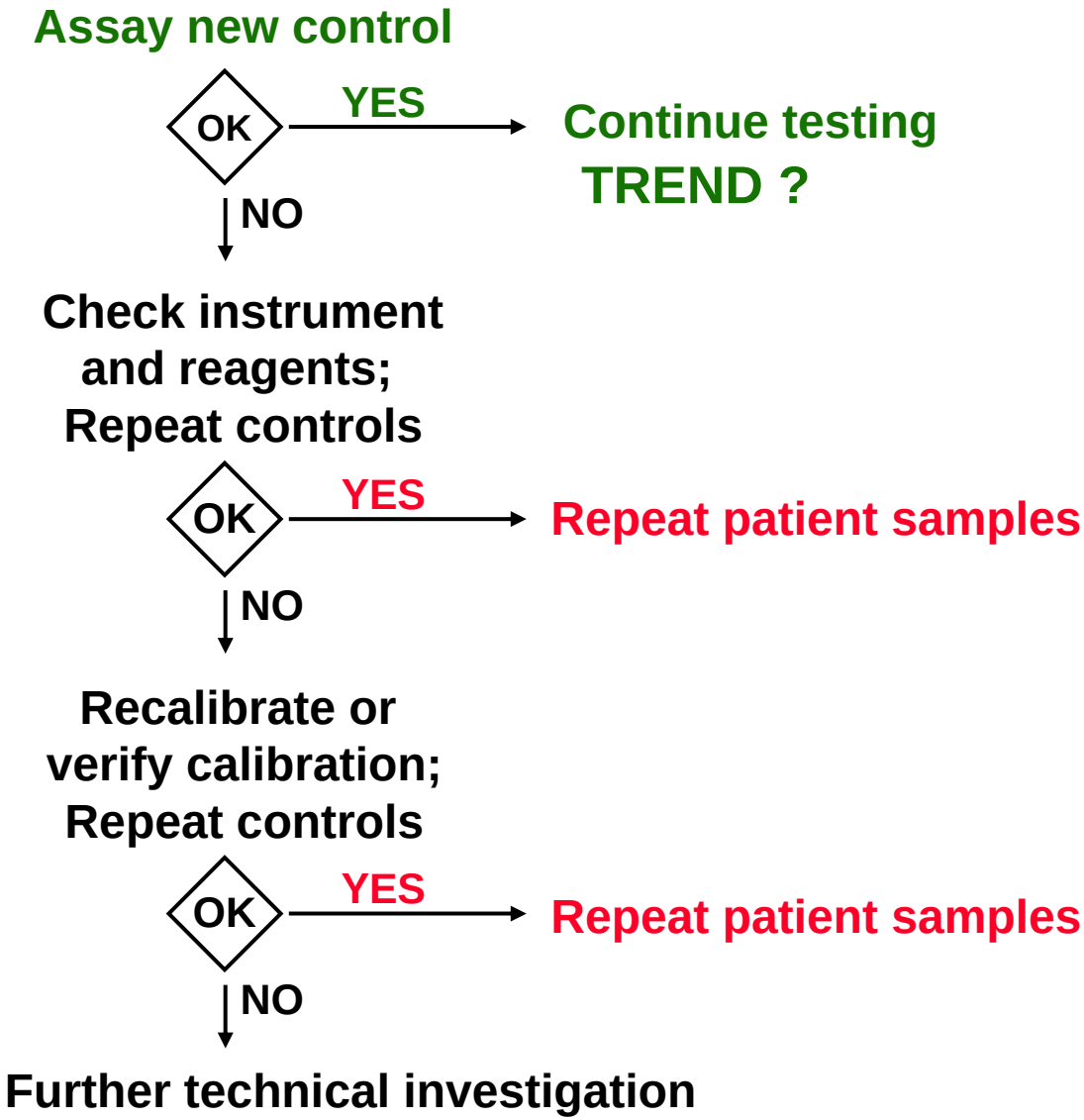
Interpretive rules are based on:

- **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**
   - **1-2$_S$ rule was used**
3. **Measurement procedure problem**

QC Fault Response

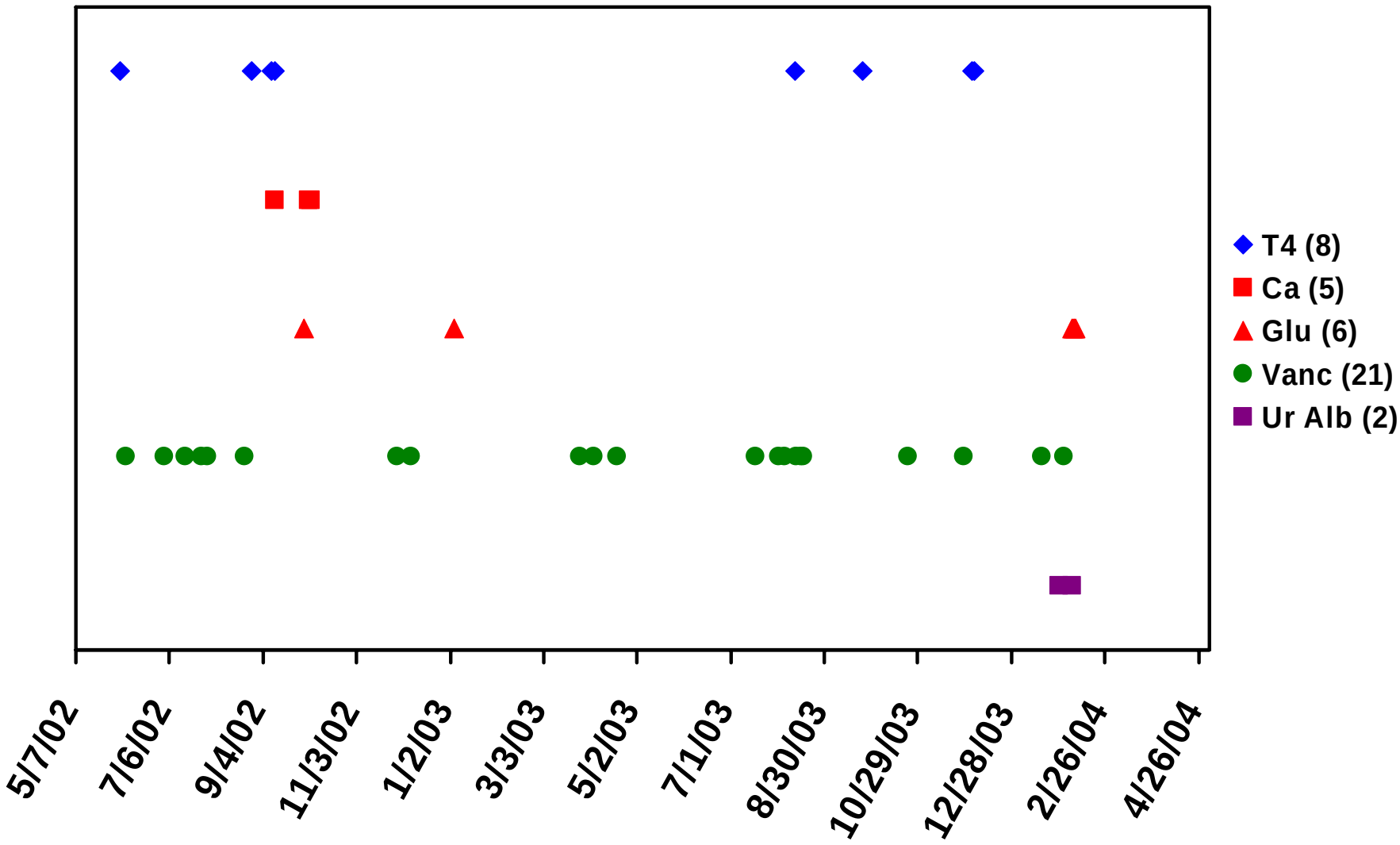


1. **Identify and correct the problem.**
   - **Do not assume an "outlier"**

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**

QC alerts requiring intervention

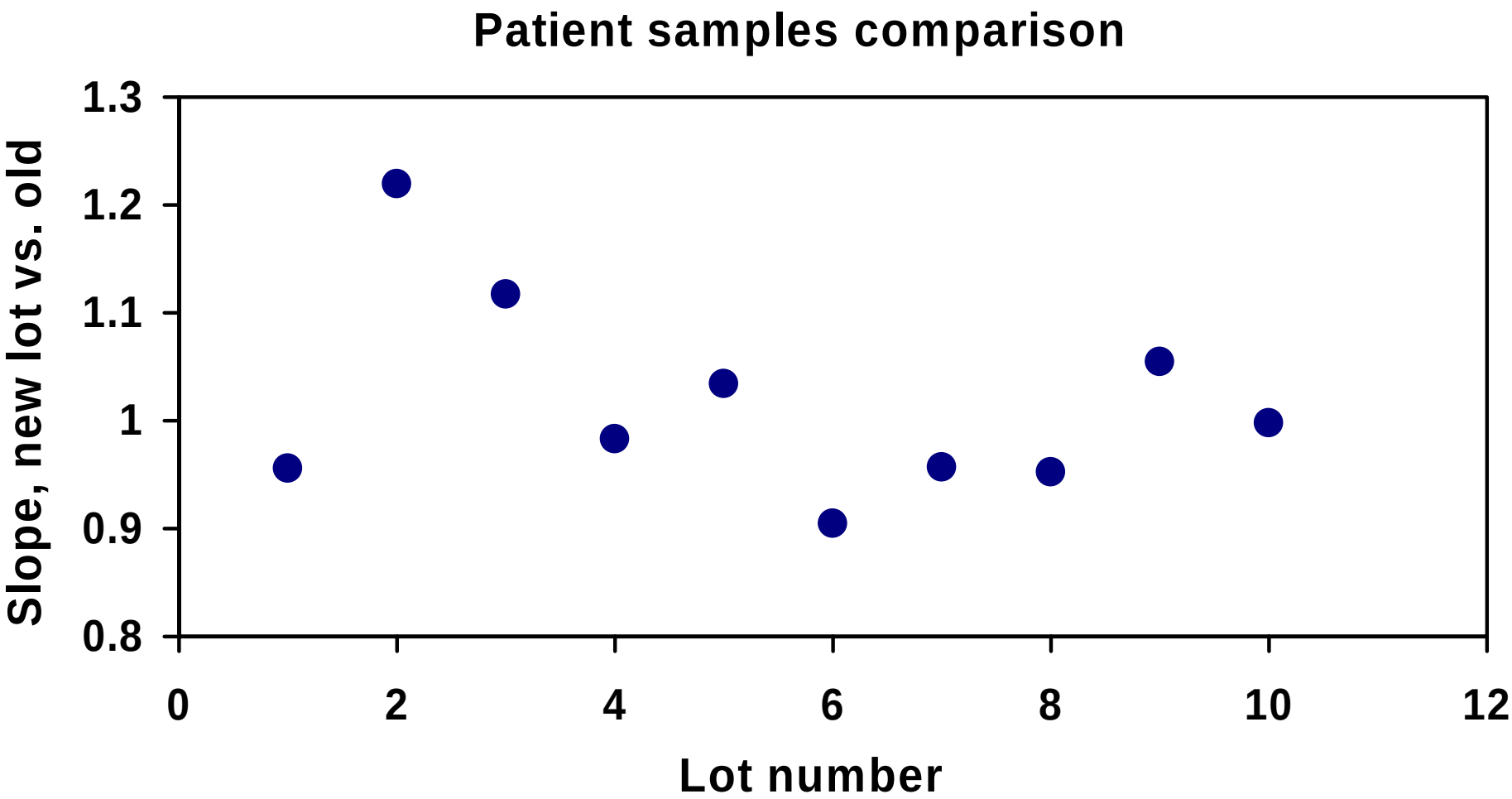
(Does not include QC material degradation, nor new lot mean adjustment issues)



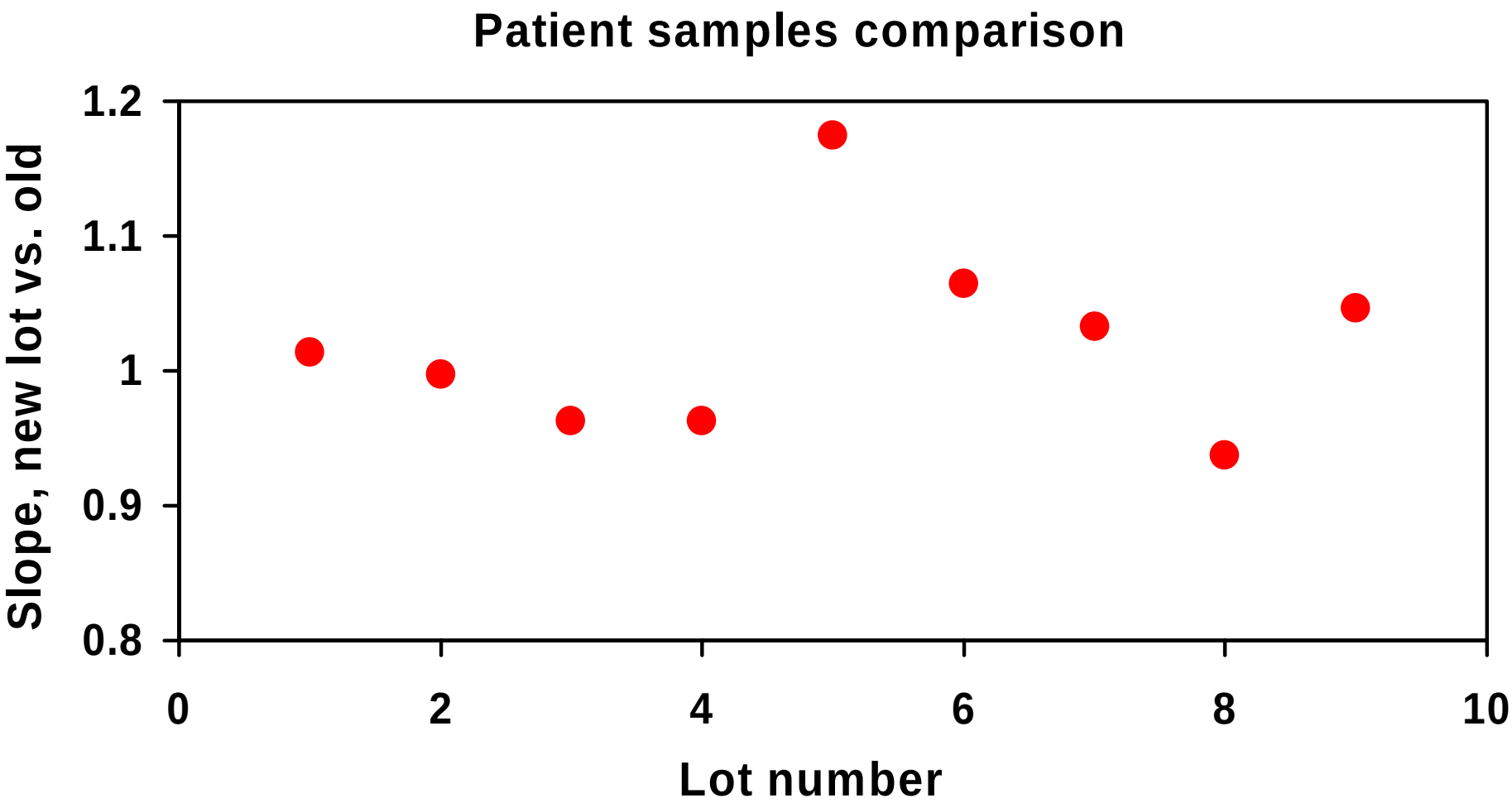
Most common causes of variability in patient results

- **Calibrator lot to lot variability**
- **Reagent lot to lot variability**
  - **which always requires a re-calibration**

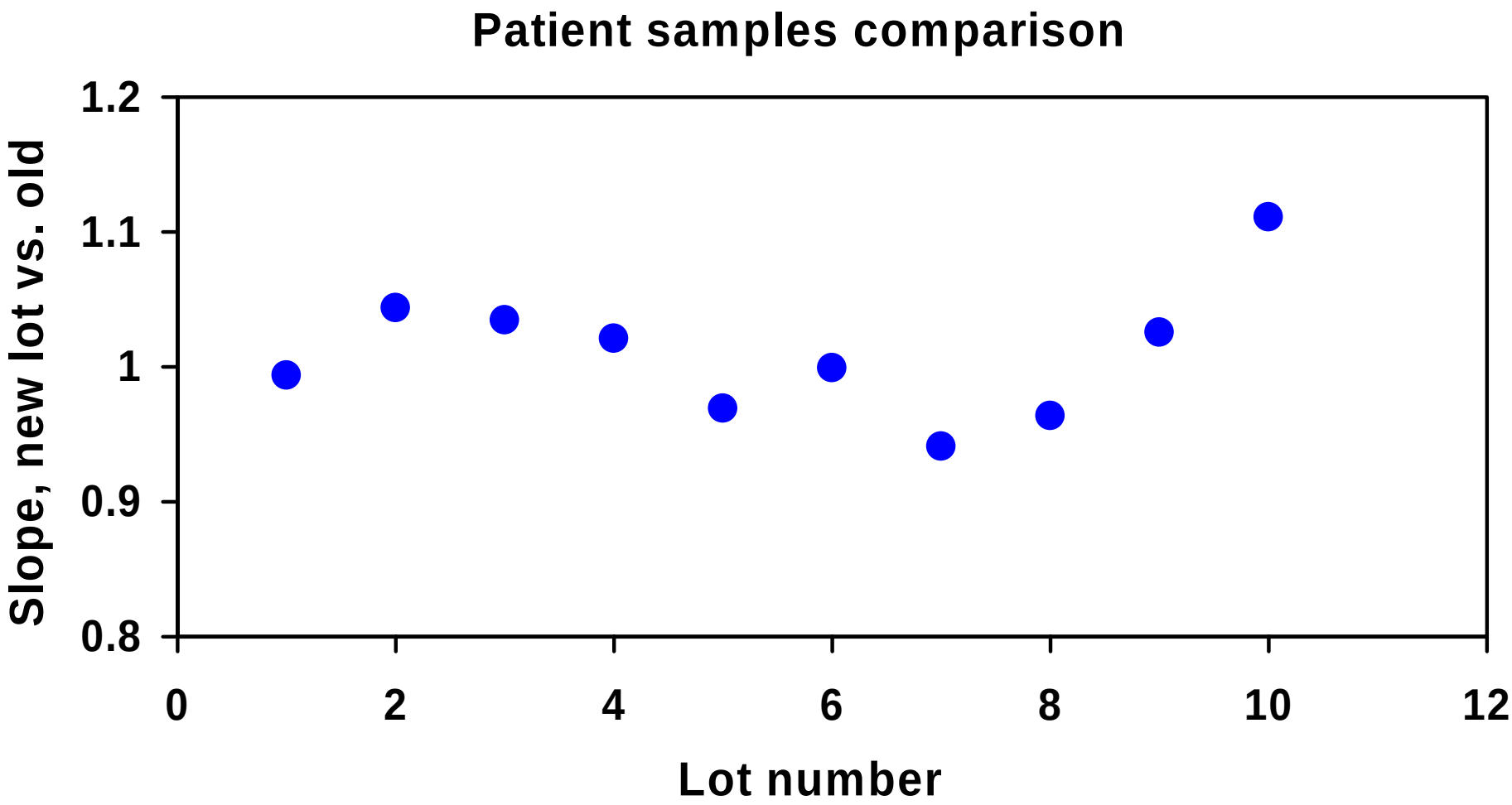
Lot to lot variability: T4



Lot to lot variability: TSH



Lot to lot variability: Troponin I



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

	POC Meter	Lab	Meter	Lab
Mean, pg/mL	94	50	1586	1785
SD, pg/mL	14	5	357	160
CV	16%	10%	23%	9%

Hemoglobin A1c

	POC Meter	Lab	Meter	Lab
Mean, %	4.4	5.8	9.4	10.7
SD, %	0.3	0.2	0.5	0.4
CV	6%	4%	5%	4%

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