# Quality Control

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# Definition

- QC systems monitor the analytical process; detect and minimize errors during the analysis and prevent reporting of erroneous test results.
- It uses statistical analysis of test system data
- Requires following published rules
  - Westgard Rules

# Consequences

- Potential consequences include:-
  - patient misdiagnosis
  - delays in treatment
  - increased costs
- Even a small calibration bias can effect treatment rates:
  - 1% +ve bias in cholesterol result
    → 5% increase in patients exceeding the treatment cut-off
  - 3% +ve bias
    → 15% increase in patient treatment.

# What is a Control?

- material that contains the substance being analyzed
  - include with patient samples when performing a test
- used to validate reliability of the test system
  - run after calibrating the instrument
  - run periodically during testing

# Types of QC

- Internal
- Daily
- Establishment of reference ranges
- Validation of a new reagent lot and/or shipment
- Following instrument repair

- External
- Proficiency testing
  - Determination of laboratory testing performance by means of intralaboratory comparisons
  - CAP, CLIA, The Joint Commission requirement
  - Must be integrated within routine workload and analyzed by personnel who are running the tests.
  - Ongoing evaluation of results to correct for unacceptable results
  - Used to access employee competency

# Causes of error

- Pre-analytical:-
  - errors before the sample reaches the laboratory
- Analytical:-
  - errors during the analysis of the sample
- Post-analytical:-
  - errors occurring after the analysis

# Test results

## Variations, Errors, Interferences

- Variations
- *Clinical variations* within an individual and between individuals
- *Analytical variations*-no test is perfect. All tests have some degree of variations for repeated measurements of the same sample.
- The final test result is affected by factors that occur
  - Pre-analytically
  - At the time of the test
  - After the test is completed

# Why Analytical Results Vary

## Inter-individual Variation

- Age
- Sex
- Race
- Genetics
- Long term health status

## Pre-analytical Variation

- Transport
- Exposure to UV light
- Standing time before separation of cells
- Centrifugation time
- Storage conditions

# Pre-analytical errors

- Collection
  - Was the right tube used?
  - Was venipuncture performed correctly?
  - Was the specimen properly stored?
- Identification
  - Was the blood collected from the correct patient?
  - Was the blood correctly labeled?
    - Patient name, ID, date, time of collection, phlebotomist

# Specimen identification

- One of the common sources of erroneous lab results is misidentified specimens
- The lab is required to have a clear and rational policy for identifying specimens, and handling misidentified specimens

# Prolonged venous stasis

Blocking the flow of blood with the tourniquet with eventually lead to a sieving effect. Small molecules, water and ions are forced out blood vessels and larger molecules are concentrated

- Increases Total Protein, proteins, iron (Fe), cholesterol, bilirubin
- Decreases potassium

# Supine vs. sitting or standing

- Going from lying (supine) to upright reduces total blood volume by about 700 ml
- The following may decrease by 5-15% in the supine patient:
  - Total protein
  - Albumin
  - Lipids
  - Iron
  - Calcium
  - Enzymes

# Specimens requiring special handling

- Should be placed *immediately* on ice
  - Lactate
  - Ammonia
  - Acid phosphatase
  - Plasma catecholamines

# Significantly affected by hemolysis:

- Hemolysis-rupture of red blood cell
  - Can be due to improper collection
  - End result is dumping cellular contents into blood. Mild dilution effect in some analytes
- Significant increase in potassium, magnesium, phosphorous

# Interferences

- Hemolysis
  - The release of hemoglobin into blood can effect the reactions comprising  specific tests
  - Causes serum or plasma to be red and can effect tests that are colorimetric
- Lipemia (lots of fats) and proteinemia (lots of protein)
  - Causes serum or plasma to be become turbid. This can effect colorimetric and turbidometric based tests
  - Also can cause a dilution effect. Fats and proteins are large and displace water in plasma. Can give falsely low results especially for Na

# Interferences

- Human Anti Animal Antibodies.
  - Occurs in individual that have been exposed to foreign immunoglobins
  - Can significantly increase or decrease immunoassay based tests since all utilize animal antibodies, particularly mouse. Referred to as Human Anti Mouse Antibodies (HAMA)
  - Tests usually contain reagent to clear HAMA
  - Technicians performs a dilution test to determine if HAMA are present
  - Generally have to send to another lab to test by alternate method or different antibody

# Types of Control Materials

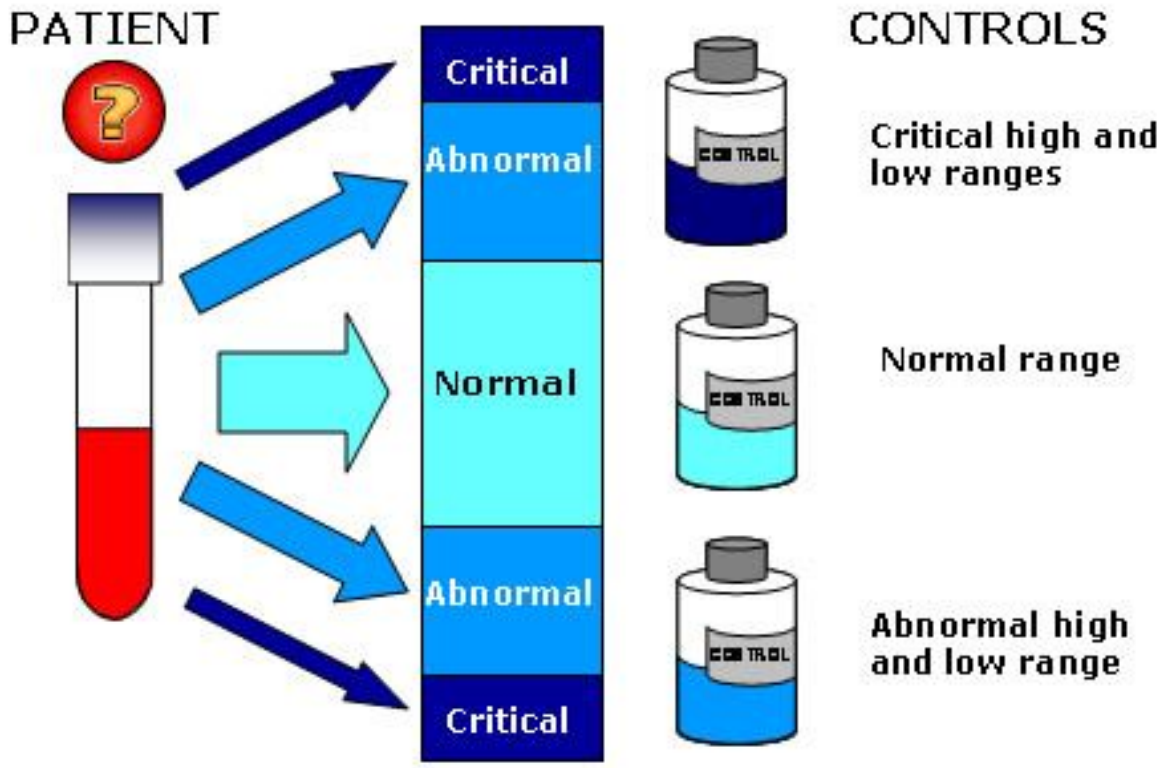
- may be frozen, freeze-dried, or chemically preserved
- requires very accurate reconstitution if this step is necessary

# Sources of Controls Materials

- commercially prepared
- made “in house”
- obtained from another laboratory, usually central or reference laboratory

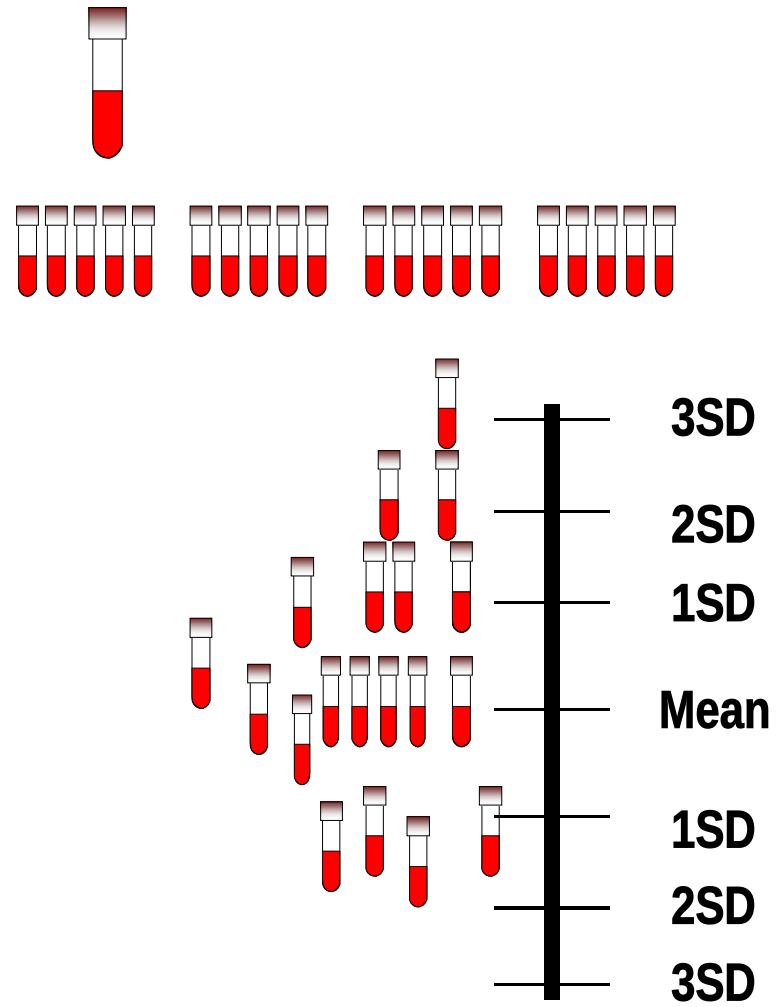
# Choosing Control Materials

- values cover medical decision points
- similar to the test sample
- controls are usually available in high, normal, and low ranges



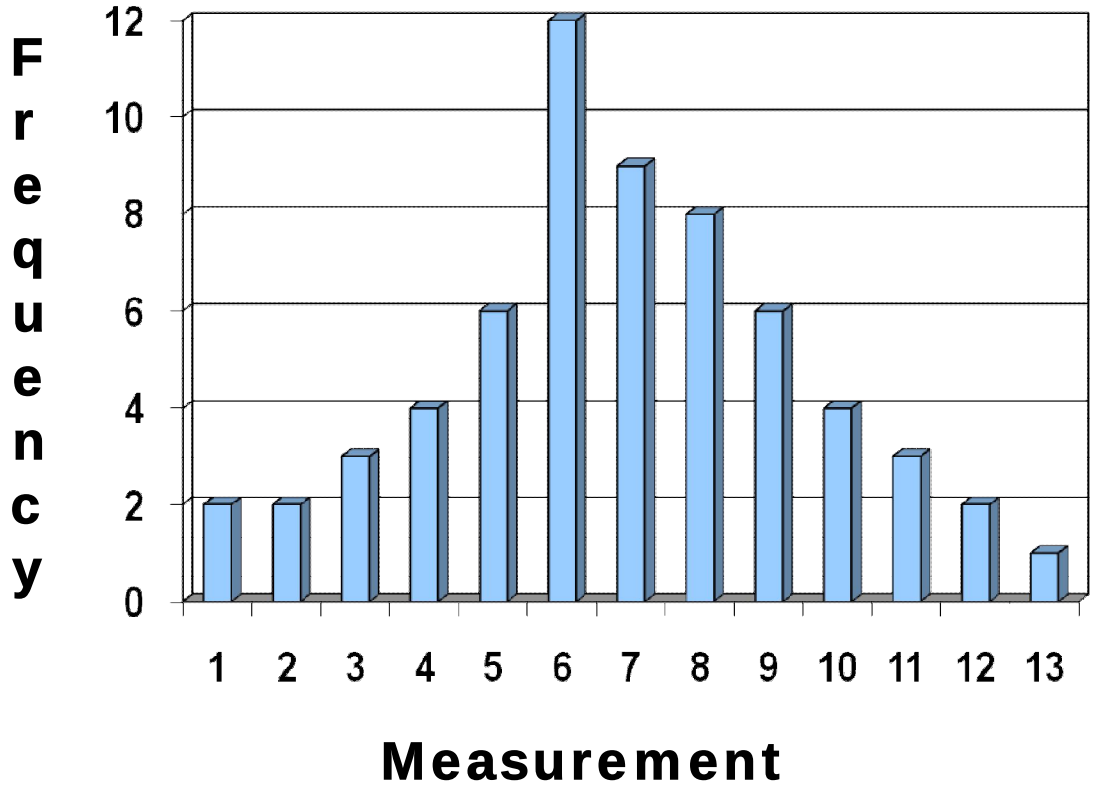
# Steps in Implementing Quantitative QC

- obtain control material
- run each control 20 times over 30 days
- calculate mean and +/-1,2,3 Standard Deviations



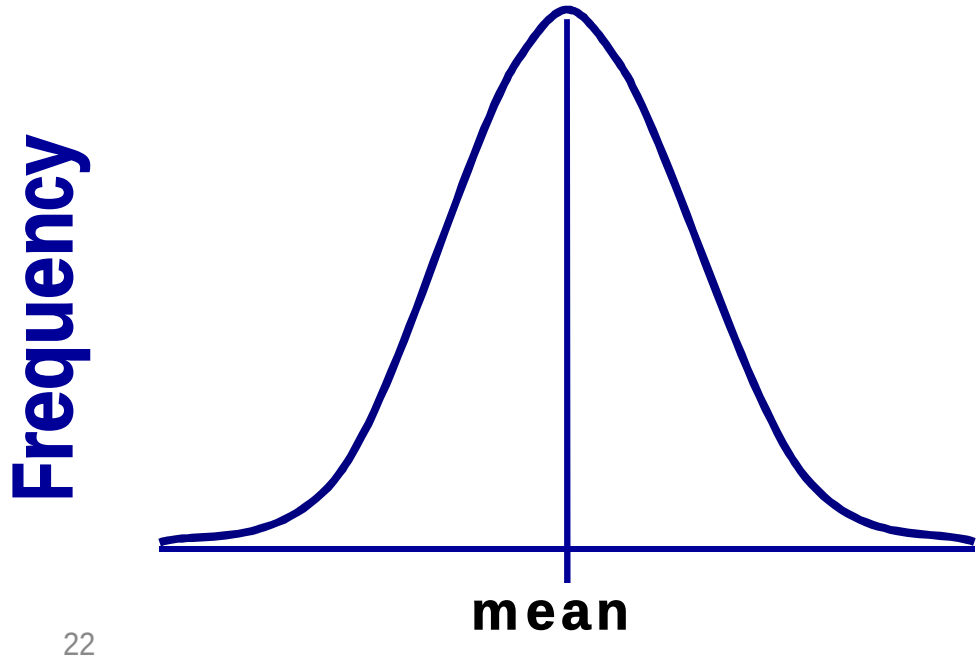
# Measures of Central Tendency

Although variable, sets of data are distributed around a central value



# Normal distribution

- all values symmetrically distributed around the mean
- characteristic “bell-shaped” curve
- assumed for all quality control statistics



Considering the terms accuracy and precision:

The first distribution A

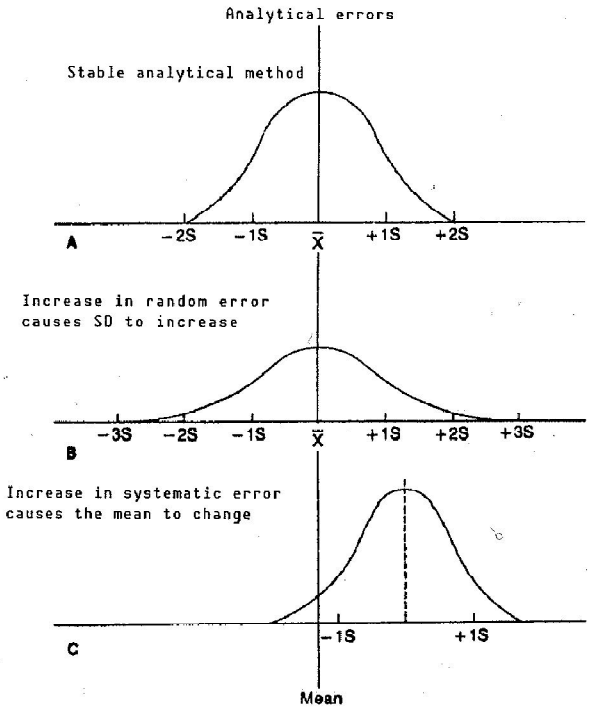
demonstrates accuracy as its mean is located in the center of the curve.
demonstrates precision as all the data is grouped together as represented by 'well rounded' bell curve.

Distribution B

has accuracy, but lacks precision as the data is more spread out resulting in a 'flatter' curve.

Distribution C

the nice peak indicates precision, but it is off the mean.



Quality Control is used to monitor the **accuracy** and the **precision** of the assay.

What are accuracy and precision?

# Definitions

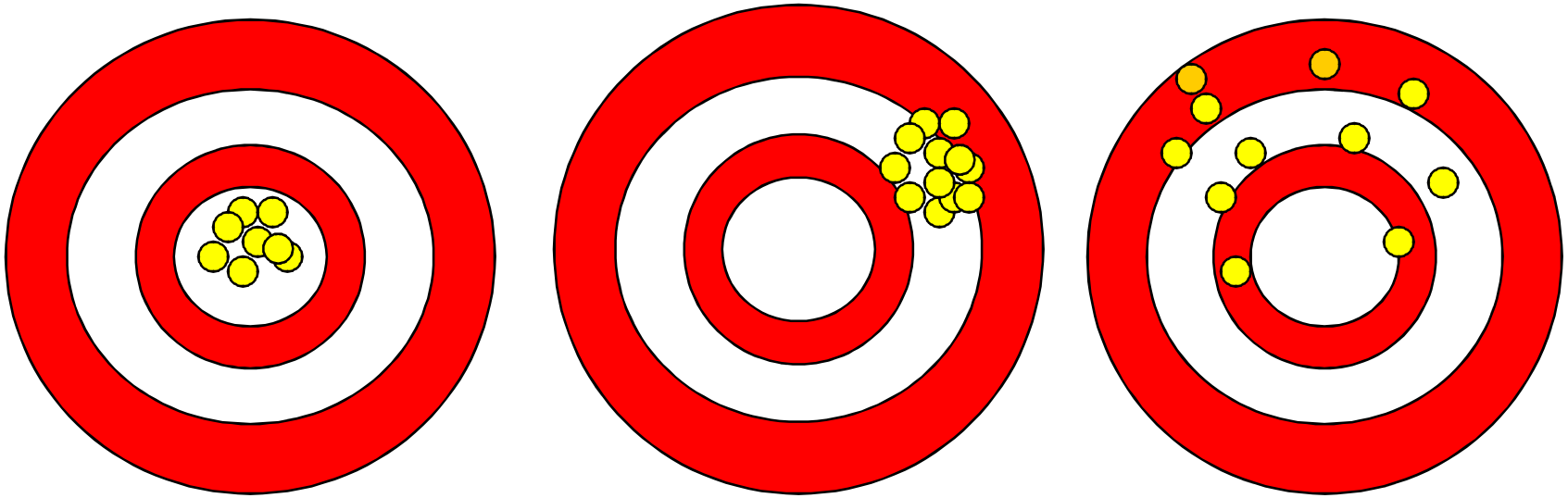
| | |
|---|---|
| **Accuracy** | **The closeness of measurements to the true value** |
| **Precision** | **The amount of variation in the measurements** |
| **Bias** | **The difference between the expectation of a test result and an accepted reference value** |

# Accuracy and Precision

Accurate and Precise

Precise but Biased

Imprecise



**Accurate = Precise but not Biased**

# Standard Deviation (SD)

SD is the principle measure of variability used in the laboratory

$$SD = \sqrt{\frac{\sum (x_1 - \bar{x})^2}{n-1}}$$

**Standard Deviation – Statistical Formula**

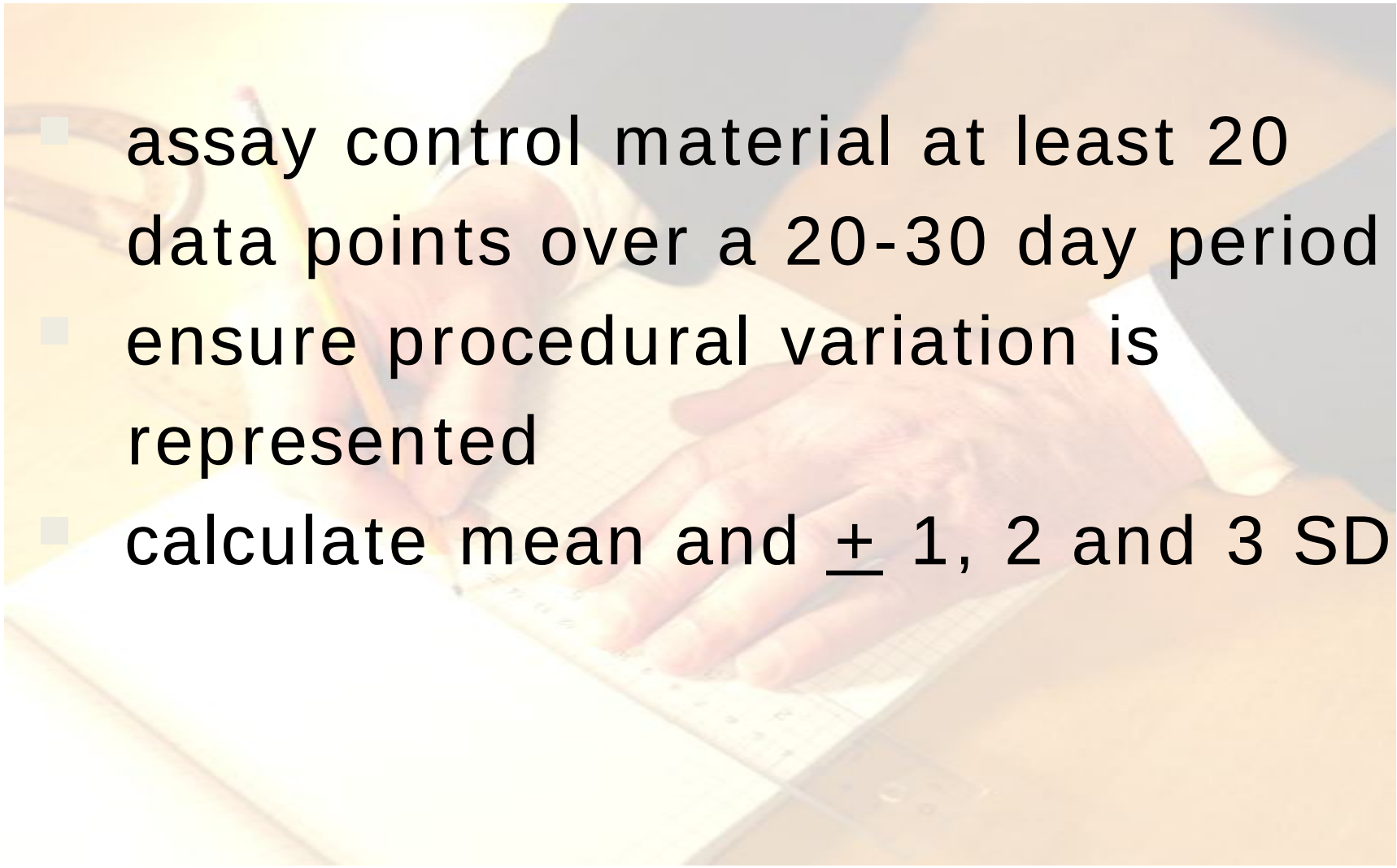
# Coefficient of Variation

The coefficient of variation (CV) is the SD expressed as a percentage of the mean.

$$CV = \frac{SD}{mean} \times 100\ \%$$

- CV
- CV is used to compare methods
- CV ideally should be less than 5%

# Statistics for Quantitative QC



- assay control material at least 20 data points over a 20-30 day period
- ensure procedural variation is represented
- calculate mean and $\pm$ 1, 2 and 3 SD

# Number of Controls

Interpretation depends on number of controls run with patients' samples.

- **Good**: If one control:
  - accept results if control is within ± 2SD unless shift or trend
- **Better**: If 2 levels of controls
  - apply Westgard multirule system

# Detecting error

- **random error**: variation in QC results with no pattern- only a cause for rejection if outside 2SDs.
- **systematic error**: not acceptable, correct the source of error

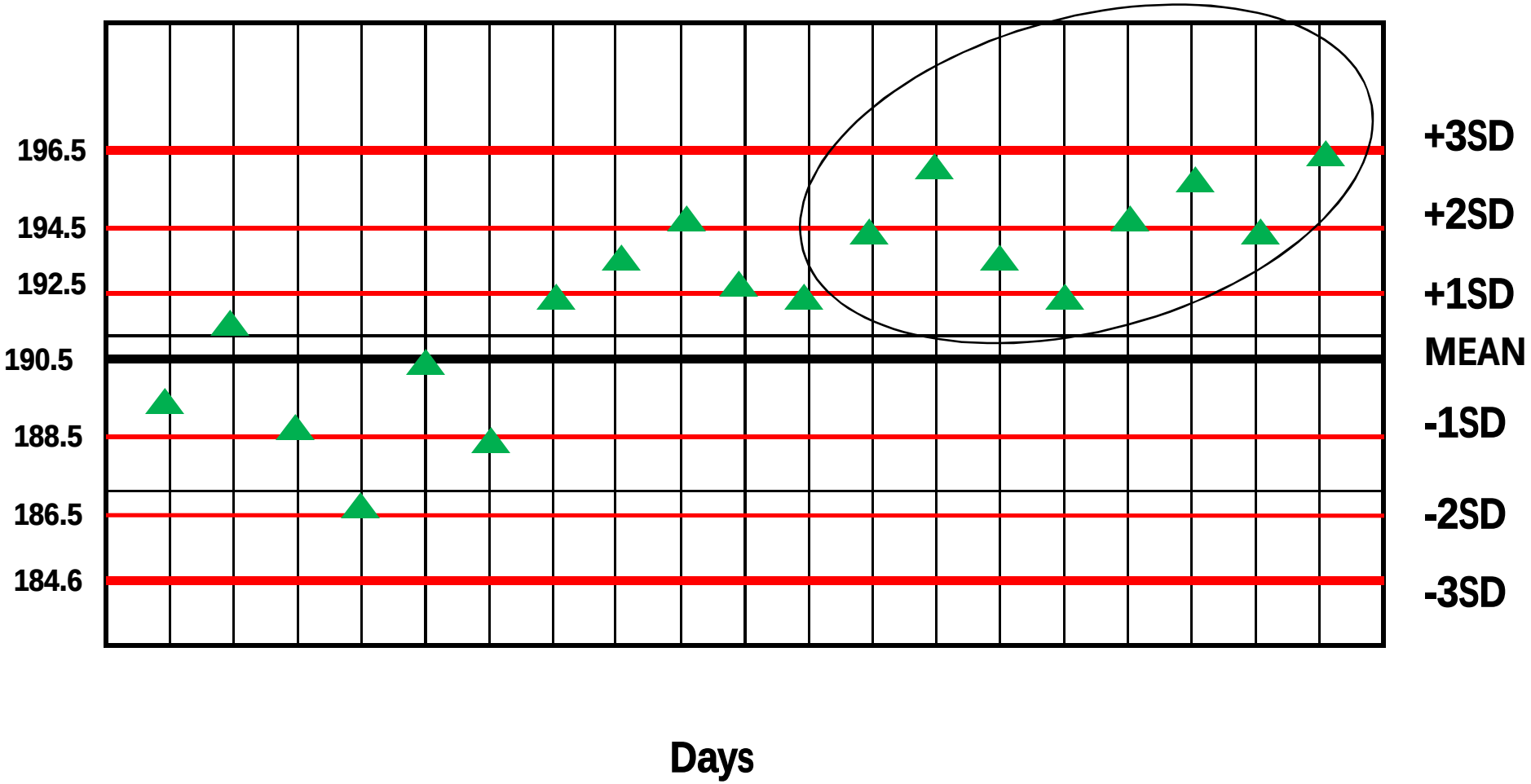
  Examples:

  – **shift**–control on one side of the mean 6 consecutive days

  – **trend**–control moving in one direction– heading toward an “out of control” value

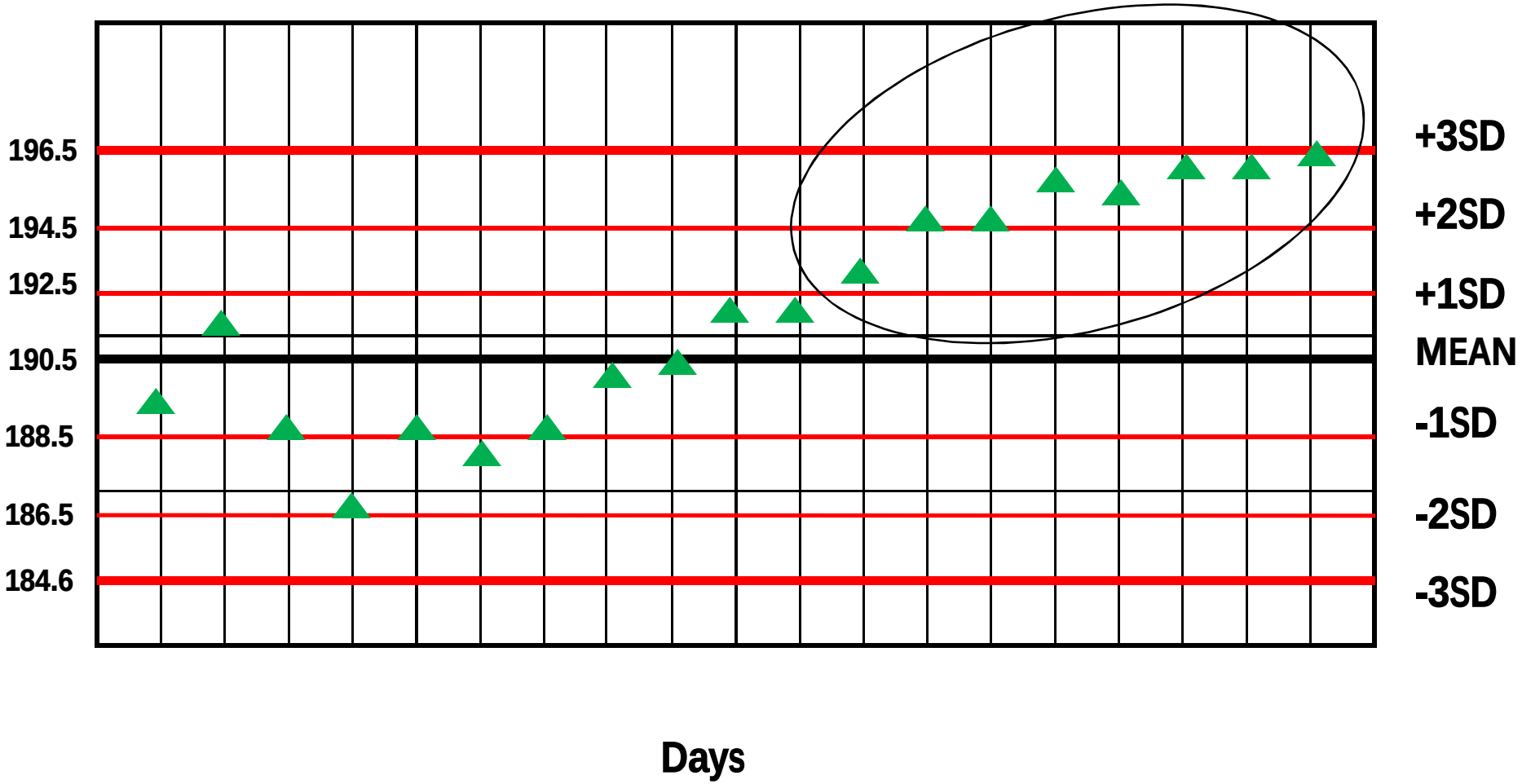
# Levey-Jennings Chart

## Shift



# Levey-Jennings Chart

## Trend

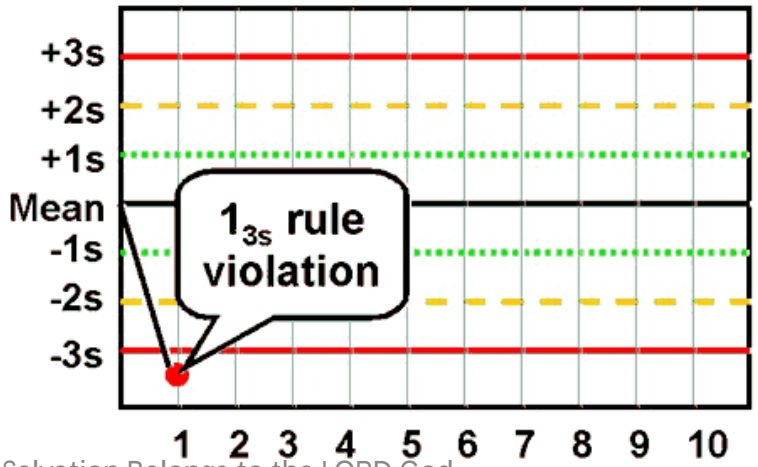


Other rules

# WESTGARD RULES

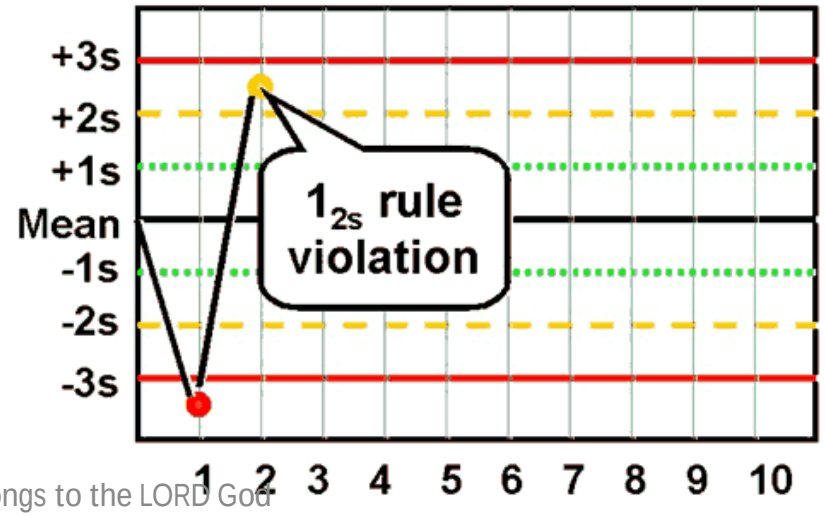
# Quality Control

- Common Westgard rules
  - $1_{3s}$
    - A single control measurement exceeds three standard deviations from the target mean
  - Action - Reject



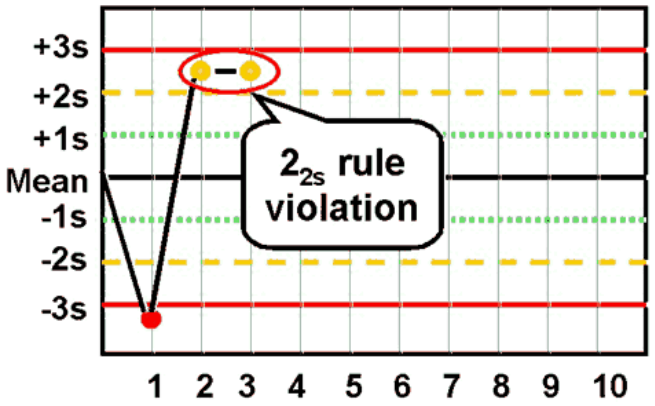
# Quality Control

- Common Westgard rules
  - $1_{2s}$
    - A single control measurement exceeds two standard deviations from the target mean
  - Action – must consider other rule violations
    - This is a warning



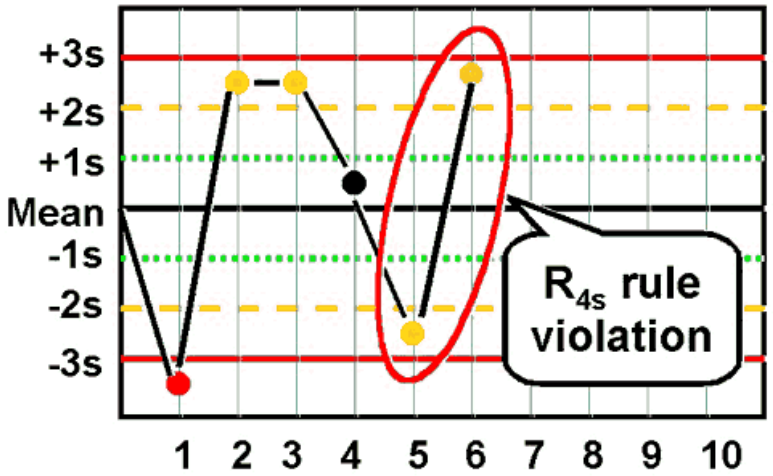
# Quality Control

- Common Westgard rules
  - $2_{2s}$
    - Two consecutive control measurements exceed the same mean plus 2S or the same mean minus 2S control limit.
  - Action – Reject



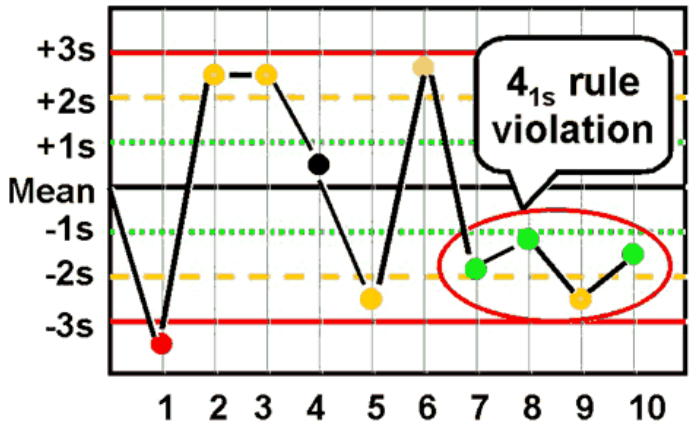
# Quality Control

- Common Westgard rules
  - $R_{4s}$
    - One control measurement in a group exceeds the mean plus 2S and another exceeds the mean minus 2S.
  - Action – Reject

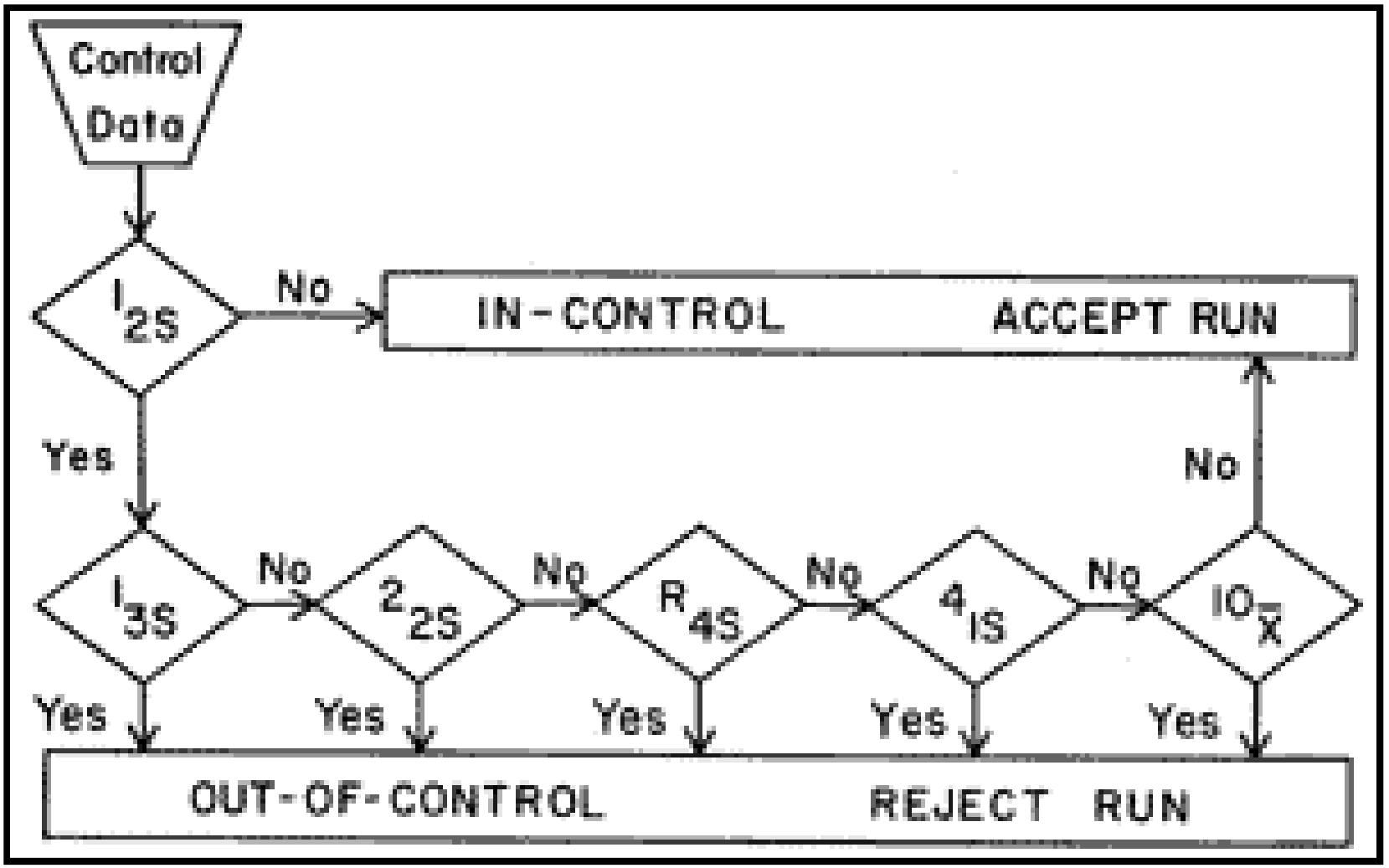


# Quality Control

- Common Westgard rules
  - $4_{1s}$
    - Four consecutive control measurements exceed the same mean plus 1S or the same mean minus 1S control limit.
  - Action – Reject



# Westgard Multirule QC



# Quality Control

- Other QC checks
  - Delta checks
    - Compares a current test result on a patient to last run patient test, flagging results outside expected physiological variation.
    - A 1981 study concluded delta checks are useful, despite a high false-positive rate.
    - But another study suggests looking at delta checks with tests that have a high clinical correlation (e.g., ALT and AST)

# If QC is out of control

- **STOP testing**
- identify and correct problem
- repeat testing on patient samples and controls after correction
- **Do not report patient results** until problem is solved and controls indicate

  proper performance

# Solving out-of-control problems

- identify problem
- refer to established policies and procedures for remedial action

# Possible Problems

- degradation of reagents or kits
- control material degradation
- operator error
- failure to follow manufacturer’s instructions
- an outdated procedure manual
- equipment failure
- calibration error

THANK YOU