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Laboratory Quality Management System

Module 12: Process Control: Quality Control for Quantitative Tests

Venue:

Presenter:

Date:

Introduction

- (QC) is a component of process control
- Monitors and allows for detecting errors in the testing system.
- Errors may be due to test system failure, adverse environmental conditions, or operator performance.
- Gives confidence that test results are accurate and reliable before patient results are reported.

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Module Outline

- Control materials
- Establishing the value range
- Graphical representation of control ranges
- Interpreting quality control data
- Using quality control information

The Quality Management System

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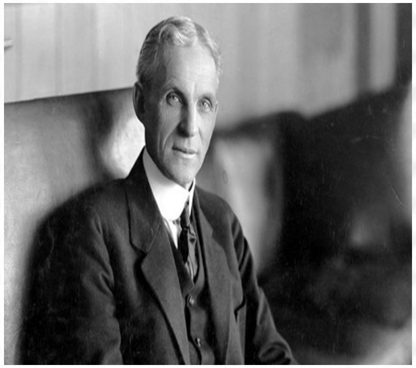
Whether you think you can or whether you think you can't, you're right!

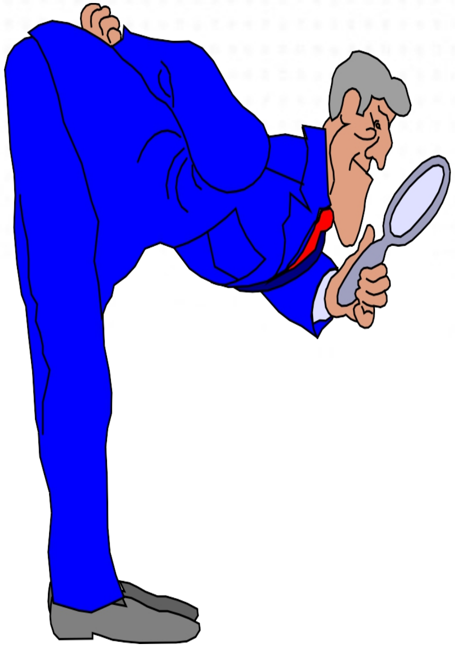
(*Henry Ford*)



Quality is……

- Invisible when GOOD

- Impossible to ignore when BAD



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Quantitative Tests

- Measure the quantity of a particular substance in a sample
- Quality control for quantitative tests is designed to assure that patient results are:
  - Accurate
  - Reliable

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Implementation steps

- Establish policies and procedures
- Assign responsibility, train staff
- Select high quality controls
- Establish control ranges
- Develop graphs to plot control values - Levey-Jennings charts
- Monitor control values
- Develop procedures for corrective action
- Record all actions taken

What is Quality Control?

- Part of quality management focused on fulfilling quality requirements *(ISO 9000:2005)*
- Included during each assay run to verify that the test is working prop

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2. Control Materials

Defining Control materials

- Contain an established amount of the substance being tested– the analyte.
- Controls are tested at the same time and in the same way as patient samples.
- The purpose is to validate the reliability of the test system evaluate the operator's performance and environmental conditions that might impact results.

Purpose of running IQC

- **Check accuracy of test system**

  -Compare observed to expected results

- **Assess precision of test system**

  -within run and between precision

- **Predict and or detect potential errors.**

  -Trend Analysis

- **Assure Stability of analytical runs**

Frequency of QC Runs

- **Stability of method**

  (daily, batch, probability of rejecting analytical run)

- **Risk of harm to patient**

  action that can be taken before error could be detected.

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QC-Quantitative Tests

Regular IQC performance along with patient samples

Manufacturer Ranges/lab ranges used as limits

Comparison of **observed results** to **expected results**

CAPA if IQCs outside of the limits

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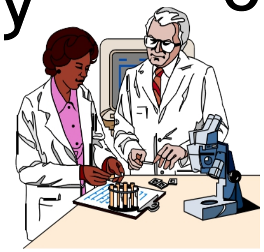
Control Vs. Calibrator

Control

- Similar to patient's samples with established concentration
- Ensure that procedure is working properly

Calibrator

- Substance with a specific concentration
- Set the measuring points of a scale



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Quality Control-Materials

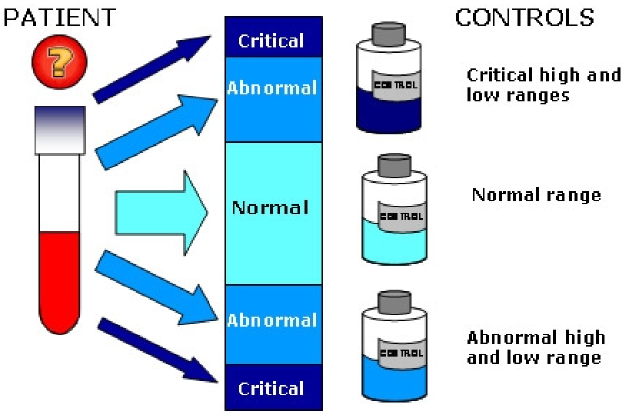
- Should approximate same matrix as patient samples

- Stable over long periods of time.

- Minimal Vial-Vial Variability.

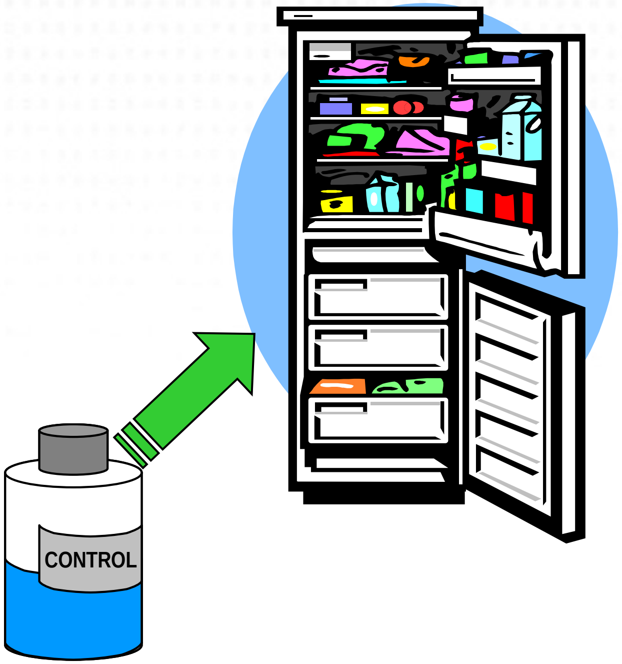
Choosing Control Materials

- Values cover medical decision points
- Similar to the test sample
- Controls are usually available in high, normal, and low ranges



Preparation and Storage of Control Material

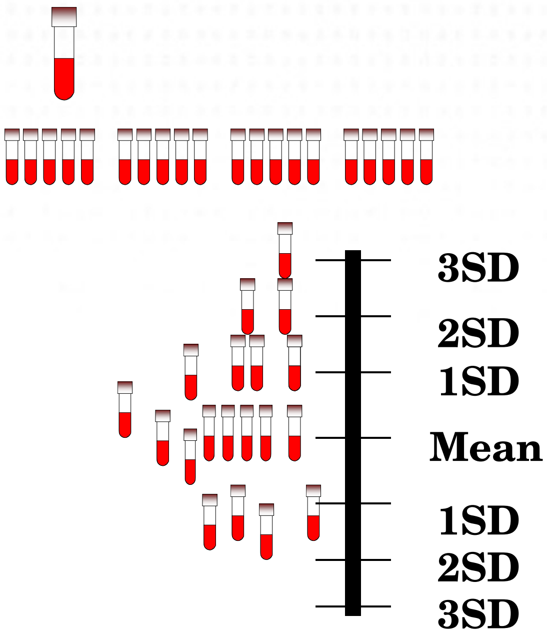
- Adhere to manufacturer's instructions
- Keep adequate amount of same lot number
- Store correctly



3. Establishing the Value range for control materials

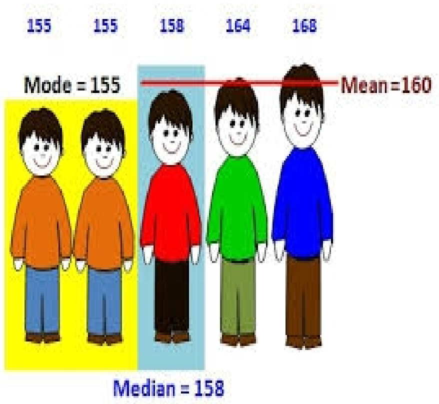
Steps in Implementing Quantitative QC

- Obtain control material
- Run each control 20 times over 30 days
- Calculate mean and +/- 1,2,3 Standard Deviations



Measures of central tendency

- Measures of central tendency provide us with a measure that describes the entire dataset using a single value that represents the center, or middle of its distribution.
- Include:
  - *Mean*
  - *Mode*
  - *Median*



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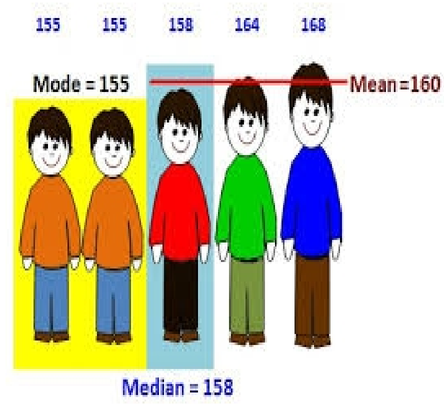
Measures of central tendency: Mean

Mean

is the sum of the values for all observations in a dataset divided by the number of observations. Also called Average.



Mean- formula

$$\bar{X} = \frac{\sum X}{n}$$

Where $\bar{X}$ = Mean

$\sum X$ = Sum of values

n = Number of values

Example

10, 15,30, 7, 42, 79 and 83

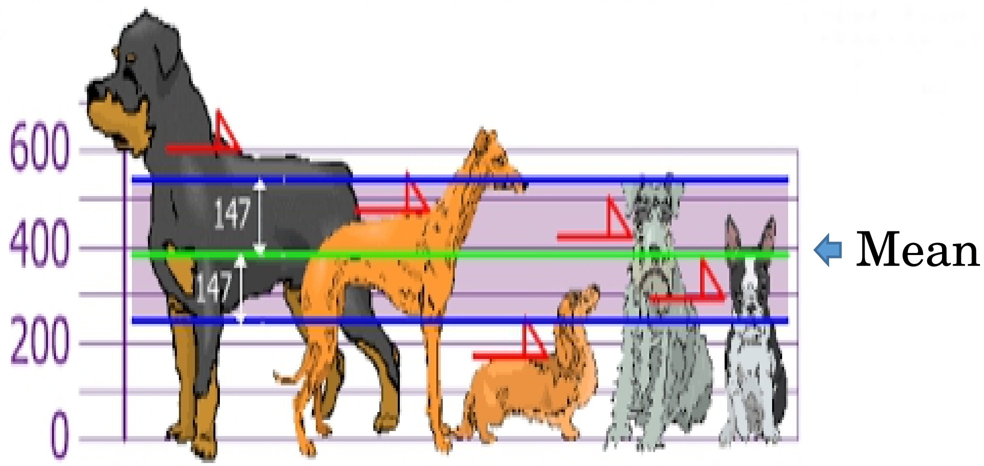
$$\bar{x} = \frac{\sum x}{n}$$

,where $\bar{x}$ is sample mean.

$$\bar{x} = \frac{10+15+30+7+42+79+83}{7}$$

Measures of spread

Describe how similar or varied the set of observed values of a dataset are.



Variance, Standard deviation, CoV, etc

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Measures of spread: Variance

Variance (σ^2) is a measurement of the spread between values in a data set

For samples:

$$\text{variance} = s^2 = \frac{\Sigma(x-\bar{x})^2}{n-1}$$

$$\text{standard deviation} = s = \sqrt{s^2}$$

Calculating Formula

$$s^2 = \frac{\Sigma x^2 - \frac{(\Sigma x)^2}{n}}{n-1}$$

For populations:

$$\text{variance} = \sigma^2 = \frac{\Sigma(x-\bar{x})^2}{n}$$

$$\text{standard deviation} = \sigma = \sqrt{\sigma^2}$$

Calculating Formula

$$\sigma^2 = \frac{\Sigma x^2 - \frac{(\Sigma x)^2}{n}}{n}$$

Measures of spread: Standard Deviation

Standard deviation is the square root of the variance

For Sampl e

$$s = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}}$$

For population

$$\sigma = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \mu)^2}{n}}$$

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Measures of spread: Coefficient of Variation (CV or CoV)

CV is the ratio of the standard deviation to the mean (usually expressed in percentage)

$$CV\ (\%) = \left(\frac{Standard\ deviation}{Mean}\right) \times 100$$

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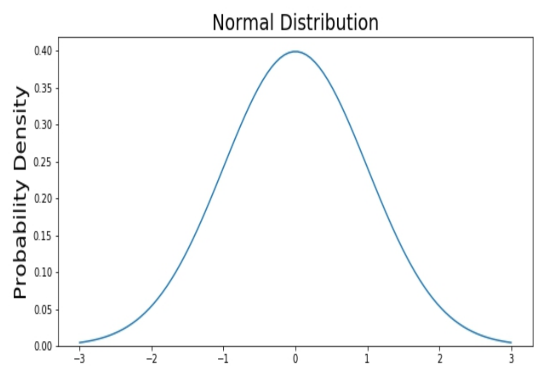
Normal distribution

A function that represents the distribution of many random variables as a symmetrical bell-shaped graph.

Most measurements in the laborat rmal population



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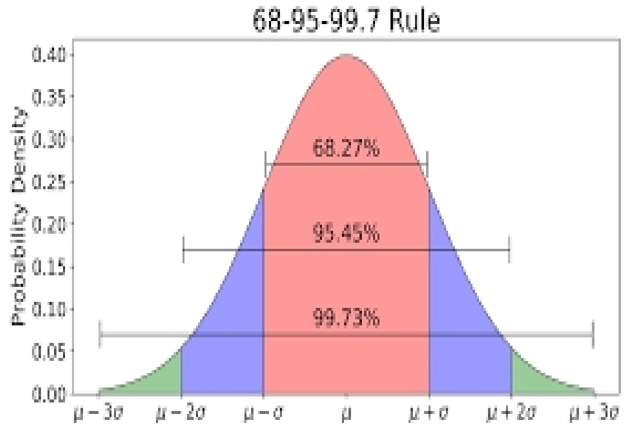
Normal distribution: The Central Limits Theorem

Also called the empirical rule (68:95:99.7)



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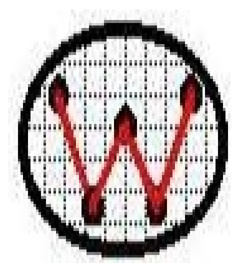
4. Graphically Representing Control Ranges

Monitoring Quantitative Quality Control Data



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Control Charts

- A graphical method for displaying control results
- Plot of Observed values and expected values
- Expected values represented by control limits (acceptable range of values) e.g. mean, 1, 2 3.

Control Charts

- When observed values falls within the control limit- method is performing properly

- When values falls outside control limit – problem may be developing

Control Charts

- Most common: Shewhart, **Levey Jennings(LJ)**, run chart
  - Mean is the target value
  - 1s, 2s, 3s are control limits for the chart
  - ±1S, **68%**, ±2S- **95%**, ±3S- **99.7%**

- used to assess method performance and continual improvement.

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Levey-Jennings (LJ) Chart

- Graphical method for evaluating whether process is in control or out of control.

- Simple data analysis and display

- Also used for trends, shifts

5. Interpreting QC data

ACTIVITY 12-1 Calculation of Mean and Standard Deviation

Purpose: To practice calculating the mean and standard deviation (SD) of a set of data to use for establishing control ranges

Suggested time: 15 minutes

Instructions: Calculate the mean and SD using Annex 12-A and the two Standard Deviation Worksheets provided.

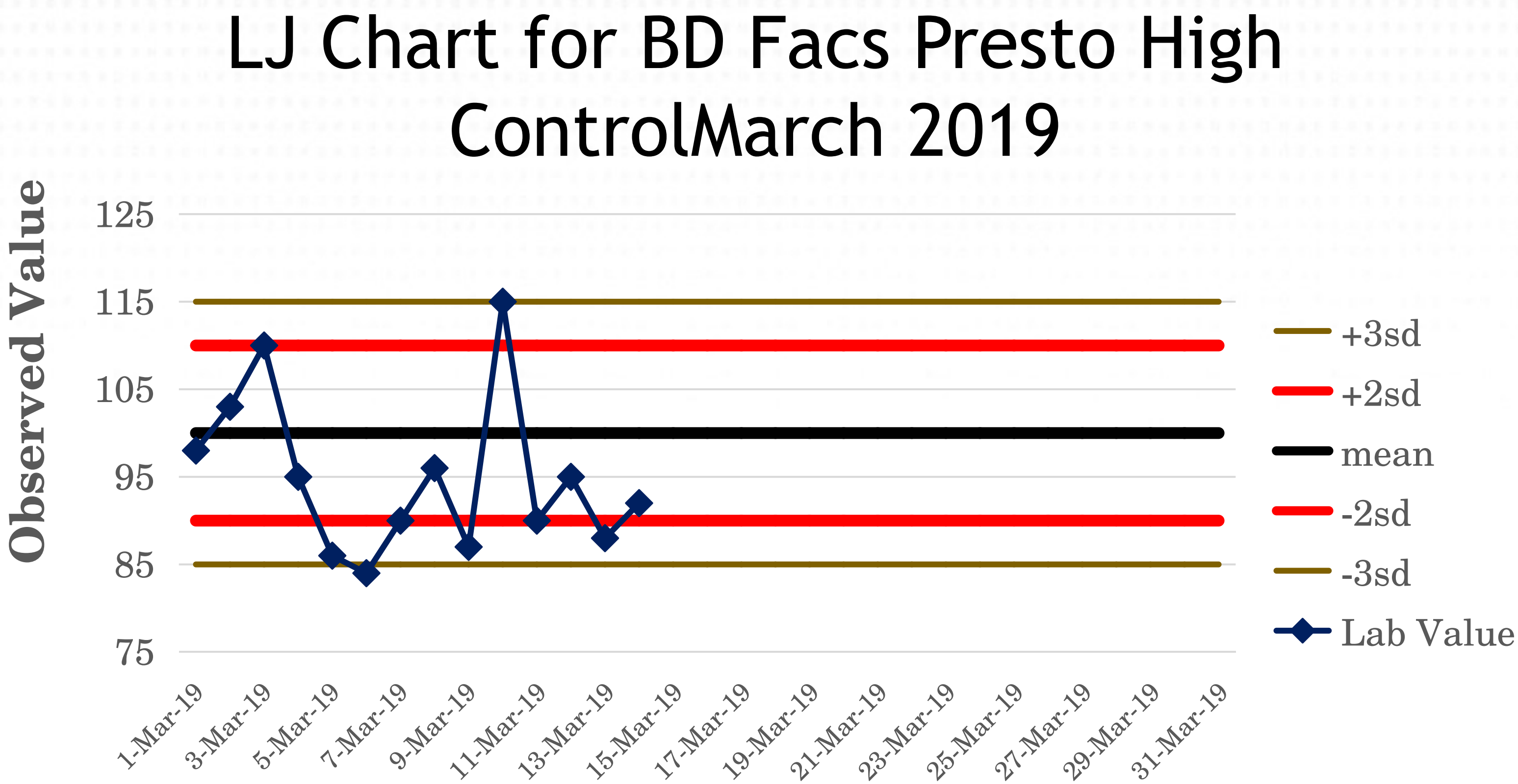
Activity 12-2 Creation of Levy-Jennings Charts

Purpose: To create Levey-Jennings Charts to monitor examination results by visualizing daily control data.

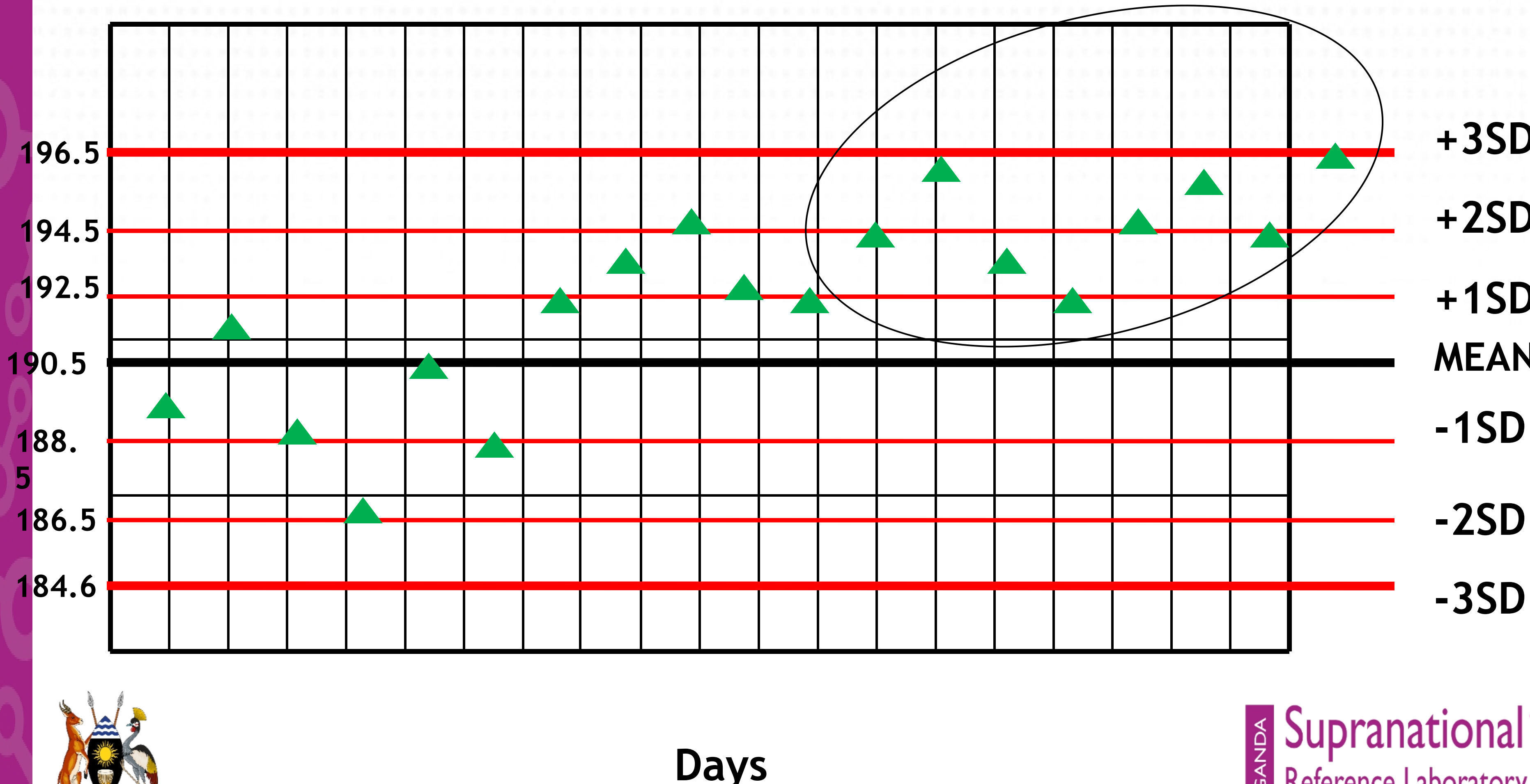
Suggested time: 15 minutes

Instructional method: Individual Assignment:

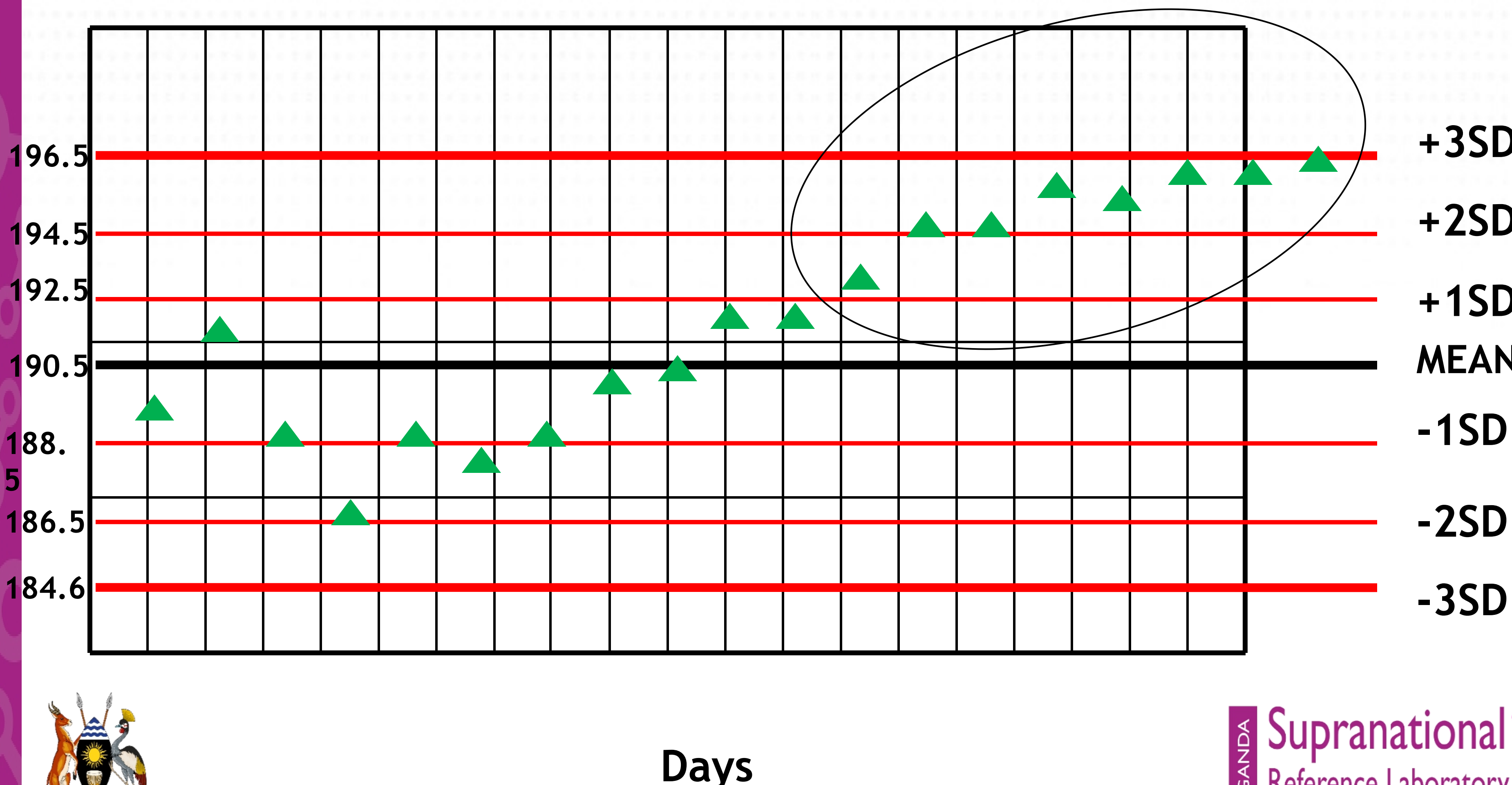
Levey-Jennings (LJ) Chart



Levey-Jennings Chart Shift



Levey-Jennings Chart Trend



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Monitoring QC Data

- **Use L-J Charts**

- Plot observed values for each run, make decision regarding acceptability of run

- Monitor over time the precision and accuracy of the equipment/method

- Review charts at defined intervals and take necessary action.

Westgard Rules

- Developed by **Dr. James O. Westgard**
- Uses decision criteria or control rules
- Allows determination of whether an analytical run is "**in-control**" or "**out-of-control**"

Dr. Westgard

Why use Westgard Rules

- Reduce Costs while maintaining a high level of certainty that our process are in control

- Reduce false rejection rates without compromising quality

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Westgard Rules

- 1_{2S} rule
- 1_{3S} rule
- 2_{2S} rule
- R_{4S} rule
- 4_{1S} rule
- 10_{X} rule

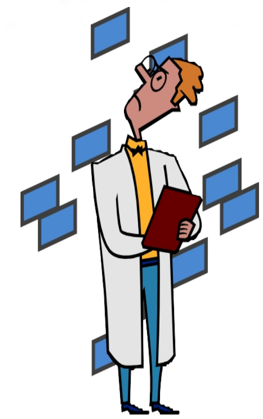
Nomenclature

- 1_{2s}- indicates 1 control value (observed) exceeds 2S control limits

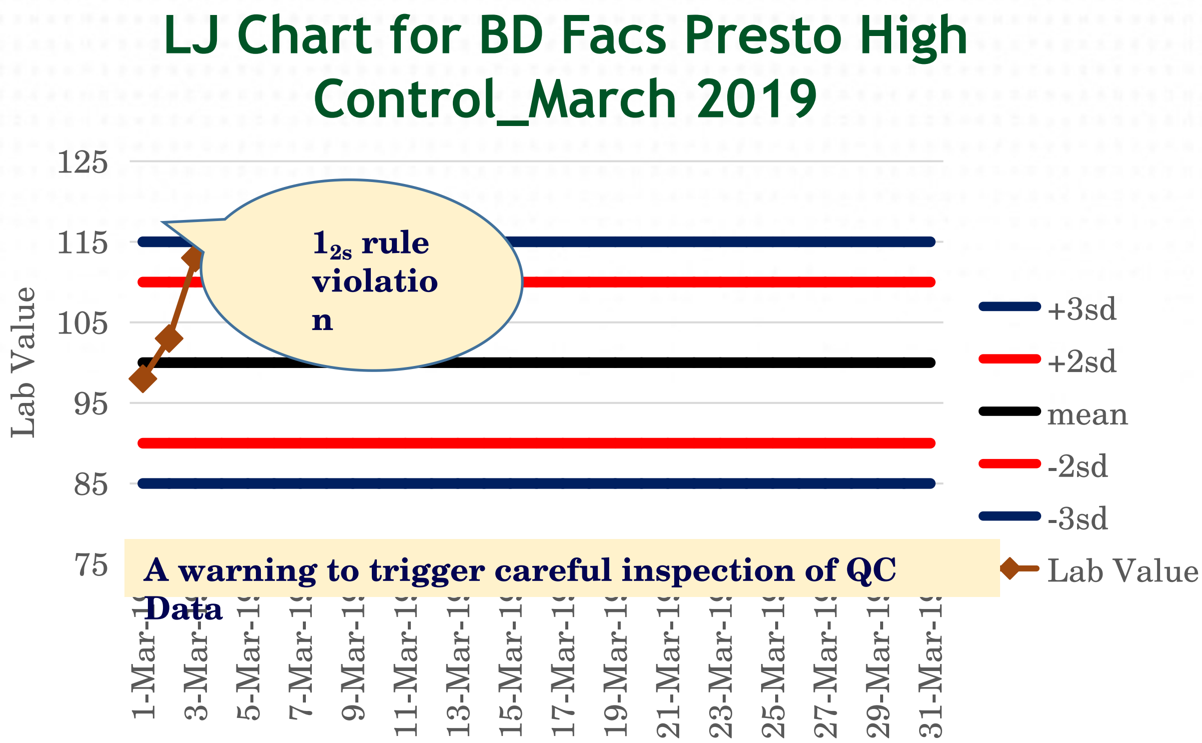
Westgard 1_{2s} Rule

1_{2S} rule: "warning rule"

- 1 control value exceeds ±2SD
- Alerts to possible problems
- Not cause for rejecting a run
- Must then evaluate the 1_{3S} rule



Westgard 1_{2s} Rule

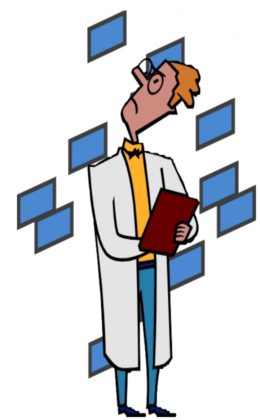


A warning to trigger careful inspection of QC Data

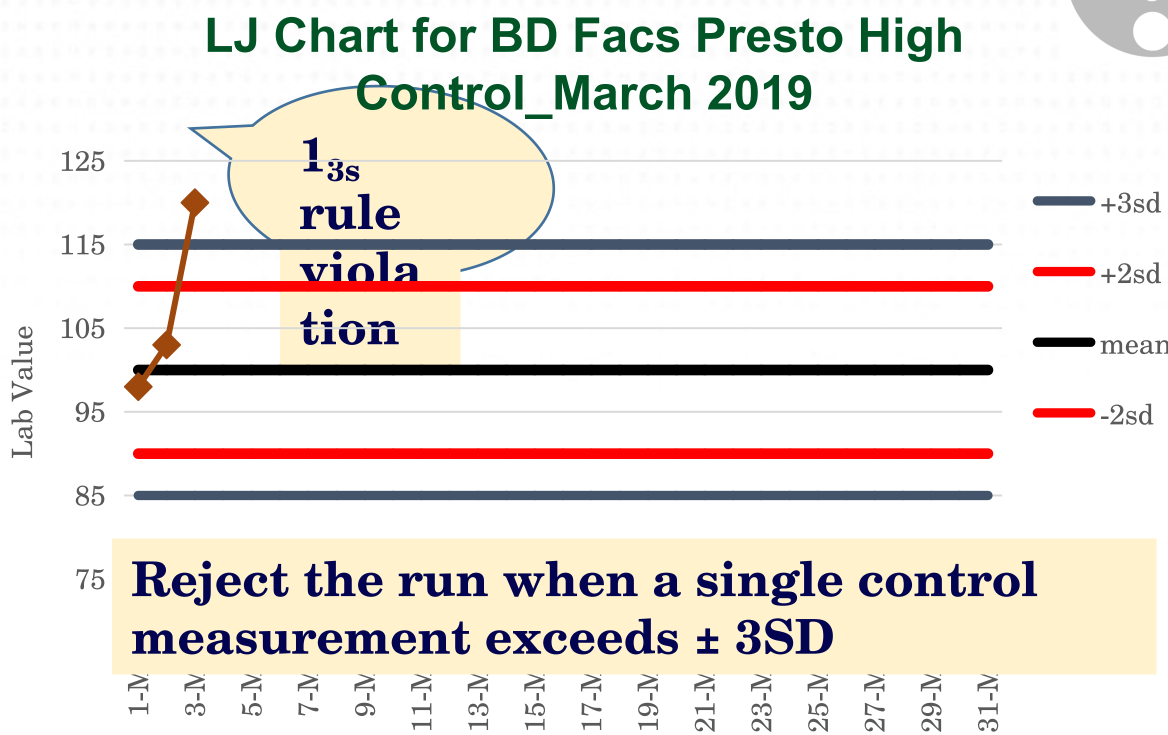
Westgard 1_{3s} Rule

<u>1_{3S} rule</u>

- 1 control value exceeds ± 3SD
- Run must be rejected



Westgard 1_{3s} Rule

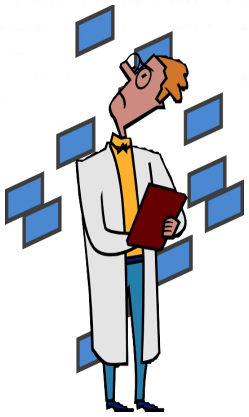


Reject the run when a single control measurement exceeds ± 3SD

Westgard 2_{2s} Rule

2_{2S} rule

- **2** consecutive control values exceed ± **2SD** in the same direction
- Patient results cannot be released
- Requires corrective Action



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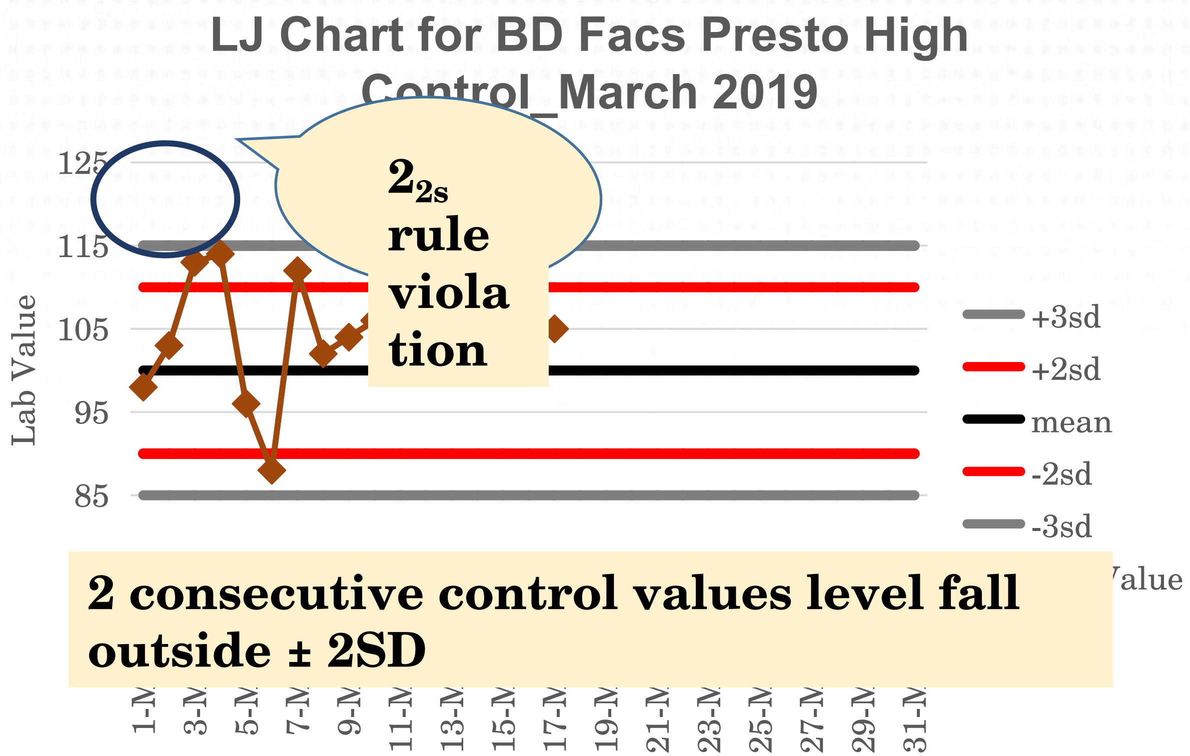
Westgard 2_{2s} Rule

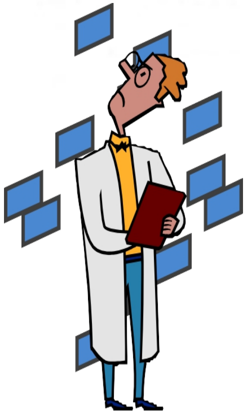


2 consecutive control values level fall outside ± 2SD

Westgard R_{4s} Rule

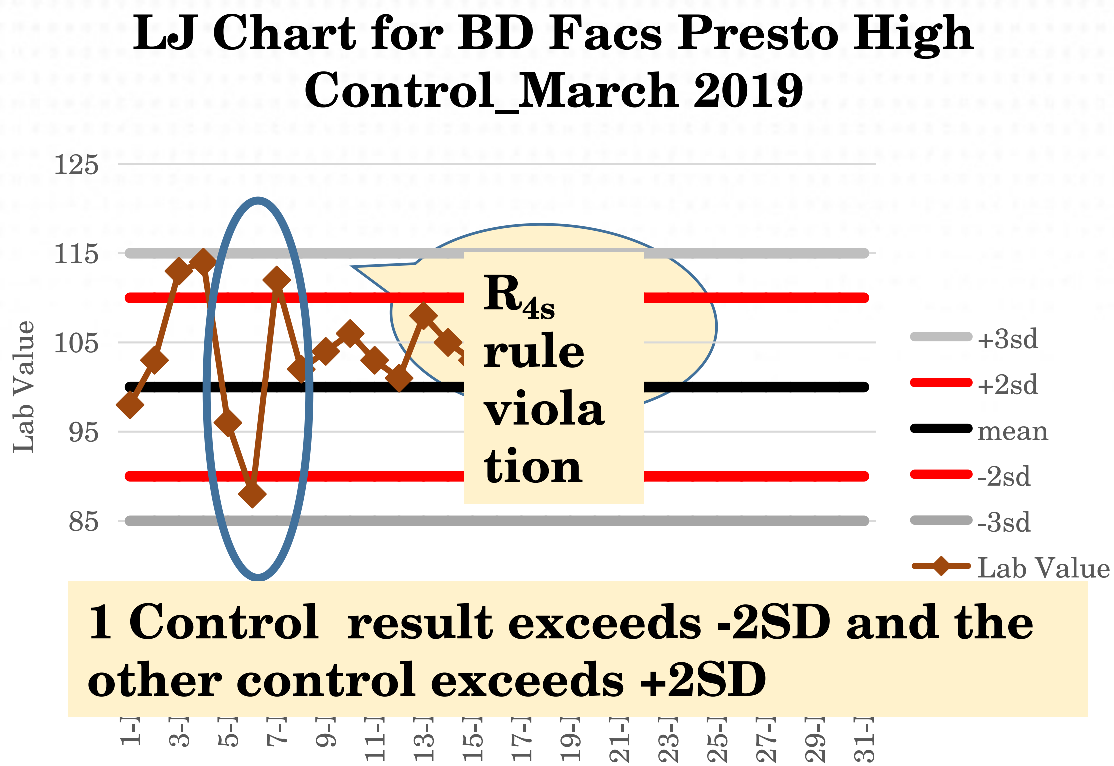
R_{4S} rule

- 1 control result exceeds the mean by –2SD, and the other control exceeds the mean by +2SD



- The range between the two results will therefore exceed 4 SD

Westgard R_{4s} Rule

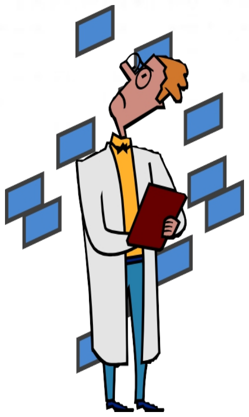


1 Control result exceeds -2SD and the other control exceeds +2SD

Westgard 4_{1s} Rule

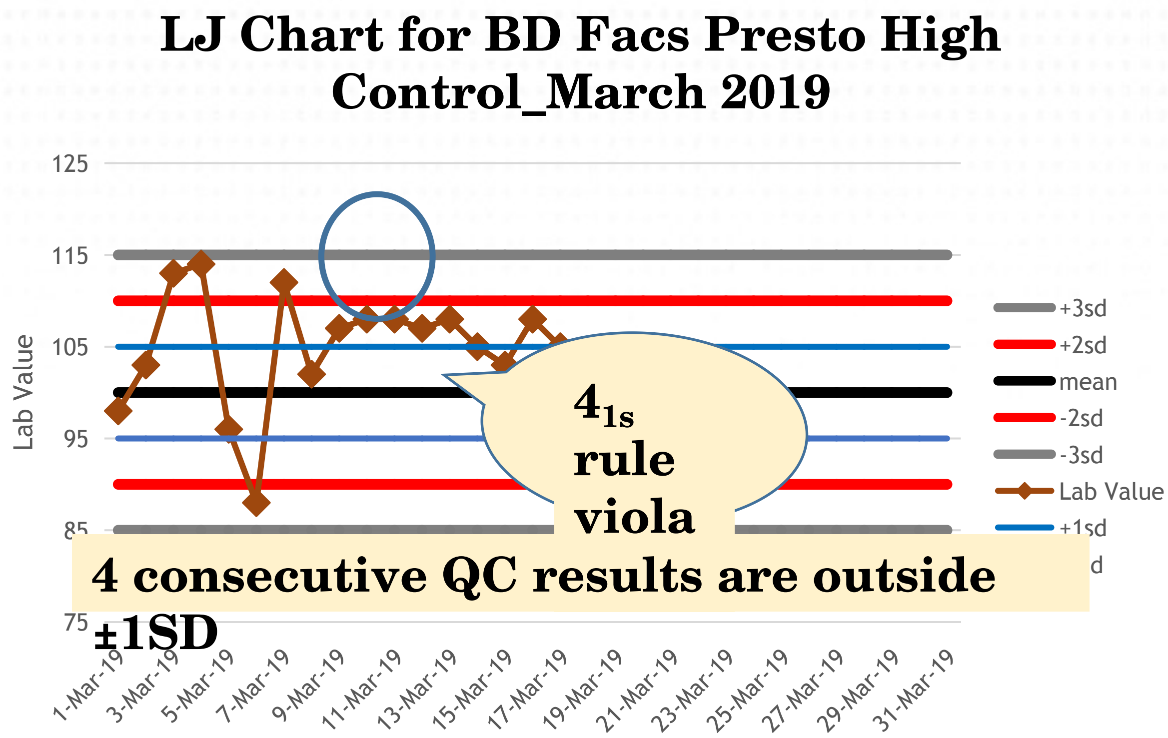
4_{1S} rule

- Requires control data from previous runs



- Four consecutive control results exceed ±1SD.

Westgard 4_{1s} Rule

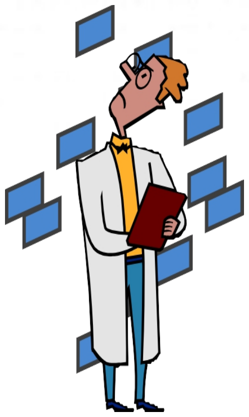


4 consecutive QC results are outside ±1SD

Westgard 10_x Rule

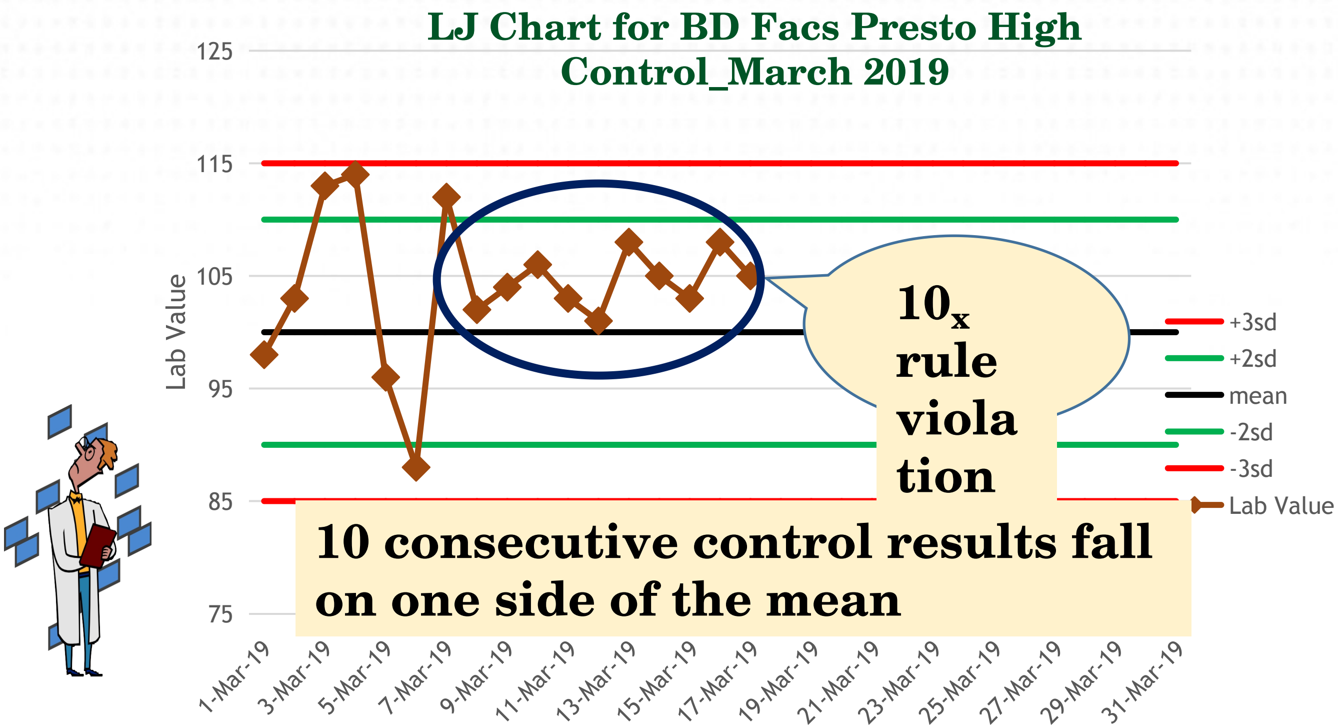
10_x rule

- Requires control data from previous runs



- 10 consecutive QC control are on one side of the mean

Westgard 10_x Rule



When a rule is violated?

- **Warning Rule:** use other rules t
  inspect the control points
- **Rejection Rule:** “Out of Contr

Stop testing

- CAPA

Do not report patient results until problem is solved and controls indicate proper performance

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Westgard MultiRule

- uses a **combination of decision criteria/control rules**, to decide whether an analytical run is **in-control** or **out-of-control.**

- Different control rules to judge the acceptability of an analytical run.

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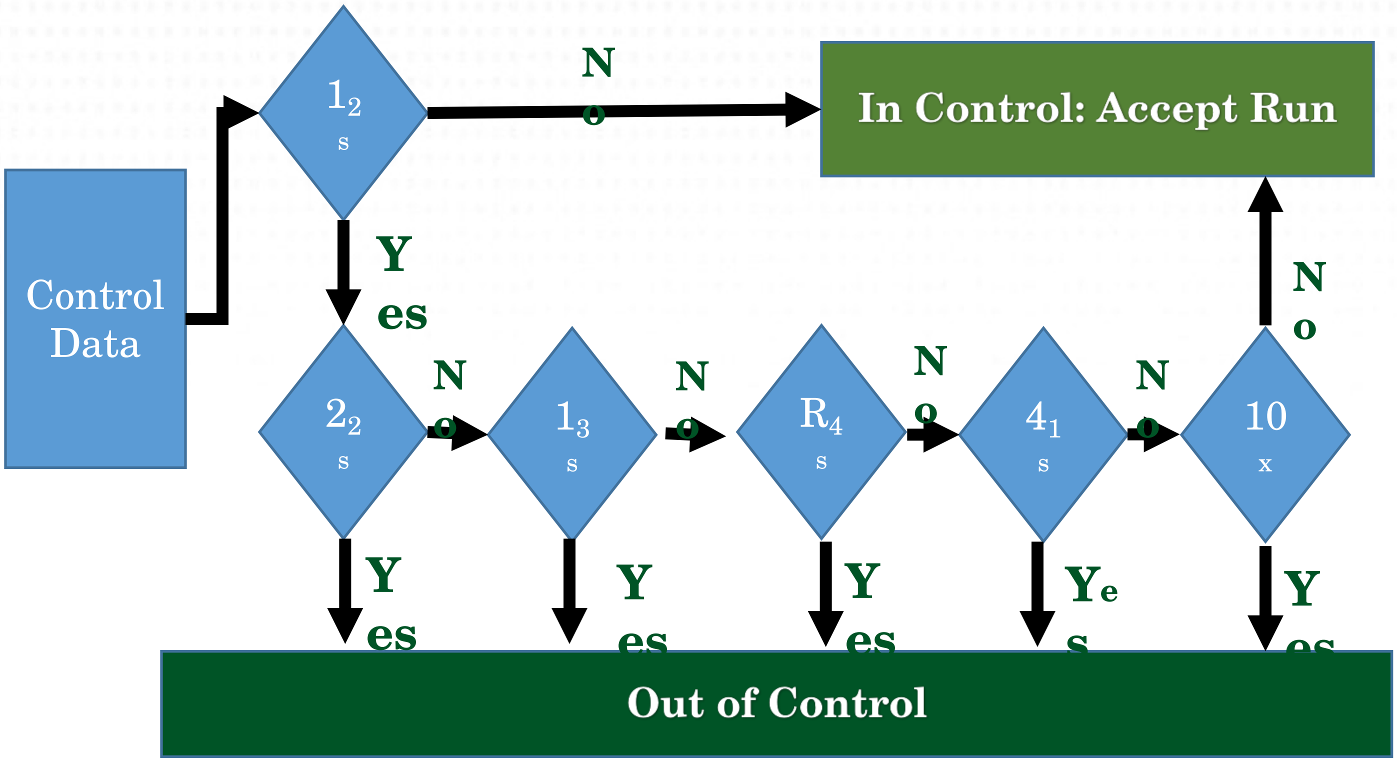
Westgard Multirule QC



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

What are accuracy and precision?

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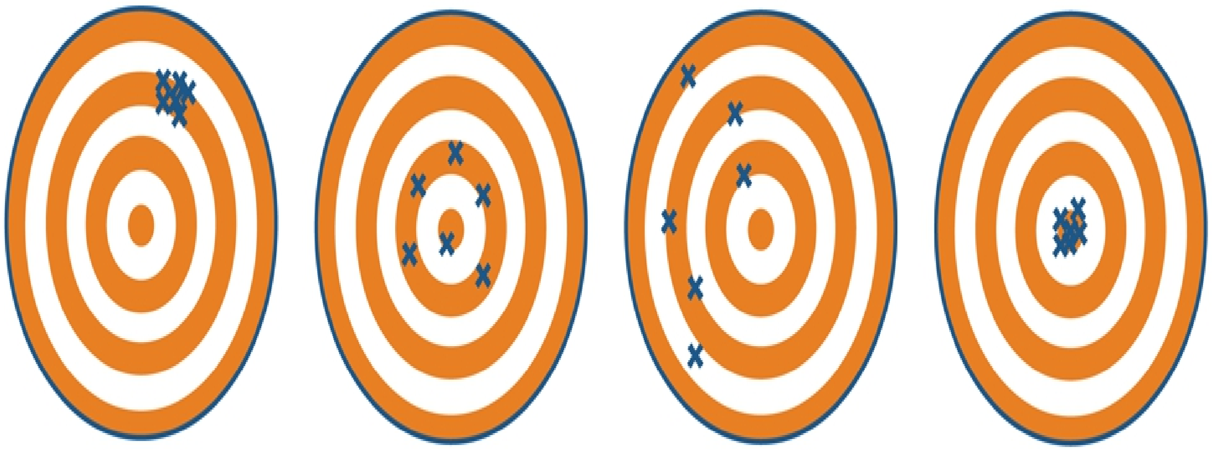
Performance Characteristics

Quality Testing

- **Accuracy/Bias:** Closeness of agreement between the measured value and the true value.

- **Precision:** Repeatability or reproducibility of measurement data.

Monitoring QC Data



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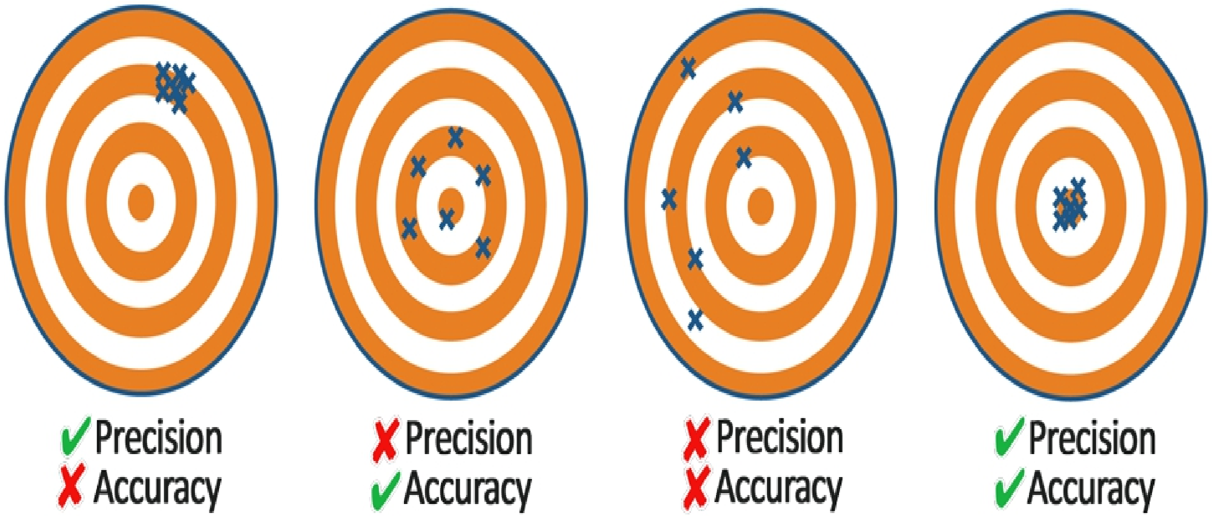
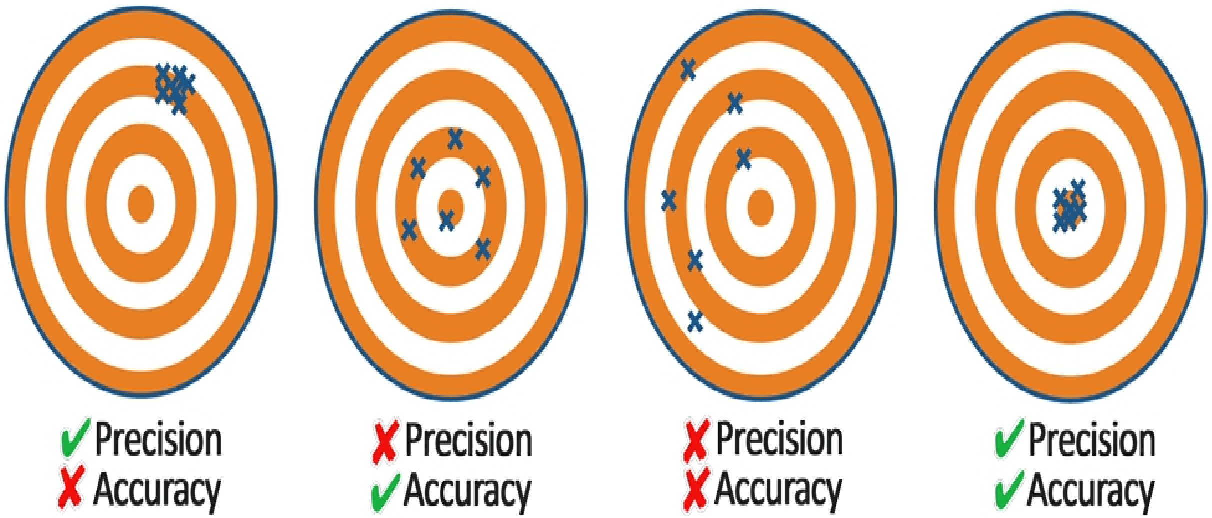
Precision Vs. Accuracy



Monitoring QC Data



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

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Performance Characteristics

- **Accuracy/Bias:** how close you are to the true value.

- **Precision:** is how close two or more measurements are to each other.

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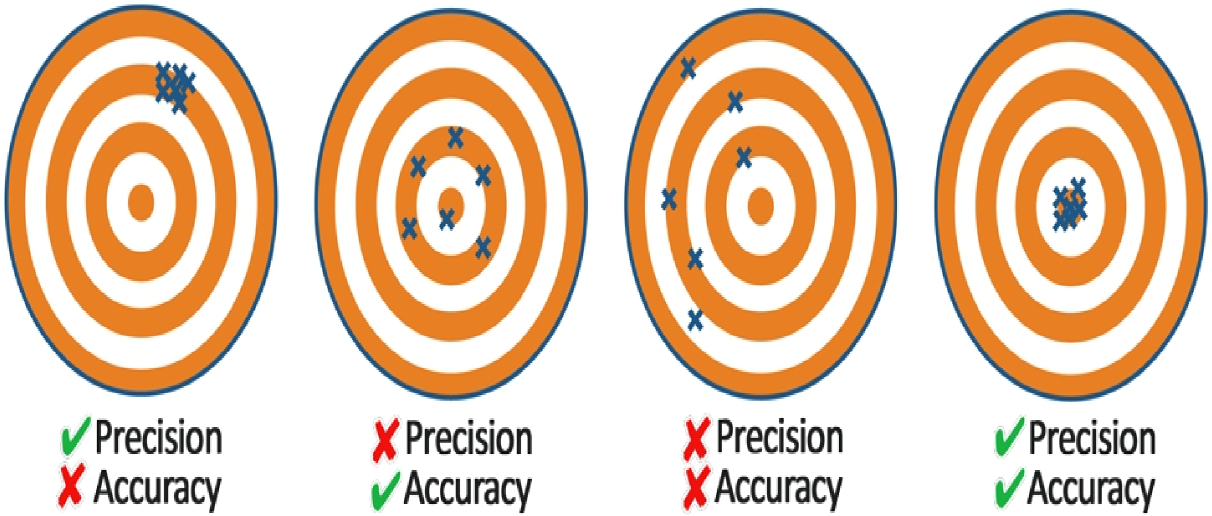
Precision Vs. Accuracy



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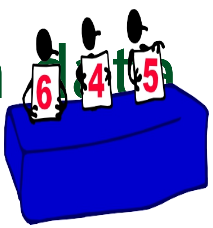
Precision

Quality Testing

- **Precision:** is how close two or more measurements are to each other.

- Within run precision and between run precision

- Precision measures **random error** in data (scatter in data)



Accuracy/Bias

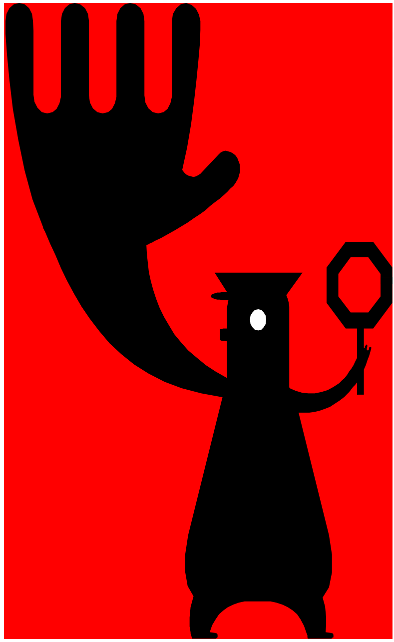
Quality Testing

- **Accuracy:** how close you are to the true value.
- Accuracy measures **systematic** in data
- Systematic errors tend to be consistent in size and direction

6. Using QC information

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



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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

Assessment

1. Differentiate between accuracy and precision.

2. What factors to consider when Selecting control material for the laboratory.

3. Name three sources of Control Materials.

4. Explain the use of a Levey-Jennings chart.

5. Describe how to correct “out of control” problems.

Summary

A quality control program for quantitative tests is essential.
It should:

- Monitor all quantitative tests
- Have written policies and procedures, followed by laboratory staff
- Have a quality manager for monitoring and reviewing QC data
- Use statistical analysis, provide for good records
- Provide for troubleshooting and corrective action

Key Messages

- A QC program allows the laboratory to differentiate between normal variation and error.
- The QC program monitors the accuracy and precision of laboratory assays.
- The results of patient testing should never be released if the QC results for the test run do not meet the laboratory target values.

References

- **ISO 15189:2012 Medical Laboratories – Requirements for Quality and Competence**

  « Clause 5.6.2, 5.6.3 & 5.6.4»

- **CLSI**
- **ASLM**

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Acknowledgement

CDC
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