How to implement a QC program?

- Establish written policies and procedures
- Assign responsibility for monitoring and reviewing
- Train staff
- Obtain control materials
- Collect data
- Set target values (mean, SD)
- Establish Levey-Jennings charts
- Routinely plot control data
- Establish and implement troubleshooting and corrective action protocols
- Establish and maintain system for documentation

Quality Control

- Qualitative Quality Control
- Quantitative QC – How to implement
  - Selection and managing control materials
  - Analysis of QC data
  - Monitoring quality control data

Designing a QC Program –

- Establish written policies and procedures
  - Corrective action procedures
- Train all staff
- Design forms
- Assure complete documentation and review

Qualitative vs.Quantitative

- Quantitative test
  - measures the amount of a substance present
- Qualitative test
  - determines whether the substance being tested for is present or absent

Stains, Reagents, Antisera

- Label containers
  - contents
  - concentration
  - date prepared
  - placed in service
  - expiration date/shelf life
  - preparer

How to implement a laboratory quality control program

Implementing a QC Program

- Select high quality controls
- Establish control range (Allowable limit of variation)
  - Collect *at least* 20 control values over a period of 20-30 days for each level of control
  - Calculate the mean ±2(SD)
- Develop Control Charts (Levey-Jennings chart)
- Each day, control values should be plotted
-
- Take immediate corrective action, if needed
  - Record actions taken

Selecting Control Materials
Calibrators

- Has a known concentration of the substance (analyte) being measured
- Used to adjust instrument, kit, test system in order to standardize the assay
- Sometimes called a standard, although usually not a true standard
- This is *not* a control

Selecting Control Materials
Controls

- Known concentration of the analyte
  - Use 2 or three levels of controls
  - Include with patient samples when performing a test
- Used to validate reliability of the test system

Control Materials
Important Characteristics

- Values cover medical decision points
- Similar to the test specimen (matrix)
- Available in large quantity
- Stored in small aliquots
- Ideally, should last for at least 1 year
- Often use biological material, consider bio-hazardous

Managing Control Materials

- Sufficient material from same lot number or serum pool for one year's testing
- May be frozen, freeze-dried, or chemically preserved
- Requires very accurate reconstitution if this step is necessary
- Always store as recommended by manufacturer

Sources of QC Samples

- Appropriate diagnostic sample
- Obtained from:
  - Another laboratory
  - EQA provider
- Commercial product

Types of Control Materials

- Assayed
  - mean calculated by the manufacturer
  - must verify in the laboratory
- Unassayed
  - less expensive
  - must perform data analysis
- “Homemade” or “In-house”
  - pooled sera collected in the laboratory
  - characterized
  - preserved in small quantities for daily use

Storage of QC Samples

- Validated batch aliquoted into smaller 'user friendly' volumes for storage
- Establish a storage protocol:
  - store at -20^{o}C
  - in use vials stored at 4^{o}C
  - use 0.5 ml vial maximum of one week
  - freeze-dried
    - (requires accurate reconstitution)
  - chemically preserved

Analysis of QC Data

How to carry out this analysis?

- Need tools for data management and analysis
  - Basic statistics skills
  - Manual methods
    - Graph paper
    - Calculator
  - Computer helpful
    - Spreadsheet
- Important skills for laboratory personnel

Measurement of Variability

- Variability occurs when control is tested repeatedly
- Variability is affected by operator, environmental conditions, and characteristics of the assay method
- The goal is to differentiate between variability due to chance from that due to error.

Establishing Control Ranges

- Select appropriate controls
- Assay them repeatedly over time
  - at least 20 data points
- Make sure any procedural variation is represented:
  - different operators
  - different times of day
- Determine the degree of variability (SD) in the data to establish acceptable range
- Determine average of values (Mean)

Calculation of Mean

$$(\bar{X}) = \frac{X_1 + X_2 + X_3 \ldots + X_n}{n}$$

X = Mean

X_1 = First result

X_2 = Second result

X_n = Last result in series

n – Total number of results

Calculation of Mean: Outliers

1. 192 mg/dL
2. 194 mg/dL
3. 196 mg/dL
4. 196 mg/dL
5. **160 mg/dL**
6. 196 mg/dL
7. 200 mg/dL
8. 200 mg/dL
9. 202 mg/dL
10. **255 mg/dL**
11. 204 mg/dL
12. 208 mg/dL
13. 212 mg/dL

Calculation of Mean

1) 192 mg/dL
2) 194 mg/dL
3) 196 mg/dL
4) 196 mg/dL
5) 196 mg/dL
6) 200 mg/dL
7) 200 mg/dL
8) 202 mg/dL
9) 204 mg/dL
10) 208 mg/dL
11) 212 mg/dL

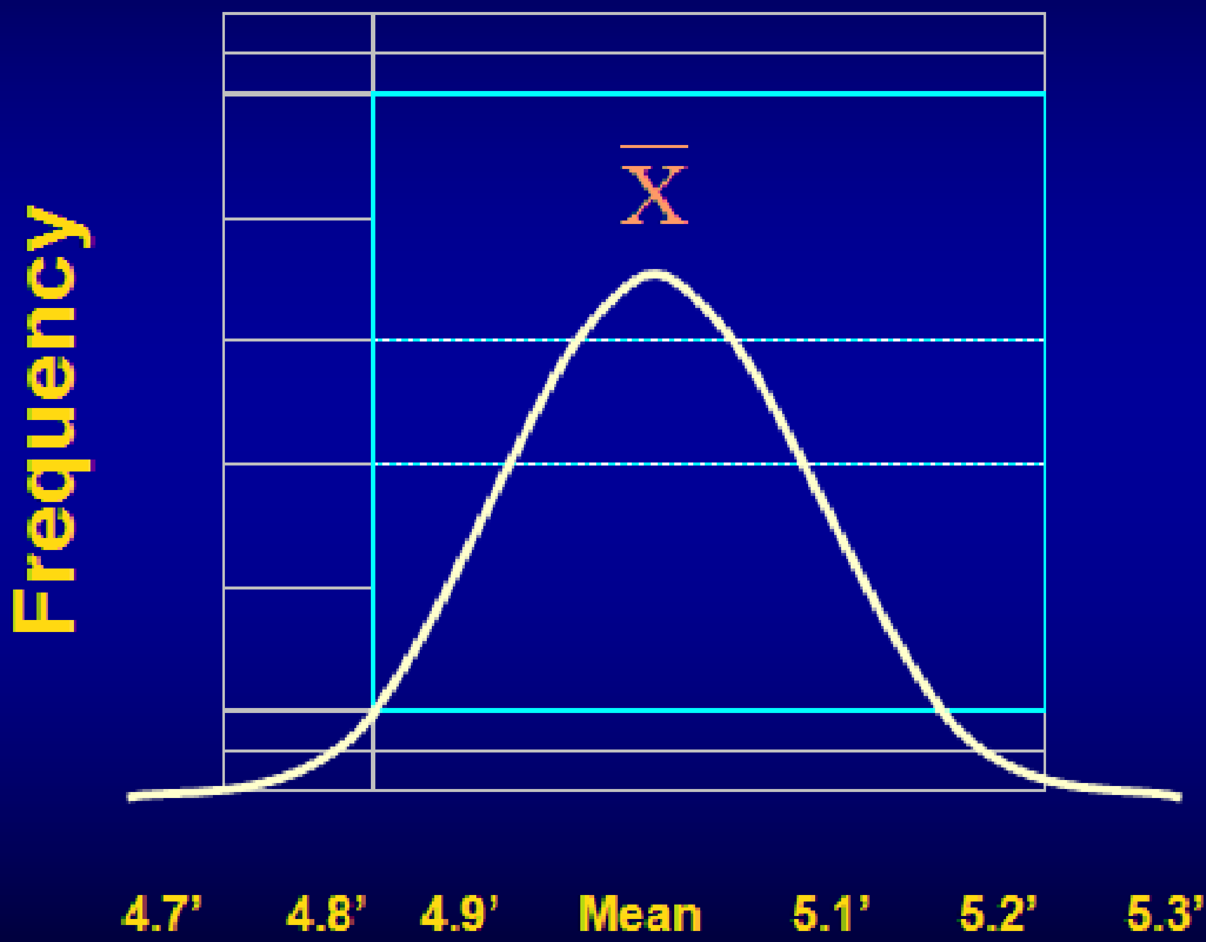
Sum = 2,200 mg/dL

- Mean = the calculated average of the values
- The sum of the values ($X_1 + X_2 + X_3 \ldots X_{11}$) divided by the number (n) of observations
- The mean of these 11 observations is ($2200 \div 11$) = 200 mg/dL

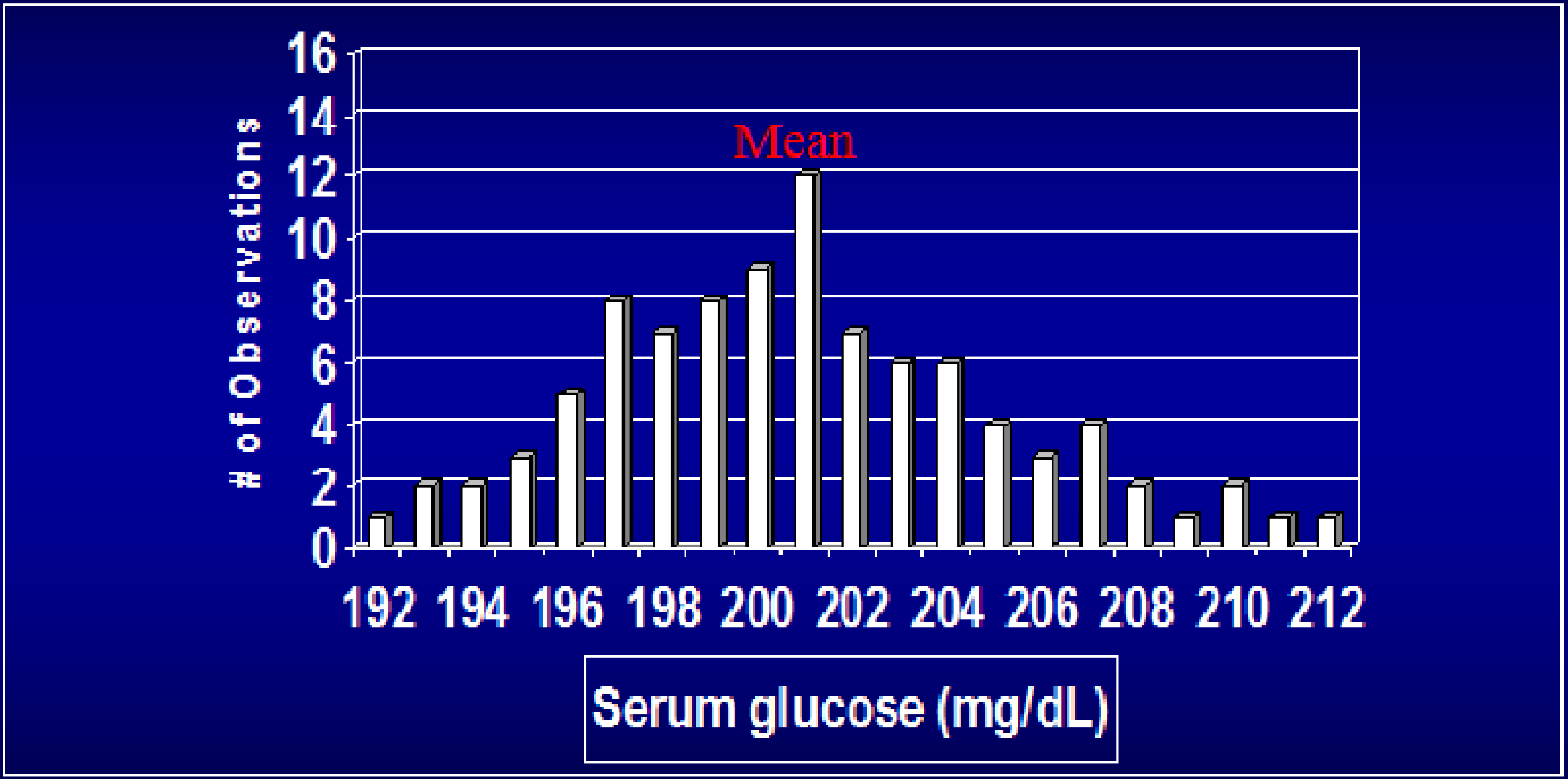
Normal Distribution

- All values are symmetrically distributed around the mean
- Characteristic “bell-shaped” curve
- Assumed for all quality control statistics

Normal Distribution

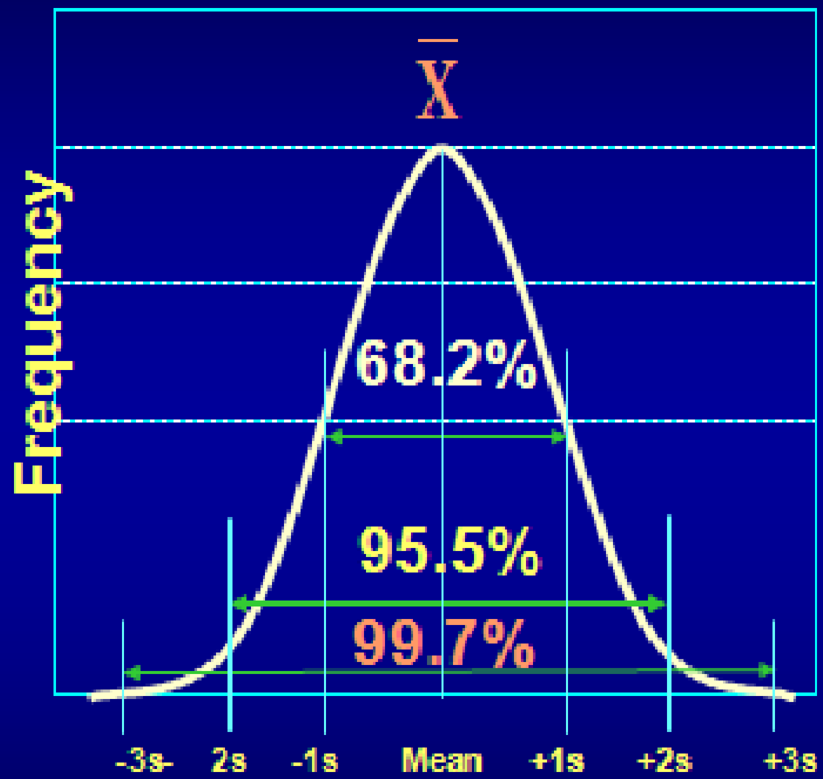


Normal Distribution



Standard Deviation and Probability

- For a set of data with a normal distribution, a value will fall within a range of:
  - +/- 1 SD 68.2% of the time
  - +/- 2 SD 95.5% of the time
  - +/- 3 SD 99.7% of the time



Monitoring of QC Data

Control chart

A graphical method for displaying control results and evaluating whether a measurement procedure is in-control or out-of-control.

Control results are plotted versus time or sequential run number;

lines are drawn from point to point to accent any trends, systematic shifts, and random excursions.

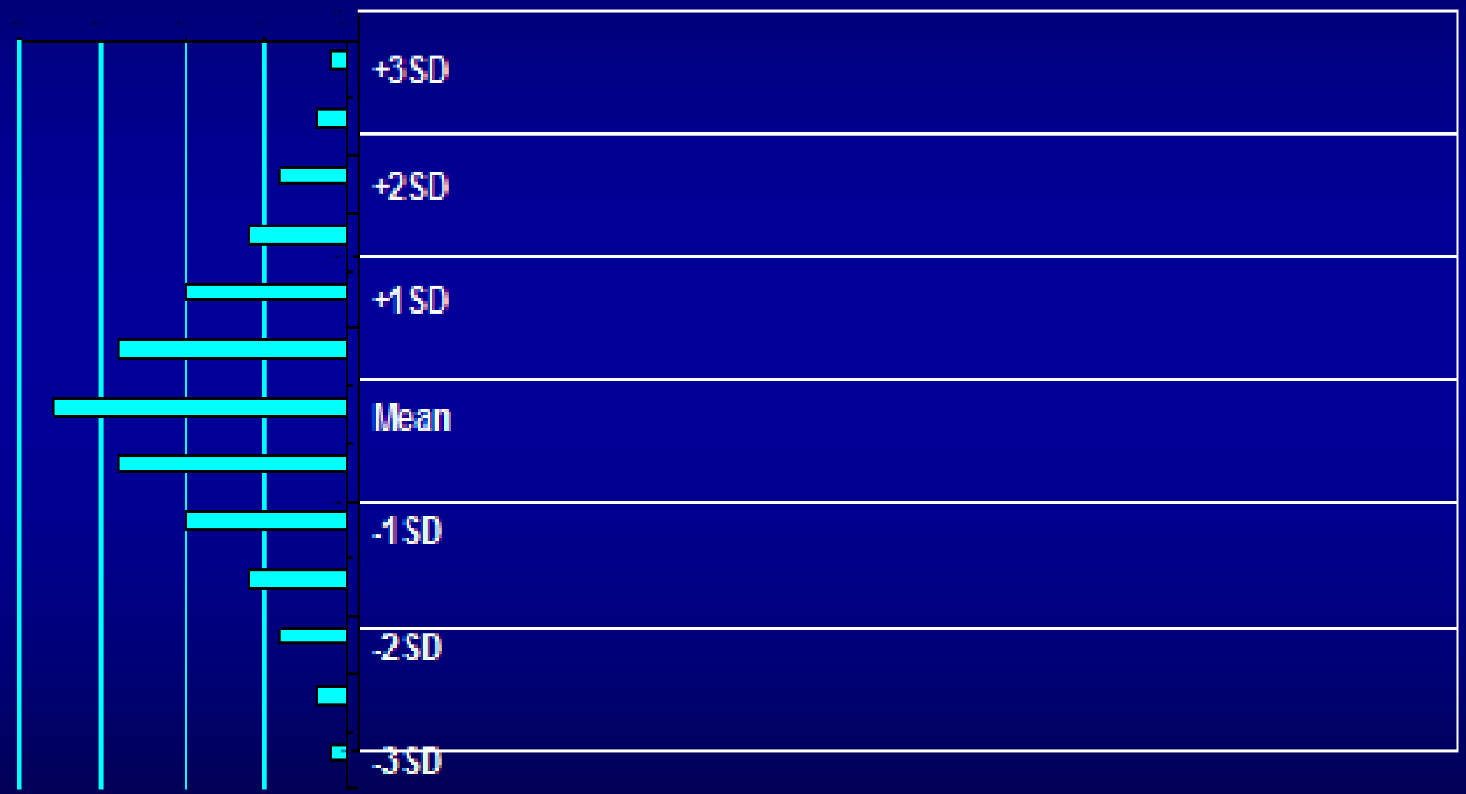
Monitoring QC Data

- Use Levey-Jennings chart
- Plot control values each run, make decision regarding acceptability of run
- Monitor over time to evaluate the precision and accuracy of repeated measurements
- Evaluate the charts daily, take necessary action, and document

Levey-Jennings Chart

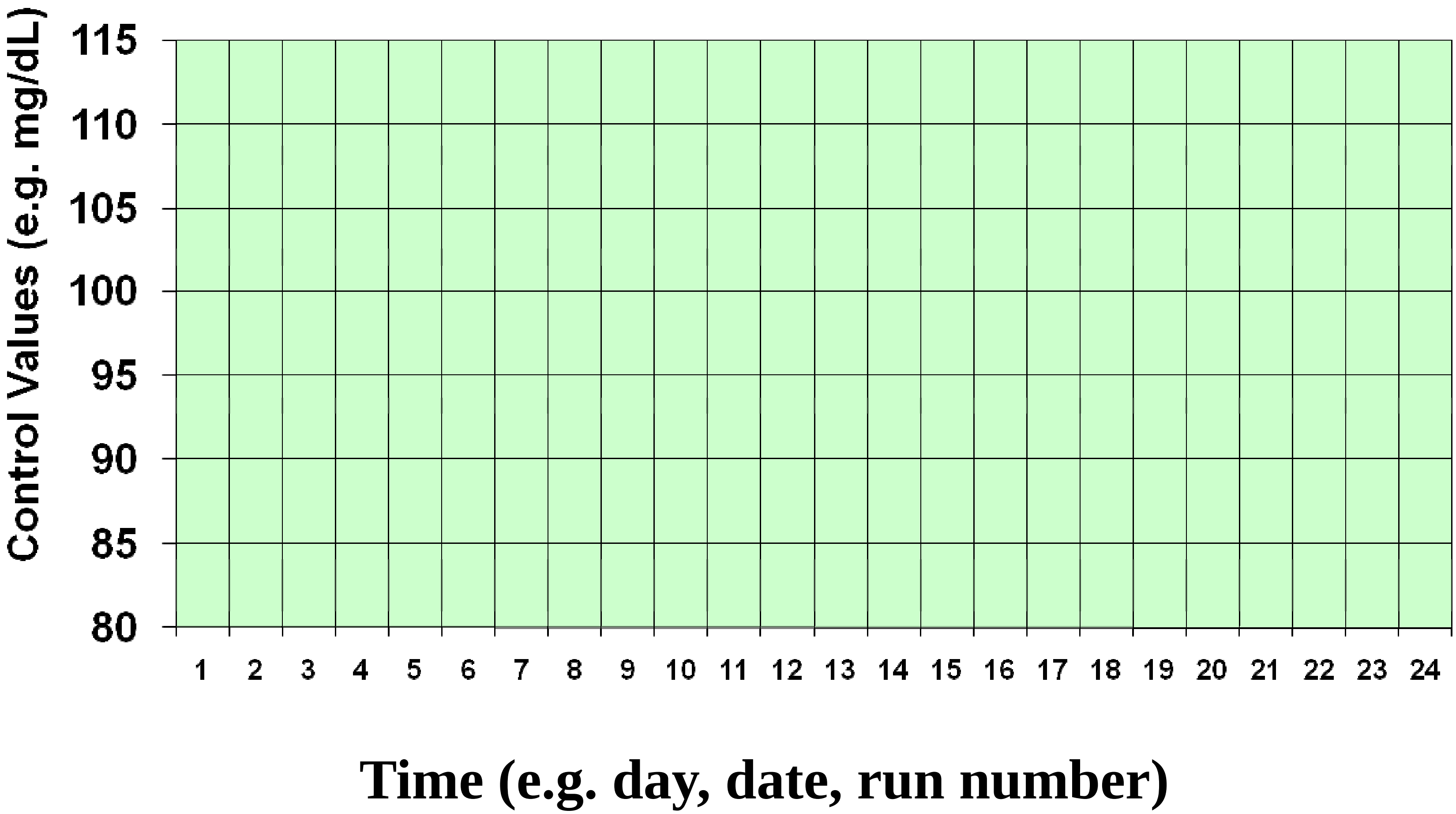
- A graphical method for displaying control results and evaluating whether a procedure is in-control or out-of-control
- Control values are plotted versus time
- Lines are drawn from point to point to accent any trends, shifts, or random excursions

Levey-Jennings Chart



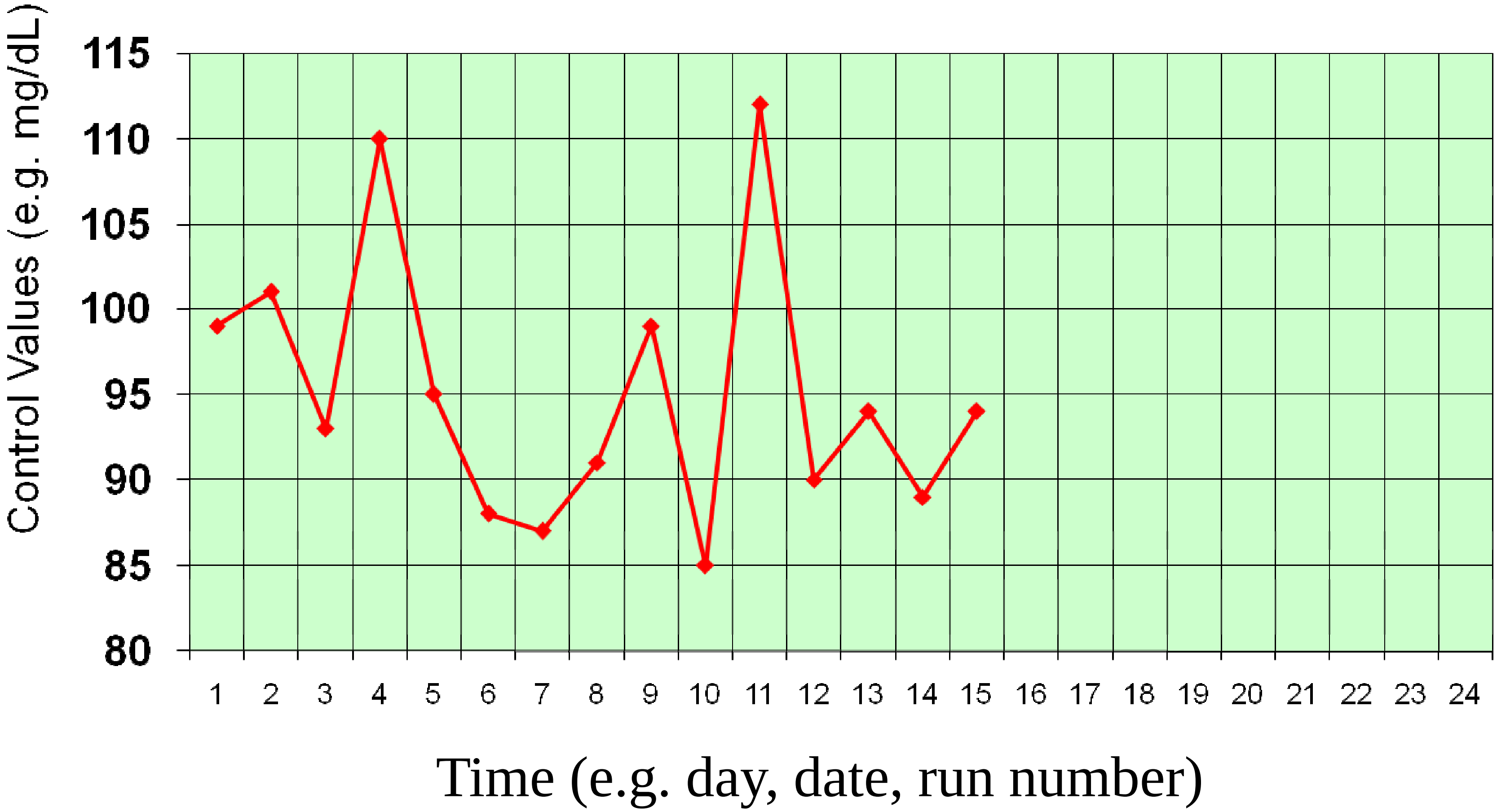
Levey-Jennings Chart -

Record Time on X-Axis and the Control Values on Y-Axis



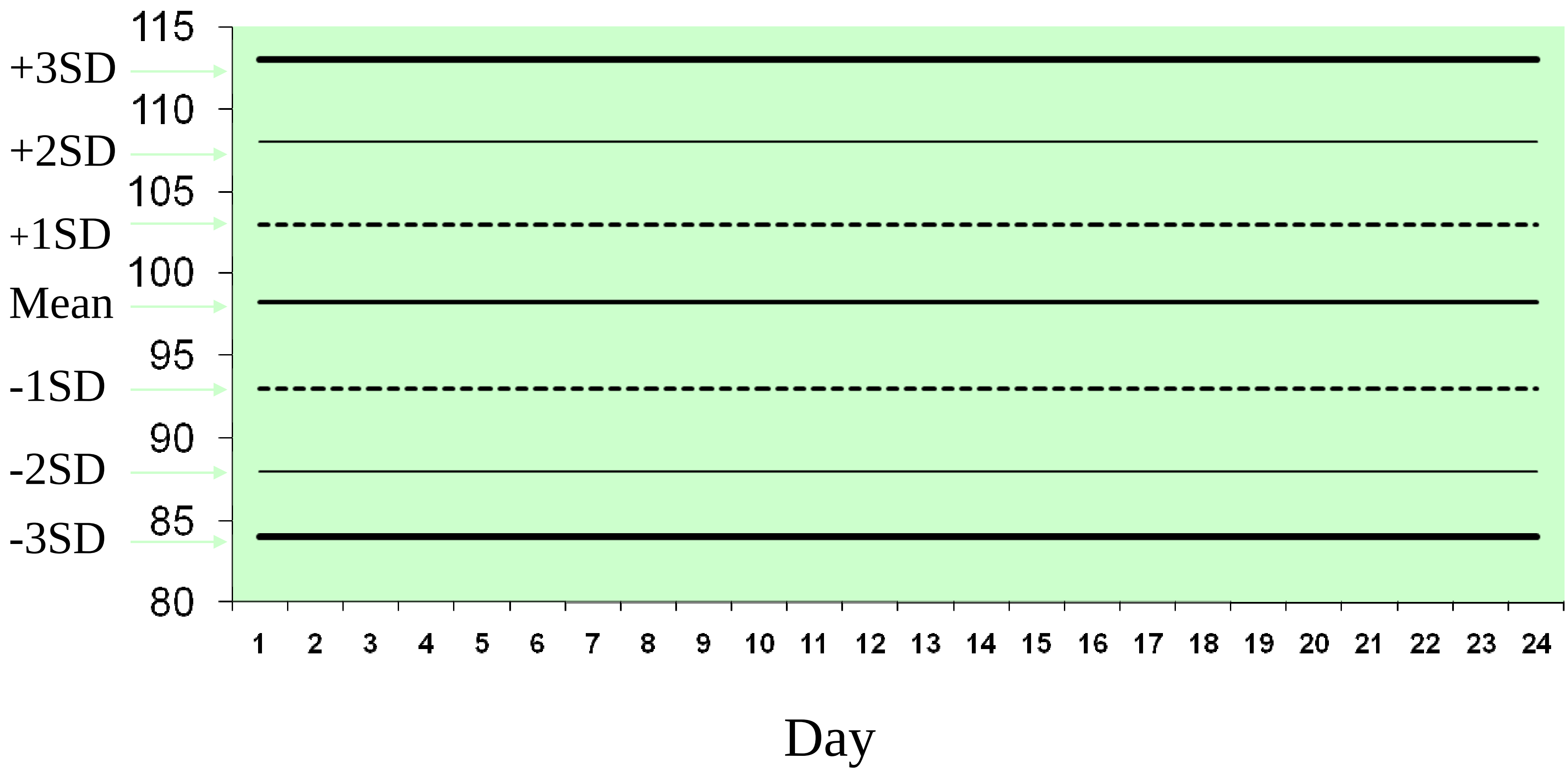
Levey-Jennings Chart -

Plot Control Values for Each Run

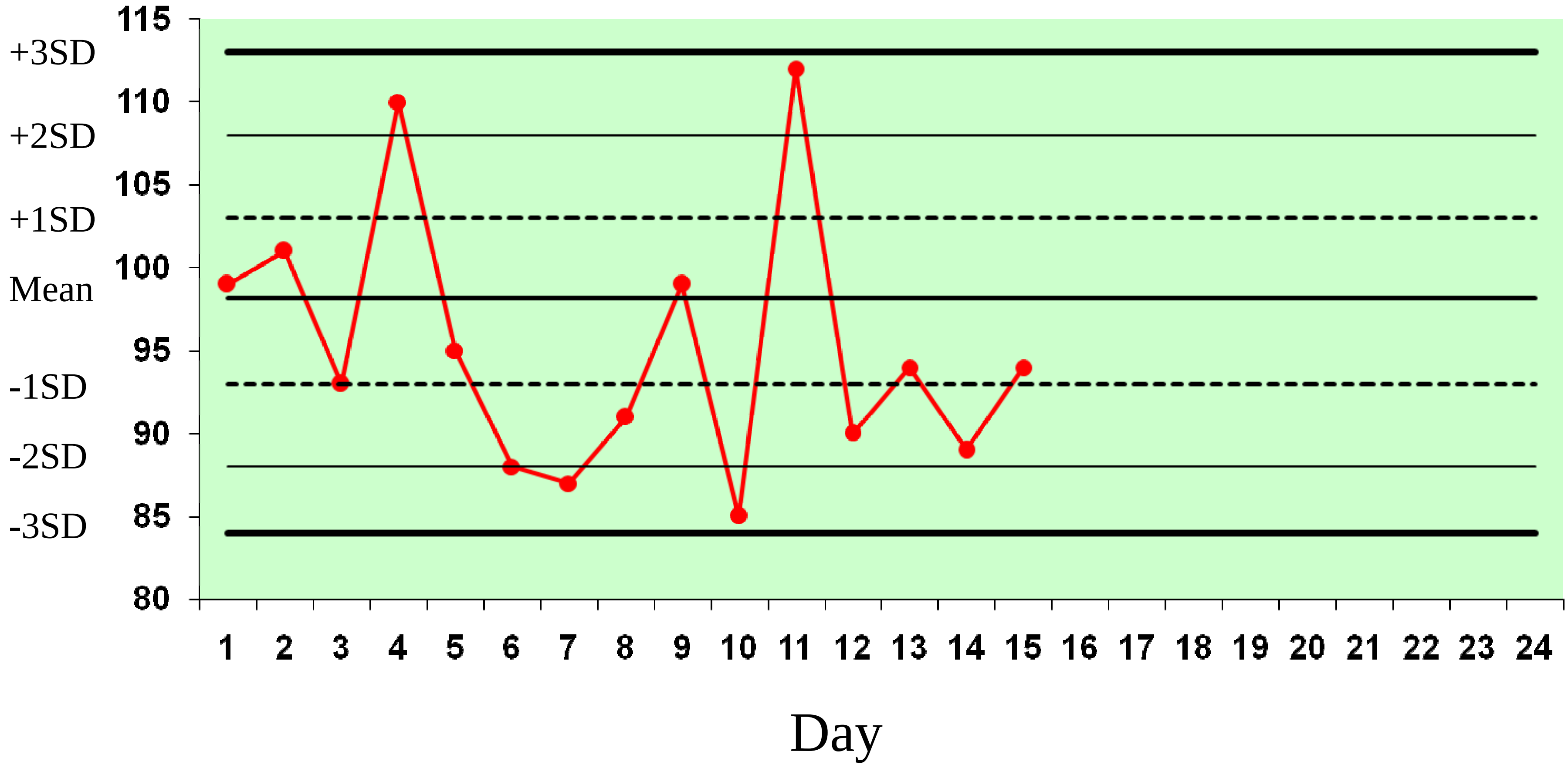


Levey-Jennings Chart

Calculate the Mean and Standard Deviation; Record the Mean and +/- 1,2 and 3 SD Control Limits

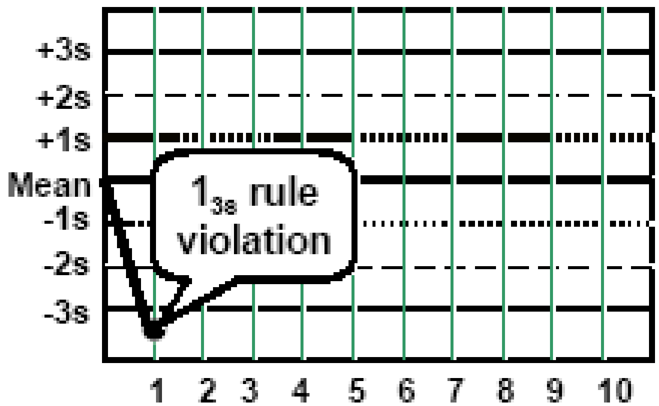


Levey-Jennings Chart -
Record and Evaluate the Control Values



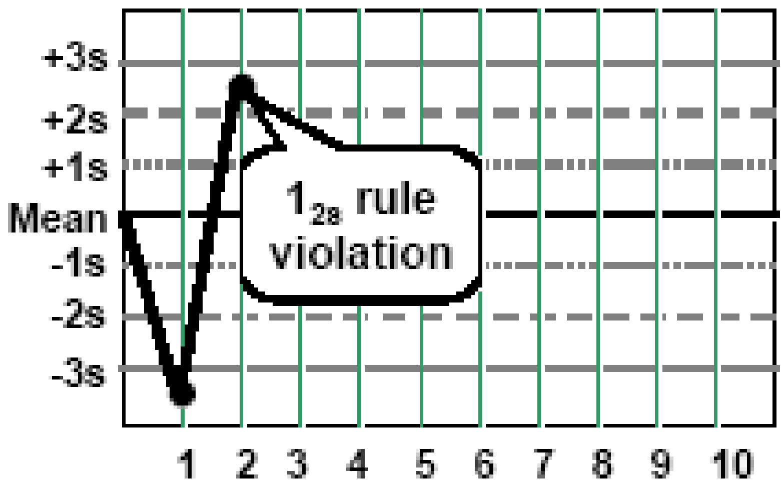
1_{3s} Rule

1_{3s} refers to a control rule that is commonly used with a Levey-Jennings chart when the control limits are set as the mean +3s and the mean −3s. A run is rejected when a single control measurement exceeds the mean +3s or the mean −3s control limit.



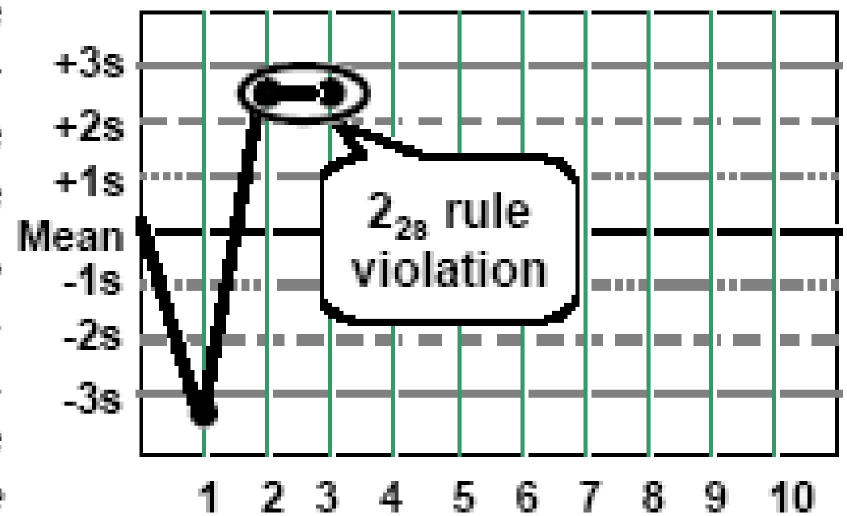
1_{2s} Rule

1_{2s} refers to the control rule that is commonly used with a Levey-Jennings chart when the control limits are set as the mean ± 2s. In the original Westgard multirule QC procedure, this rule is used as a warning rule to trigger careful inspection of the control data by other rejection rules.



1_{2s} Rule

2_{2s} refers to the control rule that is used with a Levey-Jennings chart when the control limits are set as the mean ± 2s. In this case, however, the run is rejected when 2 consecutive control measurements exceed the *same* mean +2s or the *same* mean −2s.



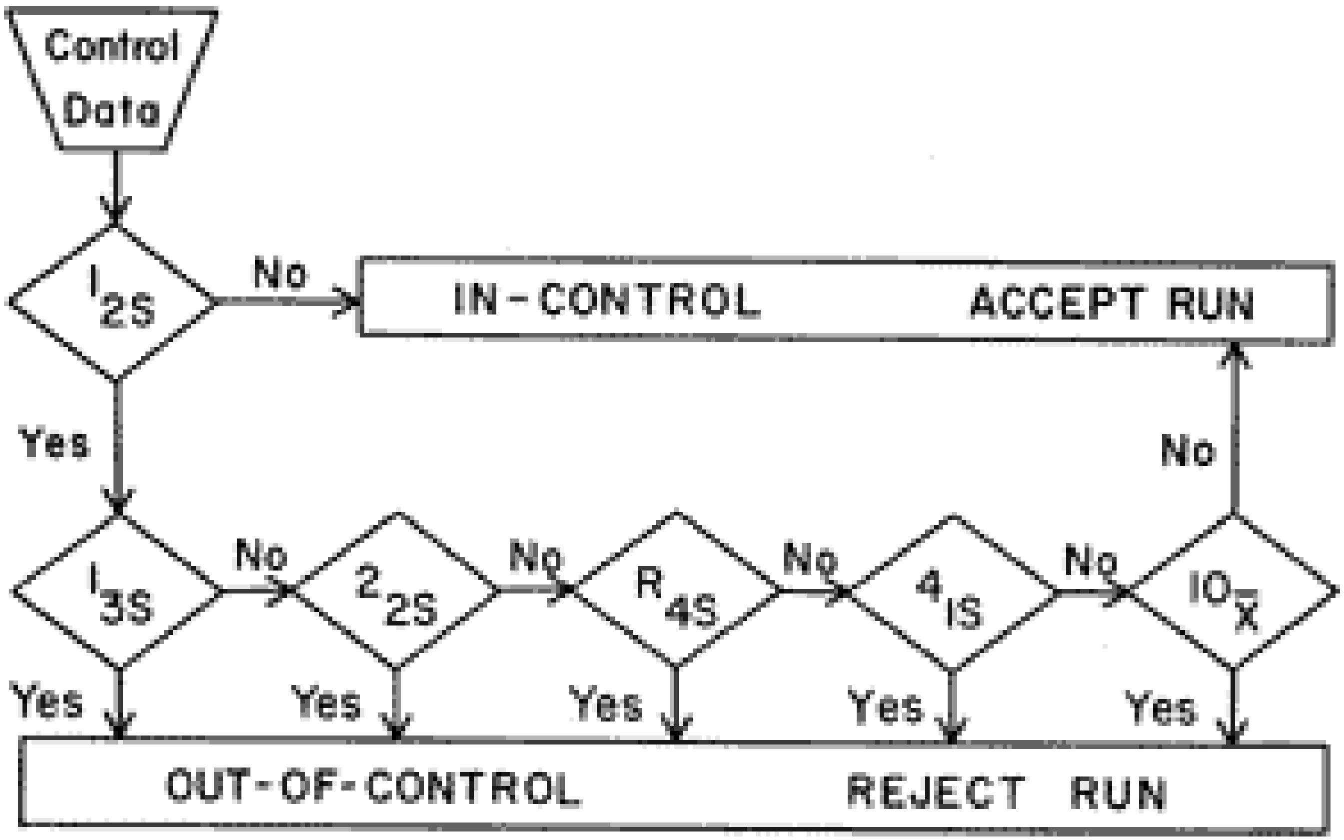
R_{4s} Rule

R_{4s} refers to a control rule where a reject occurs when 1 control measurement in a group exceeds the mean +2s and another exceeds the mean −2s.

Findings

- Control values clustered about the mean (+/-2 SD) with little variation in the upward or downward direction
- Imprecision = large amount of scatter about the mean. Usually caused by errors in technique
- Inaccuracy = may see as a trend or a shift, usually caused by change in the testing process
- Random error = no pattern. Usually poor technique, malfunctioning equipment

Evaluate data



Statistical Quality Control Exercise

- Hypothetical control values (2 levels of control)
- Calculation of mean
- Calculation of standard deviation
- Creation of a Levey-Jennings chart

When does the Control Value Indicate a Problem?

- Consider using Westgard Control Rules
- Uses premise that 95.5% of control values should fall within ±2SD
- Commonly applied when two levels of control are used
- Use in a sequential fashion

Westgard Rules

- “Multirule Quality Control”
- Uses a combination of decision criteria or control rules
- Allows determination of whether an analytical run is “in-control” or “out-of-control”

Westgard Rules

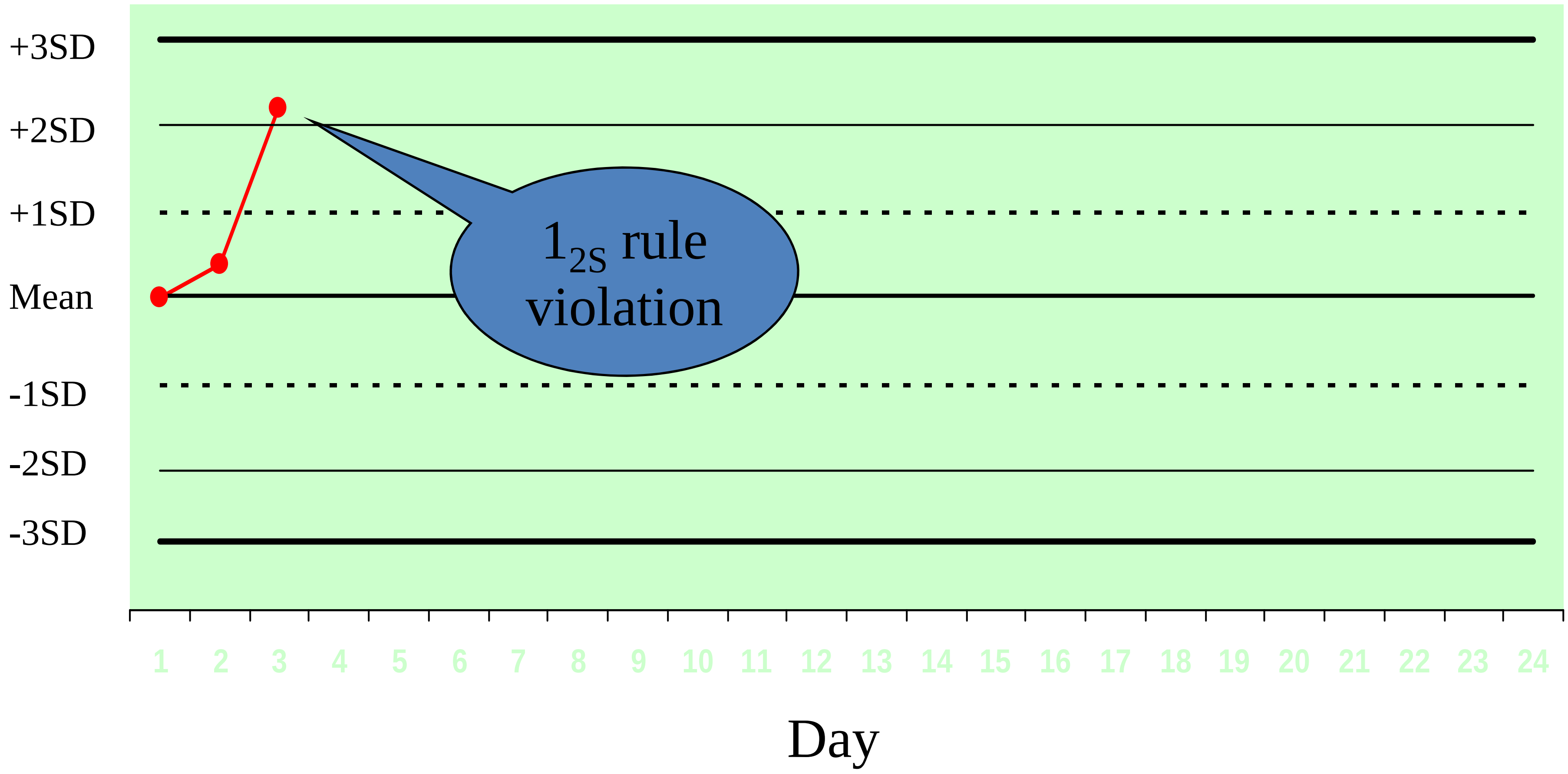
(Generally used where 2 levels of control material are analyzed per run)

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

Westgard – 1_{2S} Rule

- "warning rule"
- One of two control results falls outside ±2SD
- Alerts tech to possible problems
- Not cause for rejecting a run
- Must then evaluate the 1_{3S} rule

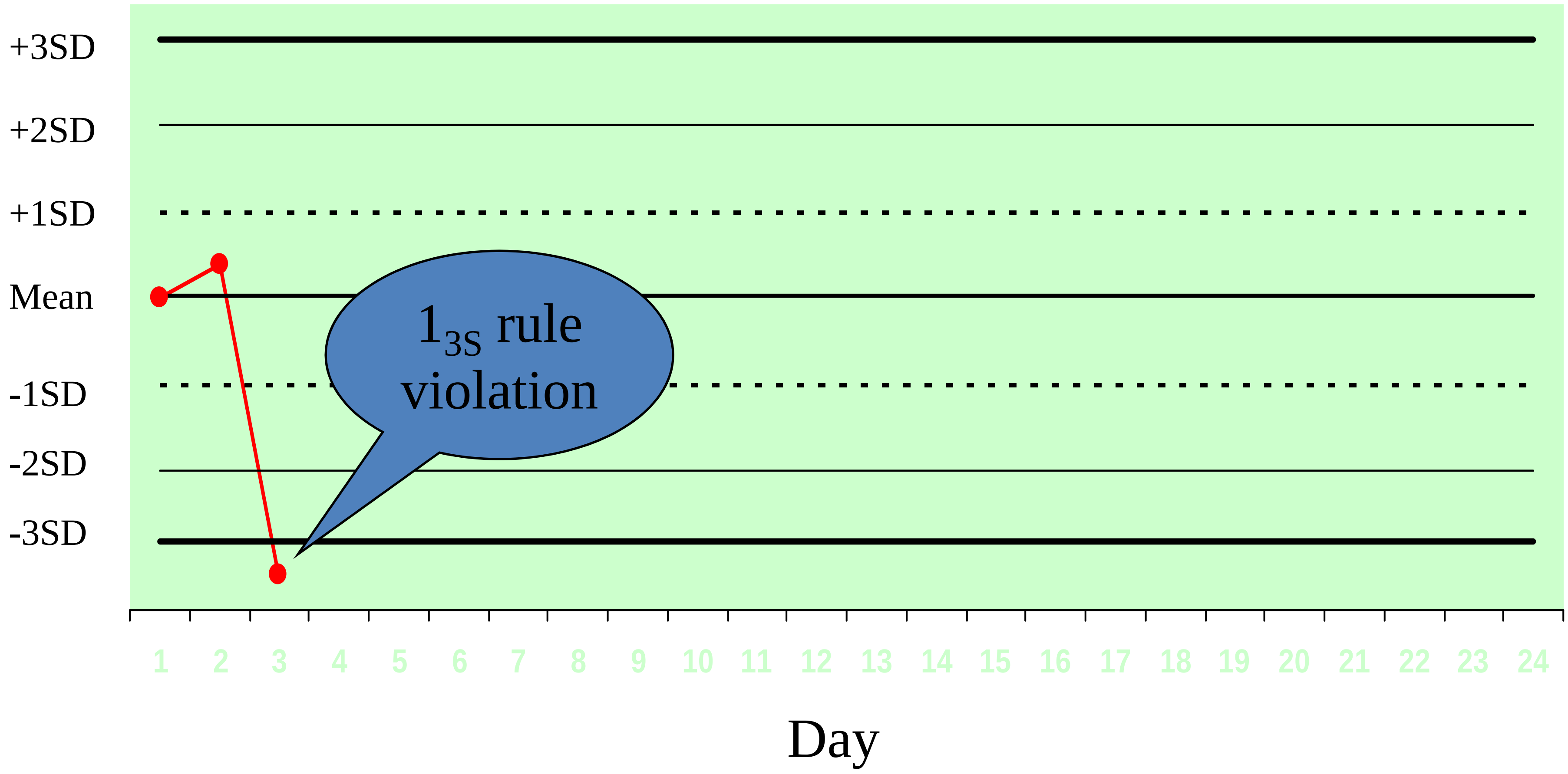
1_{2S} Rule = A warning to trigger careful inspection of the control data



Westgard – 1_{3S} Rule

- If either of the two control results falls outside of ±3SD, rule is violated
- Run must be rejected
- If 1_{3S} not violated, check 2_{2S}

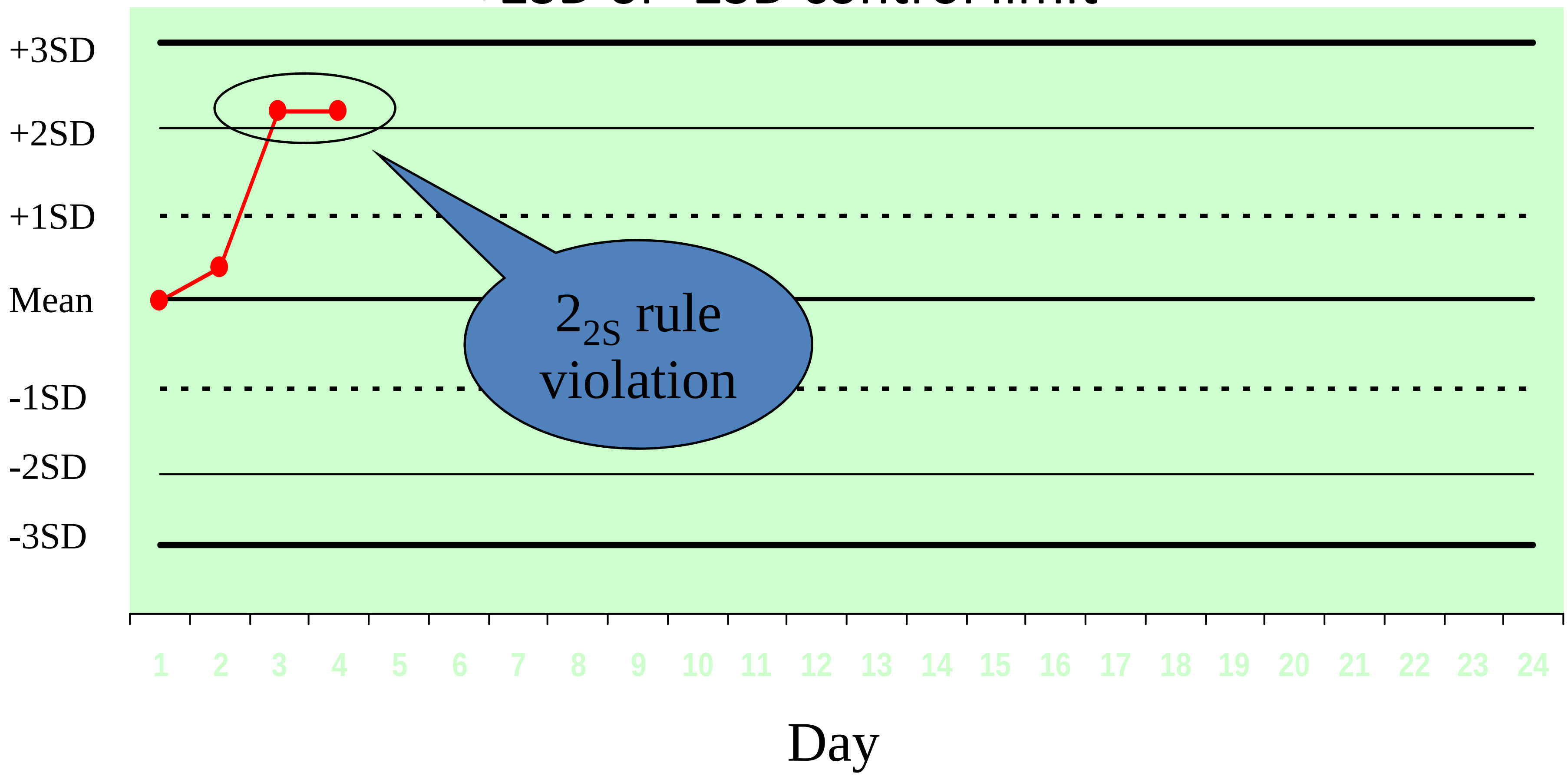
1_{3S} Rule = Reject the run when a single control measurement exceeds the +3SD or -3SD control limit



Westgard – 2_{2S} Rule

- 2 consecutive control values for the same level fall outside of ±2SD in the same direction, or
- Both controls in the same run exceed ±2SD
- Patient results cannot be reported
- Requires corrective action

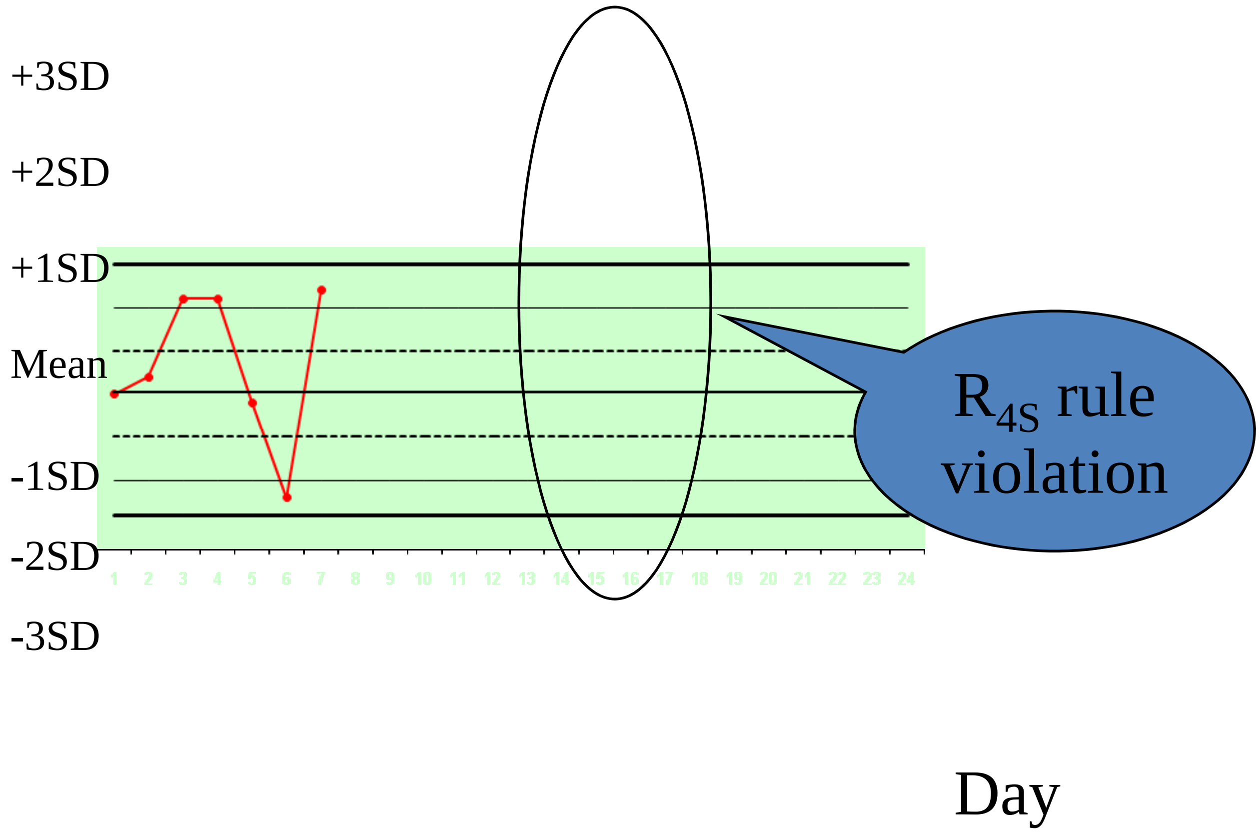
2_{2S} Rule = Reject the run when 2 consecutive control measurements exceed the same +2SD or -2SD control limit



Westgard – R_{4S} Rule

- One control 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
- Random error has occurred, test run must be rejected

R_{4S} Rule = Reject the run when 1 control measurement exceed the +2SD and the other exceeds the -2SD control limit



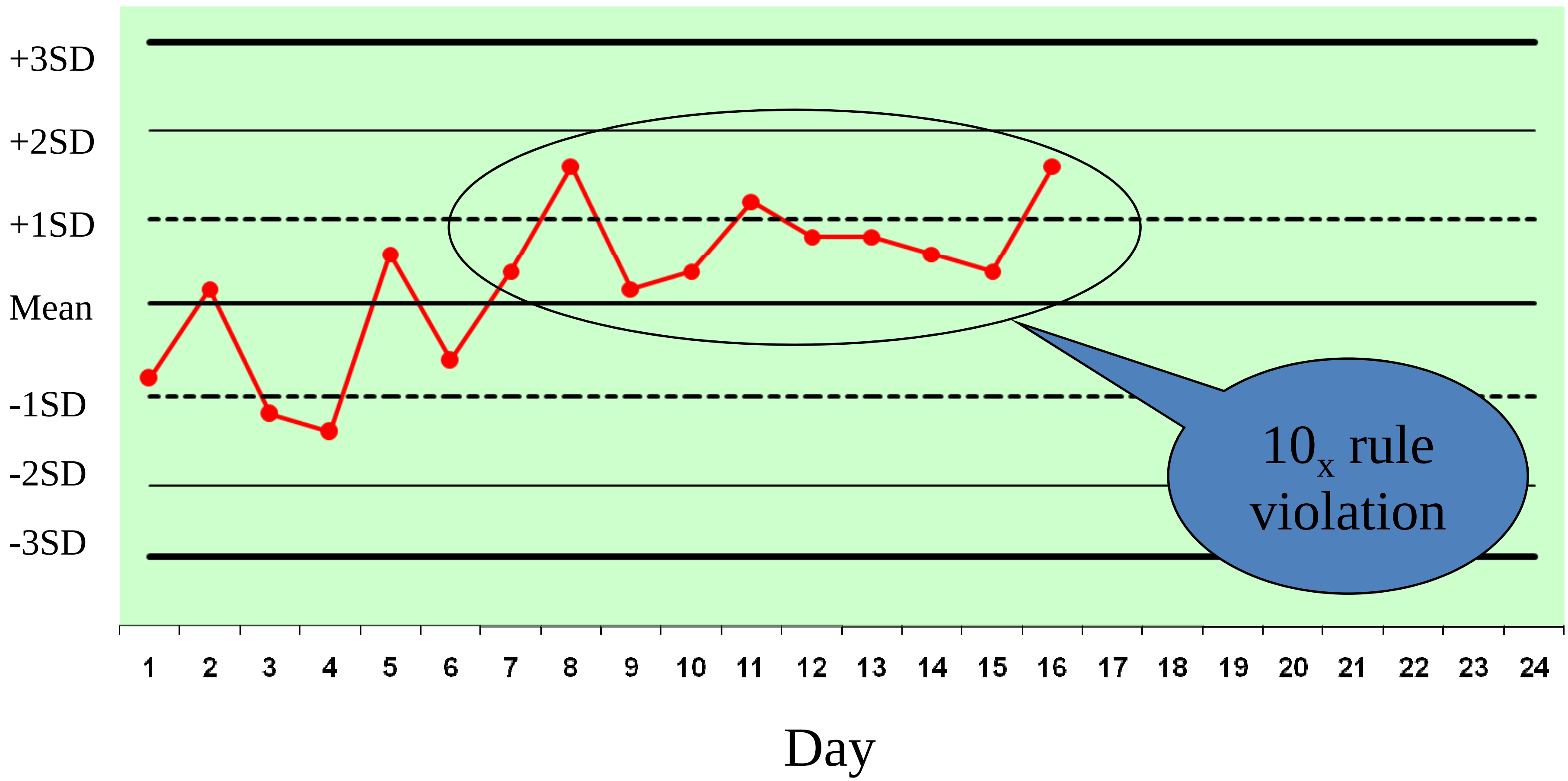
Westgard – 4_{1S} Rule

- Requires control data from previous runs
- Four consecutive QC results for one level of control are outside ±1SD, or
- Both levels of control have consecutive results that are outside ±1SD

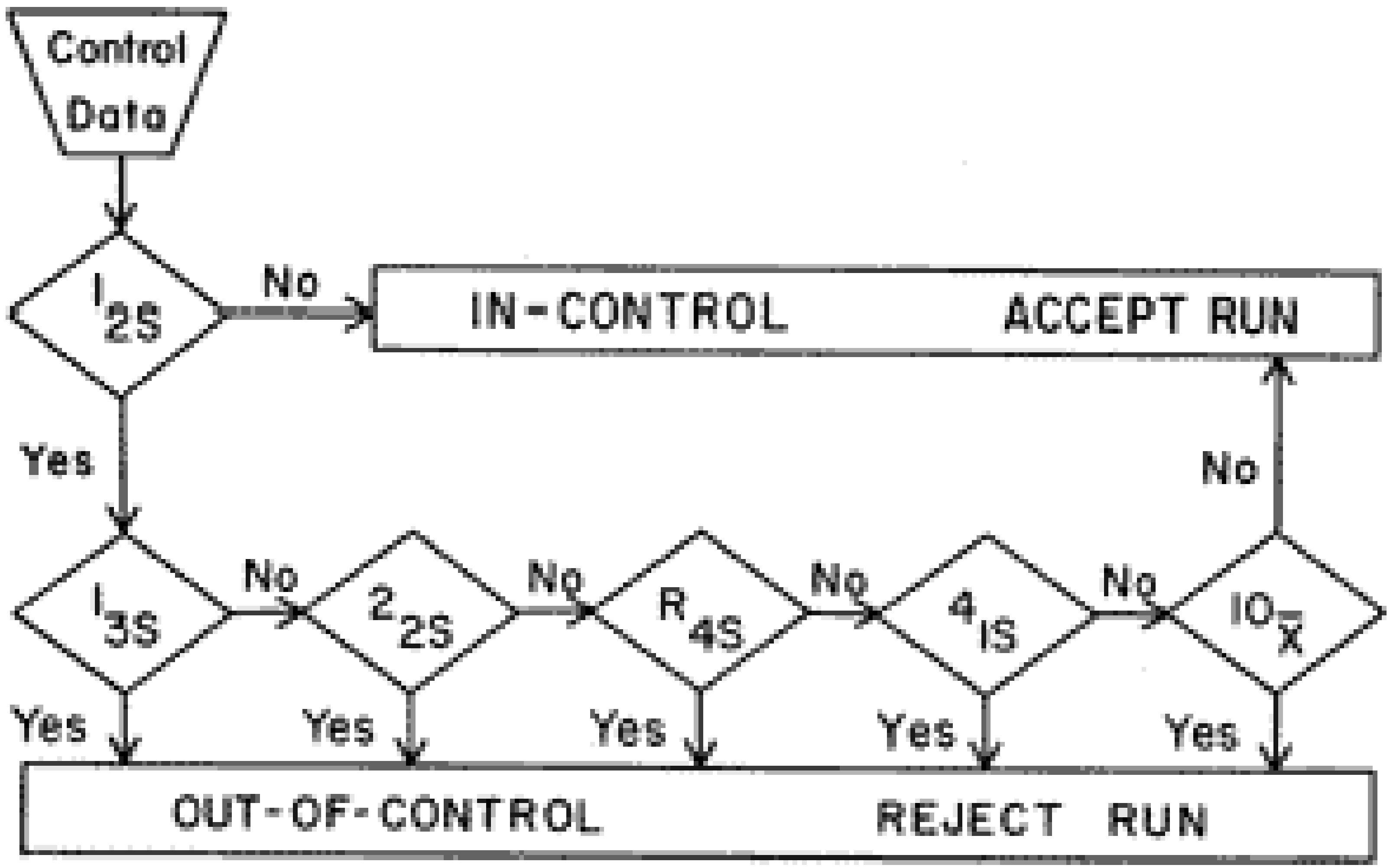
Westgard – 10_X Rule

- Requires control data from previous runs
- Ten consecutive QC results for one level of control are on one side of the mean, or
- Both levels of control have five consecutive results that are on the same side of the mean

10_x Rule = Reject the run when 10 consecutive control measurements fall on one side of the mean



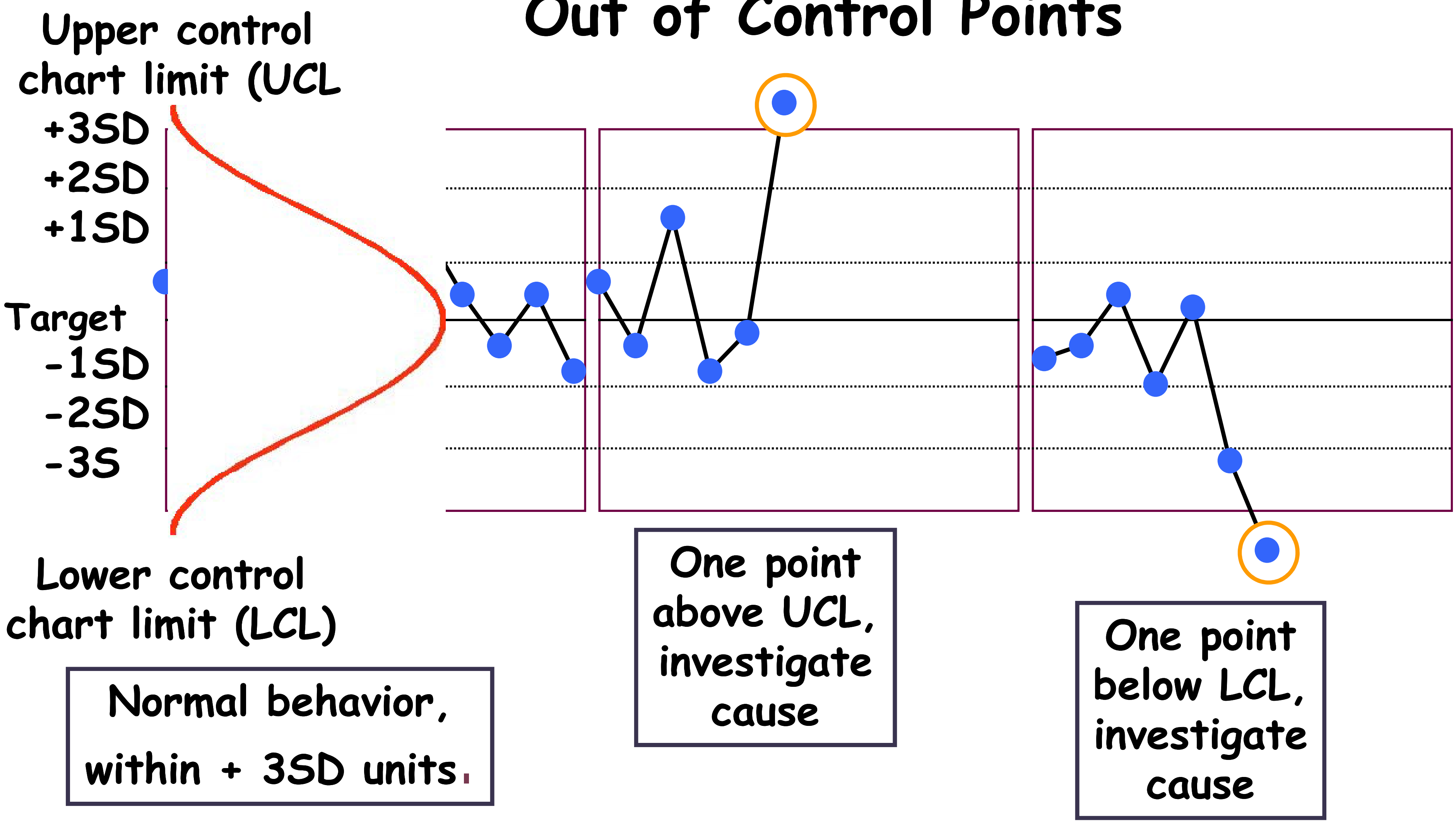
Westgard Multirule QC



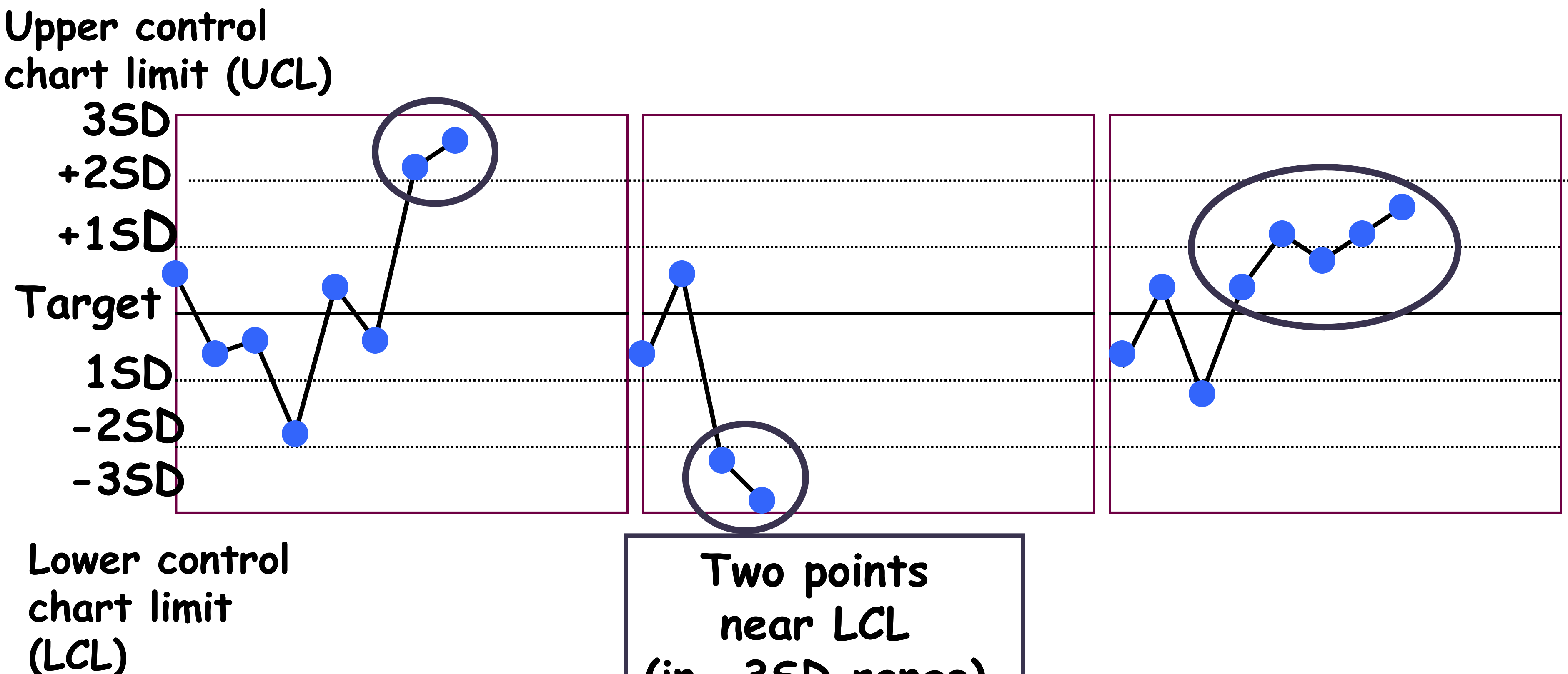
When a rule is violated

- Warning rule = use other rules to inspect the control points
- Rejection rule = “out of control”
  - Stop testing
  - Identify and correct problem
  - Repeat testing on patient samples and controls
  - Do not report patient results until problem is solved and controls indicate proper performance

Out of Control Points



Cause to Investigate



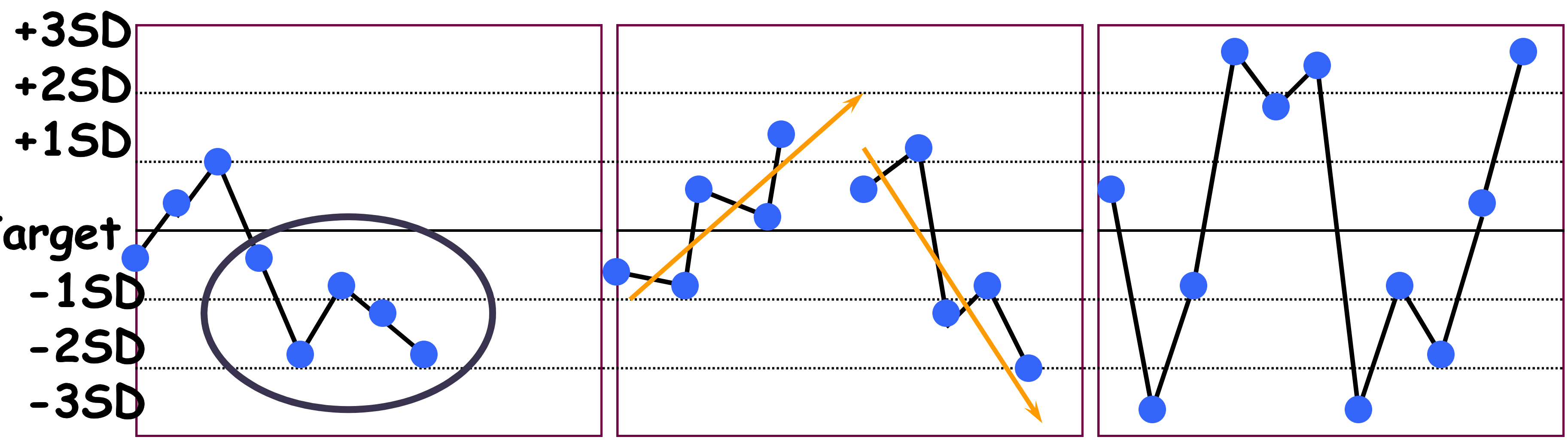
Two points near UCL (in +3SD range).

Two points near LCL (in -3SD range).

Run of 5 or more above central line.

Cause to Investigate

Upper control limit (UCL)



Lower
control limit (LCL)

Run of 5 or more below central line.

Trends in either Direction of 5 or more points.

Erratic behavior.

See Exercise

And Handout