QMS Quick Learning Activity

Controls and Control Charting

Control Charts and Trend Analysis for ISO/IEC 17025:2017

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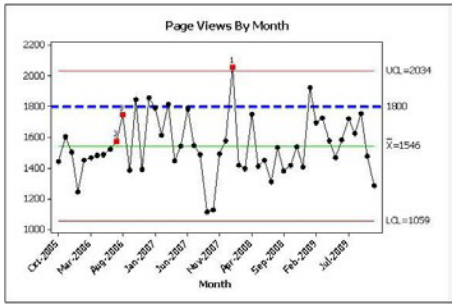
Abbreviation and Acronyms

- **RM**-Reference Materials
- **PT**-Proficiency Test(ing)
- **QMS**-Quality Management Sytem
- **QC**-Quality Control
- **STD**-Standard Deviation
- **Ct**-cycle threshold

ISO/IEC 17025 Requirements

Section 7.7 - Ensuring the validity of test results: The laboratory shall have:

- quality control procedures for monitoring the validity of tests undertaken
- data recorded so trends are detectable
- where practicable, statistical techniques applied to the reviewing of the results



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ISO/IEC 17025 Requirements

Monitoring shall be:

- Planned
- Reviewed
- Includes, as appropriate, not limited to:
  - Use of Reference Materials (RM) or Quality Control materials
  - Replicate tests using same or different methods
  - Retesting
  - Correlation of results for different characteristics

ISO/IEC 17025 Requirements

Monitoring includes: (continued)

- Use of alternative instrumentation
- Functional checks of equipment
- Use of check or working standards with control charts, where applicable
- Intermediate checks on measuring equipment
- Review of reported results
- Testing of blind samples

ISO/IEC 17025 Requirements

Monitoring includes: (continued)

- Comparison of results with other laboratories (if available and appropriate). Shall include participation in:
  - Proficiency testing (PT)
  - Interlaboratory comparisons other than PTs

Quality Management System (QMS)

The term ‘Quality Management System’ covers the quality, technical, and administrative system that governs the operations of the laboratory.

The laboratory’s QMS will have procedures for *monitoring the validity of tests and calibrations undertaken* in the laboratory.

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Quality Management System (QMS)

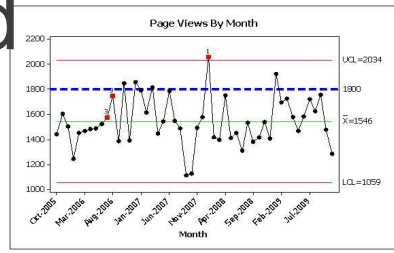
Quality Manual may state:

The laboratory monitors the quality of test results by the inclusion of quality control measures in the performance of tests and participation in proficiency testing programs. The laboratory runs Quality Control (QC) samples with each batch of samples.

ISO/IEC 17025 Requirements

Section 7.7.3

- Monitoring data analyzed and used to control, and if applicable to improve the activities of the laboratory
- If found to be outside of predefined criteria, appropriate action shall be taken to correct the problem and prevent incorrect results from being reported



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Range Control Charts

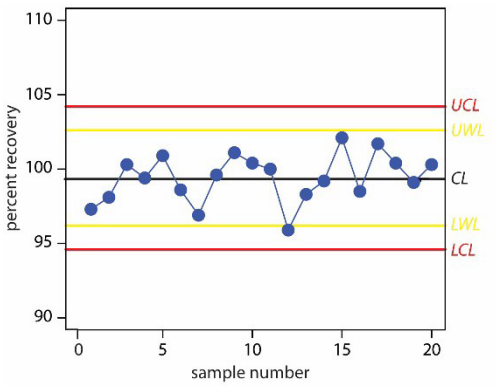
- Control Charts for Duplicate Sample Data
  - Used when impossible to use same QC over time
  - Two samples of a batch are analyzed in duplicate
    - % difference plotted
    - Absolute difference plotted

  - After 10-20 points collected calculate mean range of duplicates
  - Tables (Youden) for determining % that should fall above/below 50% line

Mean Value Control Charts Types

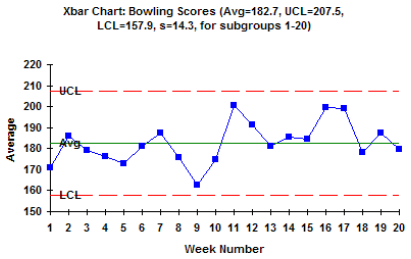
- Laboratory Control Sample (QC samples)
  - Charting the results over time of the same sample
- Matrix Spike Control Samples
  - With each batch (however defined) of samples a blank matrix sample is spiked with desired analyte.

    Recoveries (percent, count) are charted each time.



Laboratory Control Sample Control Charts

- Charting "QC samples" – must have known value associated with it.
  - Reference material
  - Old PT sample
  - Characterized by your laboratory
- Optimal QC sample
  - Similar matrix as samples
  - Value close in range of expected results

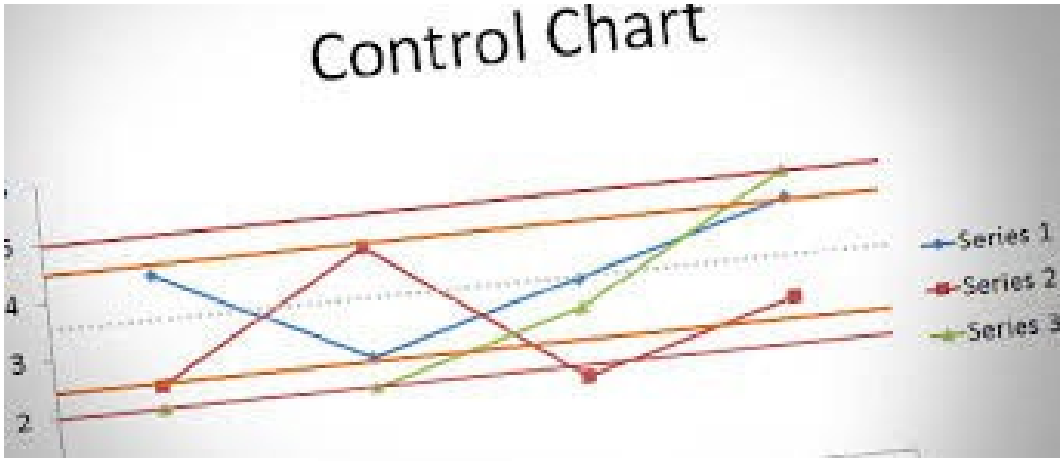


Matrix Spike Sample Control Charts

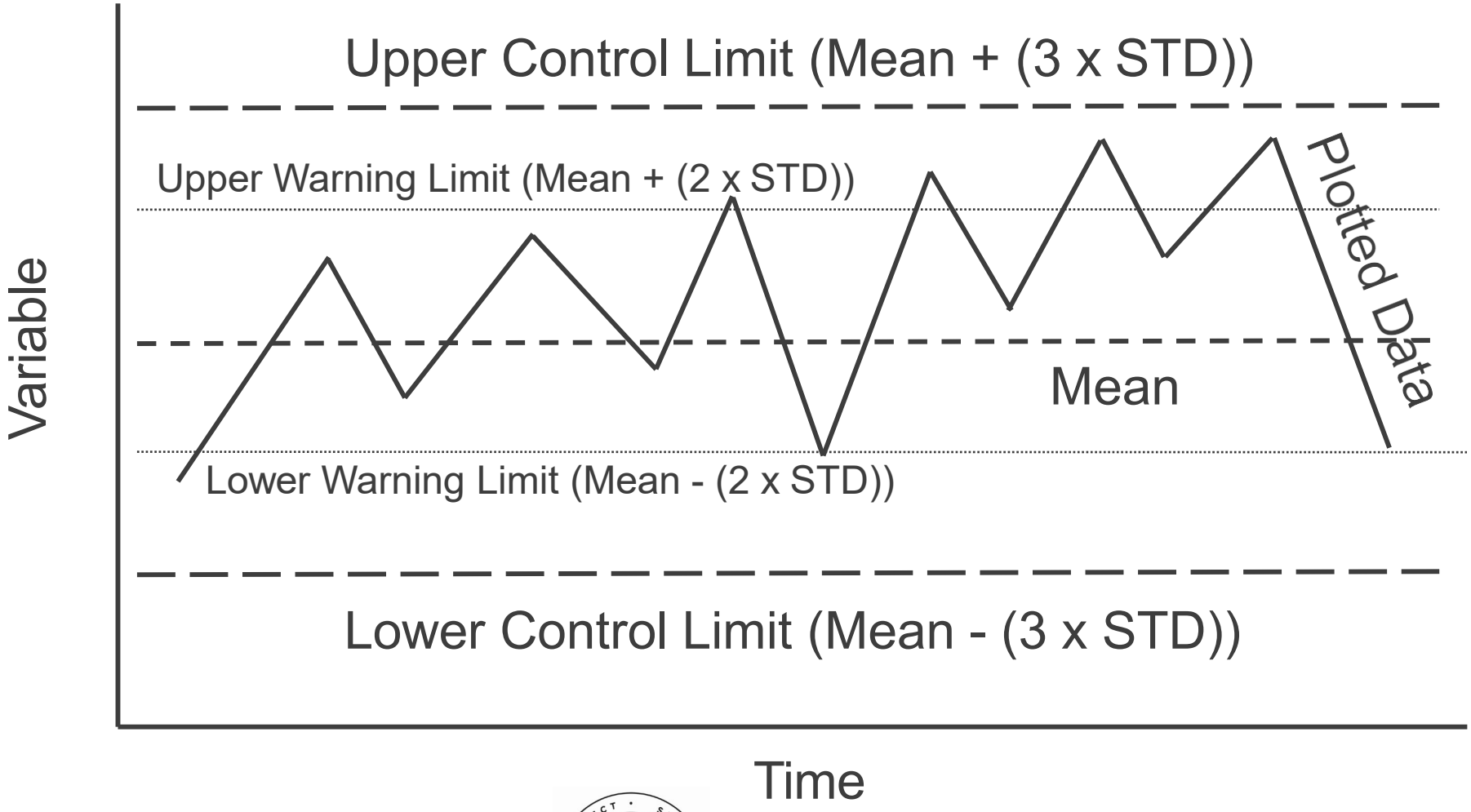
- Charting blank matrix that has been spiked with known concentration of analyte.
  - Finding blank to use is often a challenge especially when looking at trace levels
  - Used when appropriate RM is unavailable
  - RM not available in appropriate matrix
  - RM cost prohibitive

Matrix Spike Sample Control Charts

- Typical acceptance for matrix spike recovery
  - 70 – 120%
  - When large screens with many analytes or when trace levels are being analyzed acceptance can be 50 – 150%

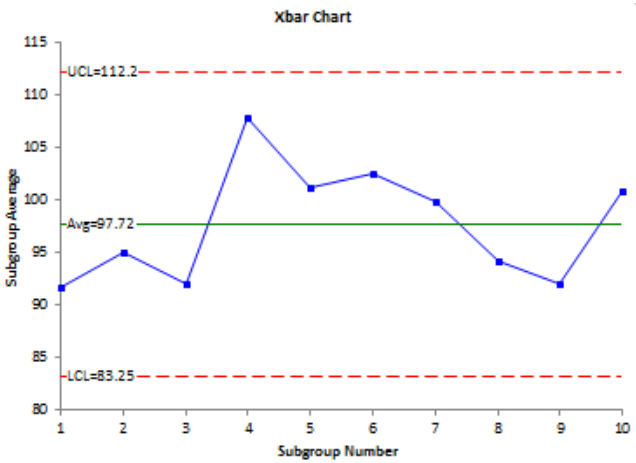


Parts of a Control Chart



Parts of a Control Chart

- X axis – time
- Y axis – variable (ex. % recovery)
- Mean
- Upper warning limit
- Lower warning limit
- Plotted data
- Upper warning limit (sometimes)
- Lower warning limit (sometimes)

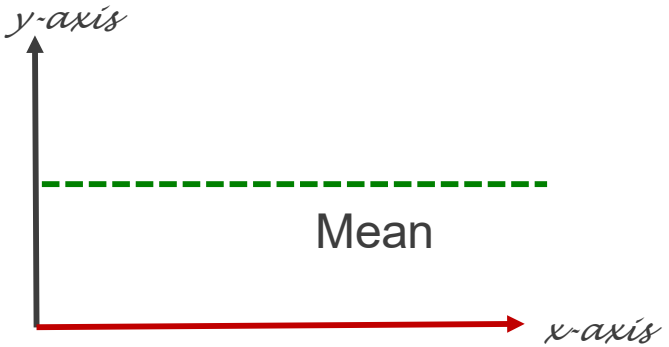


Parts of a Control Chart - Axis

- X axis
  - Each time QC sample/matrix spike is analyzed result is plotted. Could be the date run, or the instance (first time run, second time run, etc.)
- Y axis – variable (ex. % recovery, Ct value)

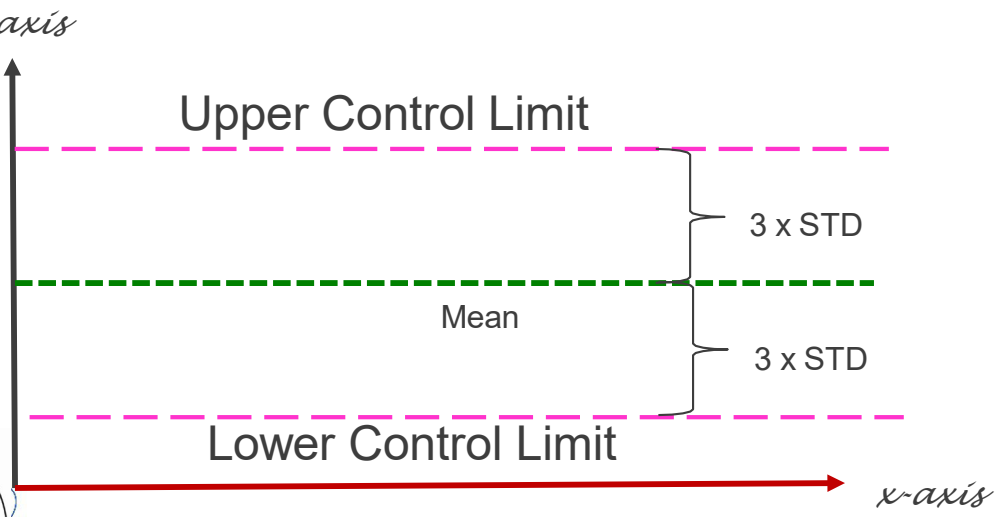
Parts of a Control Chart - Mean

- If a RM is being used that has a certified value with statistics (i.e. an acceptable range or standard deviation)
  - Use given mean
  - After ~20 point have been run, recalculate using own in-house statistics
- If a spiked sample or in-house material is being used
  - Run ~20 times (using all analysts that will be running the analysis on samples)



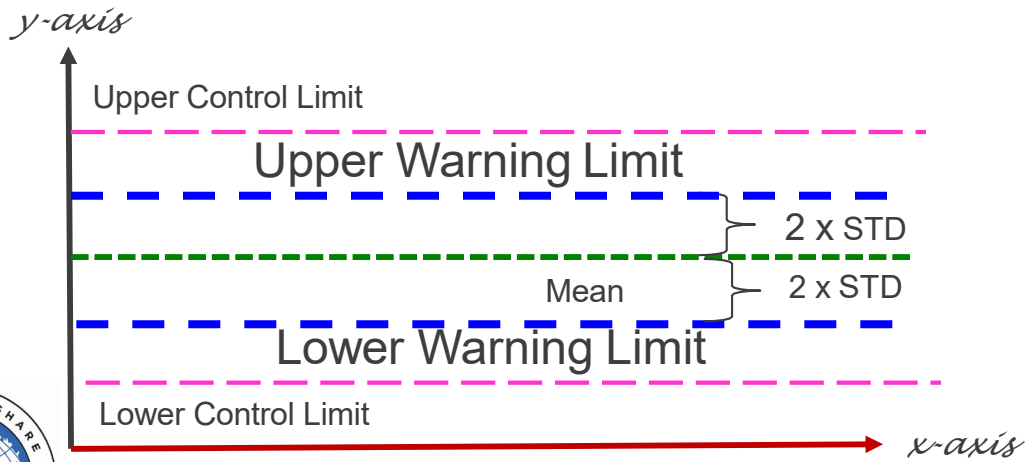
Parts of a Control Chart – Upper/Lower Control Limits

- Calculate standard deviation (STD) of points used to determine mean
- Upper and lower control limits
  - calculated by multiplying the STD x 3
  - Add (STD x 3) to mean (Upper Control Limit)
  - Subtract (STD x 3) from mean (Lower Control Limit)



Parts of a Control Chart – Upper/Lower Warning Limits

- Some control charts will have upper and lower warning limits
  - Calculate STD of points used to determine mean
- Upper and lower warning limits
  - calculated by multiplying the STD x 2
  - Add (STD x 2) to mean (Upper Limit)
  - Subtract (STD x 2) from mean (Lower Limit)



Parts of a Control Chart –Plotted Value

- Value of the control being charted
  - % recovery
  - Ct value
  - Fluorescence reading

Control Charting Statistics

- QMS will set interval at which control charting statistics (average, upper/lower control limits, etc.) are recalculated.

Statistical Control

- Control limits based on probability
- System in statistical control
  - 2/3 of values should be within mean ± 1 STD
  - 19/20 or 95% of values should be within ± 2 STD ***(Upper/Lower Warning Limits)***
  - "All" or 99.7% of values should fall within ± 3 STD ***(Upper/Lower Control Limits)***

Out of control!

- Laboratory's QMS will describe when a process (method) is considered "out of (statistical) control"
  - When the QC falls outside of the upper or lower limit
  - Two or more consecutive values fall outside 2 STD (outside the upper or lower warning limits) on the same side of the mean
  - A series of seven or eight consecutive values fall all above or all below the mean
  - An increasing or decreasing trend is detected (TRENDING analysis)

Control Charts - Trending

- Control charts reviewed to catch problems and make corrections before the process goes “out of control”
- QMS will determine interval at which control charts are reviewed

Control Charts – Qualitative Trending

- Qualitative (presence/absence) analyses ***do not*** need to have control charts for charting QC; however, the laboratory's QMS may require this
- Qualitative analyses ***do*** need to be evaluated for trending. This can be done using control charts

Control Charts – Qualitative Trending

- Qualitative analyses done using instruments can have numeric values. For example
  - Microbiology PCR analysis
    - Ct value of positive control
    - Ct value of positive sample looking at whether or not sample confirmed positive (rate of false positive)

Conclusions – Control charts

- Are used to meet the requirements of the ISO/IEC 17025 standard by providing a way for laboratories to monitor the validity of test performed
- Use RM, spiked samples, laboratory characterized materials, percent/absolute difference in duplicate samples
- Make it possible for the laboratory to track trends in analysis

References

- ISO/IEC 17025:2017
  - https://www.iso.org/standard/66912.html

- Youden WJ (1959) Graphical diagnosis of interlaboratory test results. Industrial Quality Control, 15, 24-28.