Introduction to Quality Assurance

MLS CLINICAL SEMINAR

Quality Assurance

- Monitoring of any activity that is associated with a laboratory result
- Policies, procedures, and practices to ensure laboratory results are reliable.
- Includes:
  - Record keeping
  - Calibration and maintenance of equipment
  - Quality control
  - Proficiency testing
  - Qualified personnel/training/competence

Nonanalytical Factors Related to Testing Accuracy

Laboratory Policies

- Safety manual
- Personnel policies
- Policies for critical results; specimen rejection; release of results; pipette, timer, and thermometer calibration; glassware cleaning

Laboratory Procedure Manual

Procedures should include:

- Principle and methodology of test
- Specimen requirements
- Equipment, supplies, reagents
- Preparation of materials
- Calibration/calibration verification procedures (if applicable)
- Control procedures
- Corrective action when QC or calibration fails
- Test procedure (step by step instructions)
- Limitations
- Result reporting/reference ranges/critical results/analytical measurement range
- References

Laboratory Procedure Examples

https://trh.ellucid.com/documents/view/8634/active/3

https://trh.ellucid.com/documents/view/7963/active/3

Phase of Testing

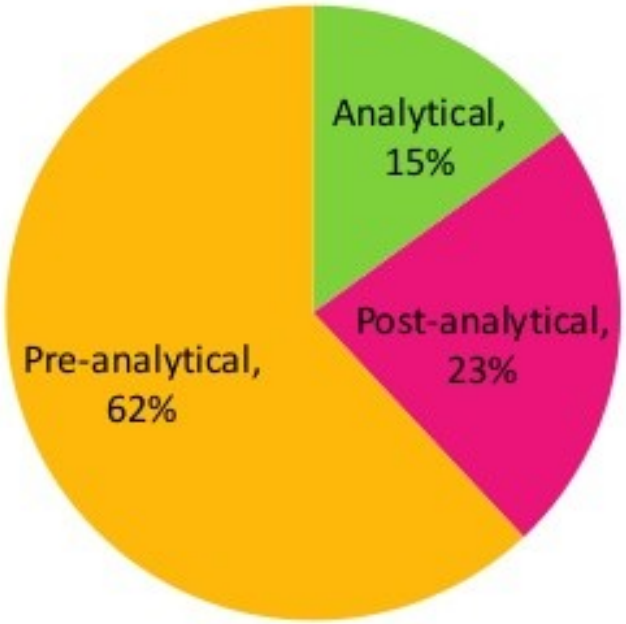
Preanalytical (preexamination)

Analytical (examination)

Postanalytical (postexamination)

Most laboratory errors occur in the preanalytical or postanalytical phase of testing

Laboratory Errors



Top Pre-analytical Errors (62%)

- Specimen collection tube not filled properly – 13%
- Patient ID error – 9%
- Inappropriate specimen collection tube/container – 8%
- Test request error – 7%
- Empty collection tube – 7%
- Others – 18%

Source: Carraro P, Plebani M. *Errors in a stat laboratory: Types and frequencies 10 years later. Clin Chem. 2007;53:1338–1342*

Test Requisitioning

Patient data (name, DOB, insurance info)

Time and date of specimen collection/collector

Source of specimen

Analyses to be performed

Individual requesting test

Diagnosis/ICD 10 code

**Info on specimen container must match exactly to the requisition

Preanalytical Errors

- Wrong test ordered
- Wrong patient
- Specimen collected at wrong time
- Specimen collected in wrong tube or container
- Blood specimens collected in the wrong order
- Incorrect labeling of specimen
- Improper processing of specimen

Analytical Errors

Oversight of instrument flags

Out-of-control quality control results

Wrong assay performed

Postanalytical Errors

Recording results inaccurately

Verbally reporting results for wrong patient

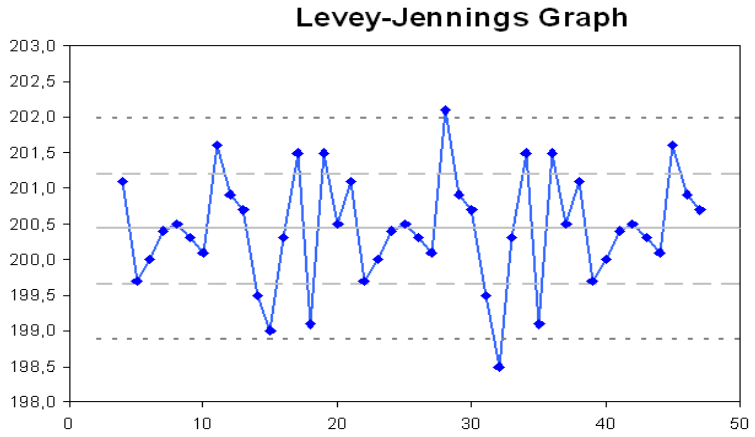
Confusion about reference ranges

LIS error

Quality Control (QC)

Procedures designed to ensure that a test method is working properly and the results meet the diagnostic needs of the clinical.

Includes testing control samples, charting the results, and analyzing them statistically



What is a QC (control) product?

A quality control product is a patient-like material ideally made from human serum, urine or spinal fluid

- Should be the same matrix as the patient sample

QC

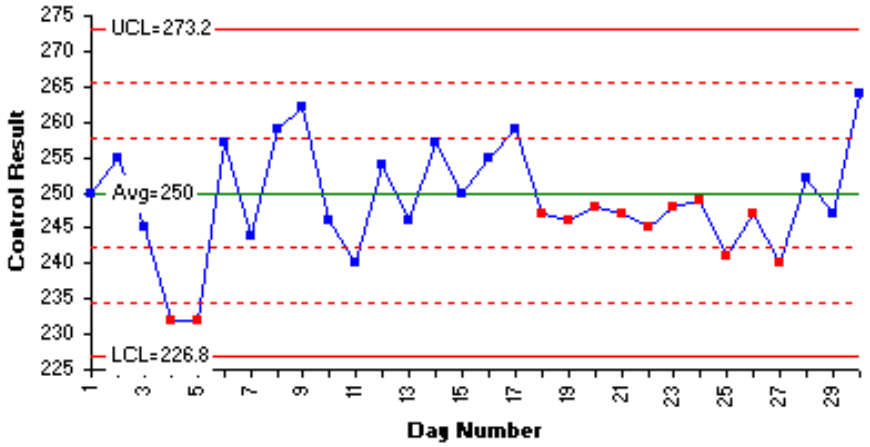
Used to monitor accuracy and precision

Required by accrediting agencies

Accuracy – how close the result is to the true value

Precision – how close repetitive values of the same sample are to one another

Levey Jennings Chart



Established for each analytical method based on calculated mean and SD

QC must be within 2SD

Monitoring Quality

Proficiency Testing (PT)

- Testing of unknown samples sent to a lab by a CMS approved PT provider
- Mandated by CMS for “regulated” analytes
- Is in addition to internal QC programs
- External to the program (subscription)
- Means of verification of laboratory accuracy

- More information can be found at: https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/CLIAbrochure8.pdf

Proficiency Testing (PT)

Identical samples sent to all labs who participate in program

Must test in the **same manner** as patient specimens

Proficiency samples must be rotated through **all** testing personnel

NEVER send out PT samples to another lab even if you routinely send out patient samples for confirmatory or additional testing

NEVER discuss PT results with another lab before the PT event due date

Each lab is evaluated and graded on results submitted as compared to results of all other labs

Must score 80% on all analytes to be in compliance (Blood bank specimens require 100%)

PT Evaluation

[redacted] City / State: [redacted]

EVALUATION
ORIGINAL

AQI-A 2016 Critical Care Aqueous Blood Gas

Test / Unit of Measure / Peer Group	Specimen	Your Result	Mean	S.D.	No. of Labs	S.D.I	Limits of Acceptability Lower	Limits of Acceptability Upper	Your Grade	Plot of the Relative Distance of Your Results from Target as Percentages of allowed Deviation
pH	AQI-01	6.59	6.594	0.013	2144	-0.3	6.55	6.64	Acceptable	Survey -100——Mean——+100
	AQI-02	7.59	7.589	0.010	2200	+0.1	7.54	7.63	Acceptable	AQI-A 2016 / AQI-C 2015 / AQI-B 2015
i-STAT CART. (EXC EC8+	AQI-03	7.40	7.385	0.008	2206	+1.8	7.34	7.43	Acceptable	-100 -80 -60 -40 -20 0 20 40 60 80 100
	AQI-04	7.54	7.535	0.009	2197	+0.6	7.49	7.58	Acceptable	
	AQI-05	6.80	6.783	0.012	2169	+1.5	6.74	6.83	Acceptable	
PCO2	AQI-01	103	99.0	4.9	2118	+0.8	91	107	Acceptable	
mm Hg	AQI-02	29	28.5	1.2	2182	+0.5	23	34	Acceptable	AQI-A 2016 / AQI-C 2015 / AQI-B 2015
i-STAT CART. (EXC EC8+	AQI-03	36	38.0	1.4	2181	-1.4	32	43	Acceptable	-100 -80 -60 -40 -20 0 20 40 60 80 100
	AQI-04	34	34.1	1.3	2188	-0.1	29	40	Acceptable	
	AQI-05	75	80.7	3.3	2171	-1.7	74	88	Acceptable	
PO2	AQI-01	55	49.9	9.8	2159	+0.5	20	80	Acceptable	
mm Hg	AQI-02	118	112.8	4.7	2180	+1.1	98	127	Acceptable	AQI-A 2016 / AQI-C 2015 / AQI-B 2015
i-STAT CART. (EXC EC8+	AQI-03	118	95.9	5.1	2167	+4.3	80	112	Unacceptable	-100 -80 -60 -40 -20 0 20 40 60 80 100
	AQI-04	108	104.0	4.6	2181	+0.9	90	118	Acceptable	x: Result is outside the acceptable limits
	AQI-05	93	58.9	9.1	2159	+3.7	31	87	Unacceptable	
Potassium	AQI-01	2.4	2.46	0.05	1656	-1.2	1.9	3.0	Acceptable	
mmol/L	AQI-02	5.3	5.26	0.05	1660	+0.8	4.7	5.8	Acceptable	AQI-A 2016 / AQI-C 2015 / AQI-B 2015
i-STAT CART. (EXC EC8+	AQI-03	3.6	3.57	0.05	1665	+0.6	3.0	4.1	Acceptable	-100 -80 -60 -40 -20 0 20 40 60 80 100
	AQI-04	4.3	4.33	0.05	1659	-0.6	3.8	4.9	Acceptable	
	AQI-05	2.4	2.33	0.05	1639	+1.5	1.8	2.9	Acceptable	

Unacceptable performance

PT Score Card

EVALUATION
ORIGINAL

AQI-A 2016 Critical Care Aqueous Blood Gas

CMS Peformance Summary for Analytes Regulated Under the Clinical Laboratory Improvement Amendments of 1988

CLIA ID #: 39D0697287 **Subspecialty :** Routine Chemistry

Regulated Analyte	Proficiency Event 2015 2			Proficiency Event 2015 3			Proficiency Event 2016 1			Current Event Performance Interpretation	Cumulative CLIA '88 Performance Interpretation	
	Test Event	Score	%	Test Event	Score	%	Test Event	Score	%			
ALT	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>
Albumin	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>
Alkaline Phosphatase	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>
Amylase	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>
AST	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>
Bilirubin, Total	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>
Blood Gas, pH	AQI-B	5/5	100	AQI-C	5/5	100	AQI-A	5/5	100	Satisfactory	Successful	
Blood Gas, PO2	AQI-B	4/5	80	AQI-C	3/5	60	AQI-A	3/5	60	Unsatisfactory	Unsuccessful	<3>
Blood Gas, PCO2	AQI-B	5/5	100	AQI-C	5/5	100	AQI-A	5/5	100	Satisfactory	Successful	
Calcium, Total	C-B	5/5	100	C-C	5/5	100				Pending	Successful	<4>

Unsatisfactory

Unsuccessful- 2 out of 3 unsatisfactory

Delta Checks

- a quality control tool
- comparison of patient result with previous result(s)
- large disparity usually indicates error in one of the results
- Can be used to detect specimen integrity errors, specimen identification errors, or other analytical errors
  - Examples: MCV in hematology or electrolytes

Patient Moving Averages

- a QC strategy using the mean patient result to continuously monitor assay performance
- can be used in chemistry and hematology
- X-bar
  - Proposed by Dr. Brain Bull in 1974
  - Evaluates RBC indices which are typically stable for patient population over time.
  - Uses small batches of 20 samples to calculate each mean. The mean of each batch is compared to the target values.

Physiologic Plausibility/Incompatible with Life

Patient results must be checked to be sure they are physiologically possible and that the results make sense when compared to other results from the same sample

- Examples:
  - Albumin cannot exceed total protein
  - Protein must be present when pathologic urinary casts are present
  - Microscopic results match macroscopic results

Patient results must be checked to make sure they are not “incompatible with life”

Process Improvement (PI)

Determining how to improve begins by recognizing a failure or a risk of failure in meeting a patient or physician need

Using Lean and Six Sigma

Combine Six Sigma quality management with Lean manufacturing strategy

Develop tangible metrics for quality improvement

Benefits of Quality Management in the Laboratory

- Improved patient care and satisfaction
- Improved staff satisfaction
- Standard process for information flow
- Consistency in way work is completed
- Work completed sooner
- Increase capacity
- Improve financial performance
- Improve employee engagement

Quality Monitors

- Review preanalytic, analytic, and postanalytic processes
- Determine monitors
- Perform regular assessments
- Establish thresholds
- Collect data
- Evaluate data
- Perform corrective actions and follow up

Reading Hospital Quality Monitors

Pre-Analytic

- Specimen quality issues
- Blood Culture Contamination Rate
- ED Order to Draw TAT

Analytic

- Brain Attack TAT
- ED TAT
- Corrected reports
- Blood Product Wastage
- Proficiency Testing results

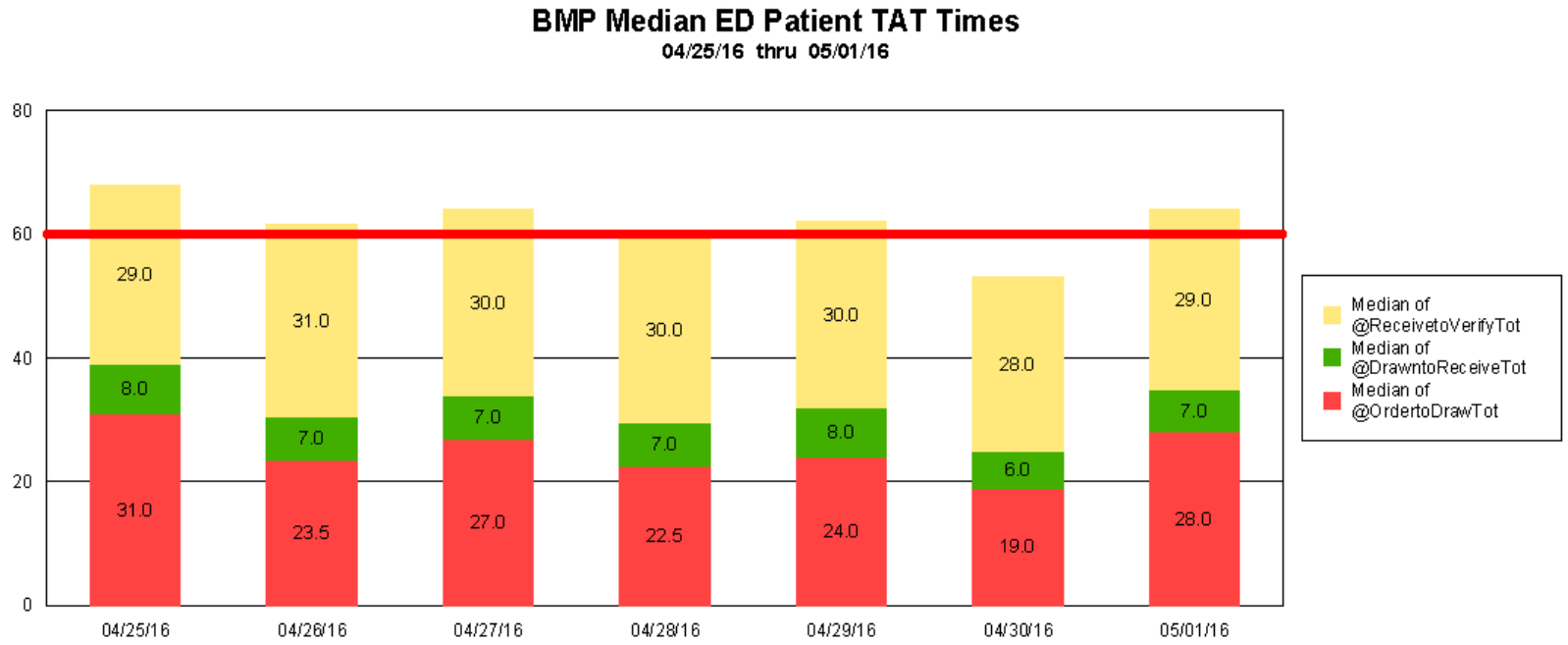
Post Analytic

- Critical Values Reporting Compliance Audit

Customer Service

- Outpatient Recollect Return rate
- Press Ganey Surveys

Turnaround Times Example



	Total					Lab					Nurse				
	Number of Tests	Order to Draw Min	Draw to Receive Min	Receive to Verify Min	Order to Verify Min	Number of Tests	Order to Draw Min	Draw to Receive Min	Receive to Verify Min	Order to Verify Min	Number of Tests	Order to Draw Min	Draw to Receive Min	Receive to Verify Min	Order to Verify Min
04/25/2016	159	31.0	8.0	29.0	68.0	95	41.0	8.0	29.0	78.0	64	22.5	8.0	28.5	59.0
04/26/2016	154	23.5	7.0	31.0	61.5	102	29.0	8.0	30.0	67.0	52	17.5	6.0	31.5	55.0
04/27/2016	168	27.0	7.0	30.0	64.0	118	32.0	7.5	30.0	69.5	50	19.5	7.0	29.0	55.5
04/28/2016	136	22.5	7.0	30.0	59.5	93	25.0	8.0	29.0	62.0	43	19.0	6.0	31.0	56.0
04/29/2016	146	24.0	8.0	30.0	62.0	97	25.0	9.0	30.0	64.0	49	20.0	6.0	31.0	57.0
04/30/2016	115	19.0	6.0	28.0	53.0	70	24.5	6.0	27.0	57.5	45	17.0	6.0	28.0	51.0
05/01/2016	146	28.0	7.0	29.0	64.0	94	31.0	9.0	30.0	70.0	52	20.5	6.0	29.0	55.5
Total:	1,024					669					355				
Median:		25.0	7.0	30.0	62.0		29.0	8.0	29.0	66.0		19.0	6.0	30.0	55.0
Average:		55.2	9.8	32.4	97.4		68.9	10.5	31.7	111.1		29.5	8.3	33.6	71.4

Quality Control

MLS CLINICAL SEMINAR

QA Indicators and QC Programs

Tools to ensure that reported lab results are of the highest quality

Improves the accuracy and reliability of laboratory testing

Diagnostic Test Results

- Outcome of a diagnostic test is a result which can be either a quality control or a patient result
- Results may be:

Quantitative

Semi-quantitative

Qualitative

- All tests require the use of quality control

Definition

Quality Control- statistical process used to monitor and evaluate the analytical process

Procedures to detect errors in:

- test procedure
- integrity of reagents
- tech performance
- lab instruments

Achieved by use of control substances

- Control charts are used to plot and compare current value to historical results
- Calculate mean and SD to establish control limits

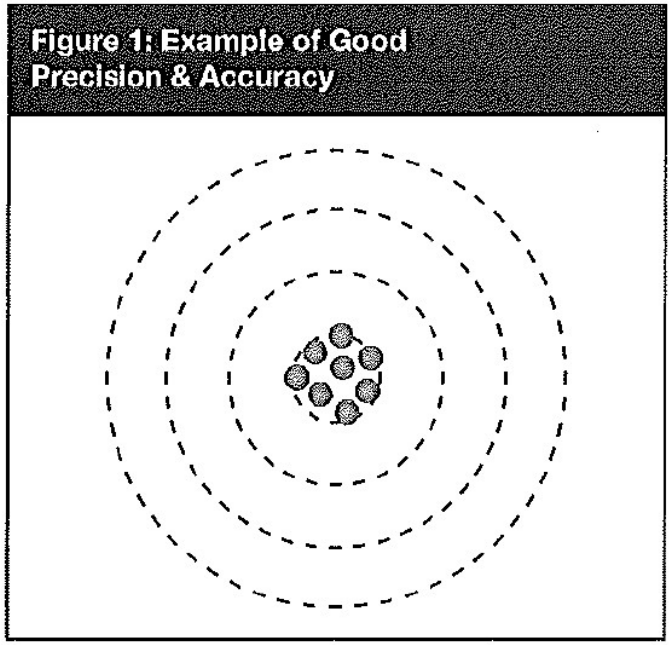
Quality Control ("Controls")

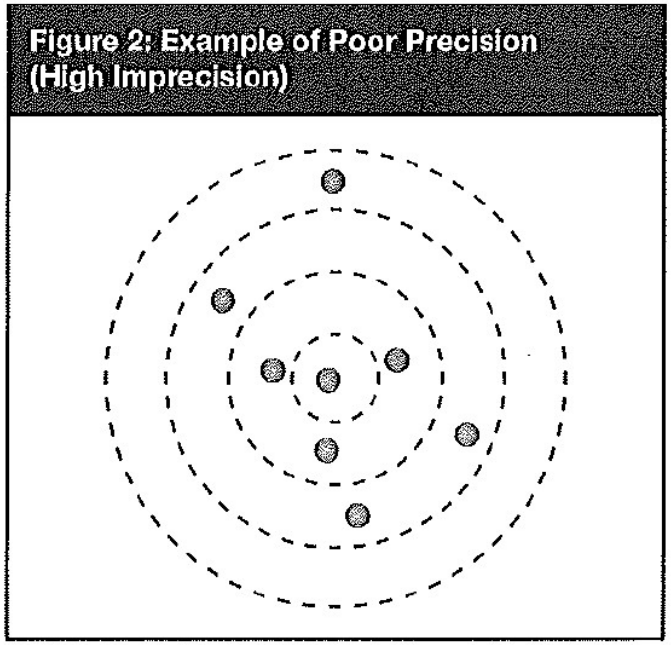
- liquid (ready to use), frozen, or lyophilized
- assayed or unassayed
- same matrix as patient samples (matrix effect)
- have long-term stability
- must contain appropriate analyte levels to span the clinical range (normal, high, low)
- at least 2 levels of QC must be analyzed at least once a day (follow CLIA/manufacture regulations)

How do I test QC?

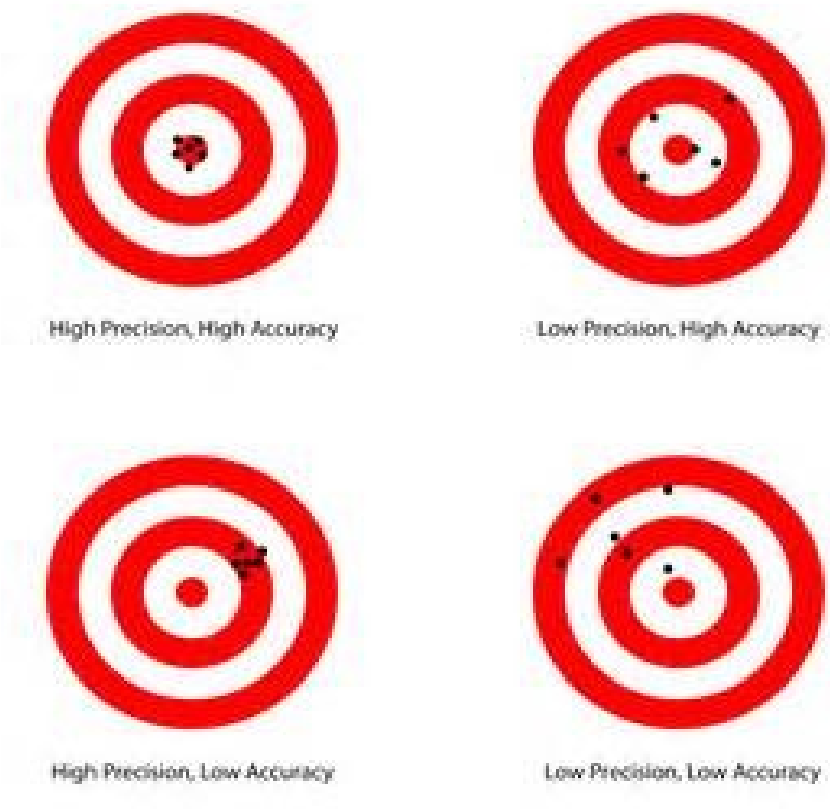
- In the same manner as patient samples
- Normal and abnormal controls are tested at least daily
- Used to create a QC database that the laboratory uses to validate the test system
- All QC results must be within established ranges in order to report patient results

Accuracy and Precision





More Examples



Statistical Terms

Mean- average of a set of values (primary indicator of accuracy)

Median-the middle point of all data points- 50th percentile

Mode- the most frequent number

Range- difference between the high and low values

- **When data exhibit Gaussian distribution, the mean, median, and mode are the <u>same</u>**

Standard Deviation Calculation

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

Where:

s = standard deviation

$\bar{x}$ = mean (average) of the QC values

$\Sigma(x_n - \bar{x})^2$ = the sum of the squares of differences between individual QC values and the mean

n = the number of values in the data set

Standard Deviation

- Most common measure of imprecision or dispersion
- Measure of the spread or scatter of a set of observations around the mean
- Measure of **RANDOM ERROR**

Coefficient of Variation

$$CV = (s \div \bar{x})\,100$$

Where:

s = standard deviation

$\bar{x}$ = mean

Coefficient of Variation (CV)

- Measure of standard deviation expressed as a percentage of the mean
- Independent of the units of measurement
- Also a measure of random error (change in precision)
- Used to compare the relative variability between methods or tests with different means and different standard deviations

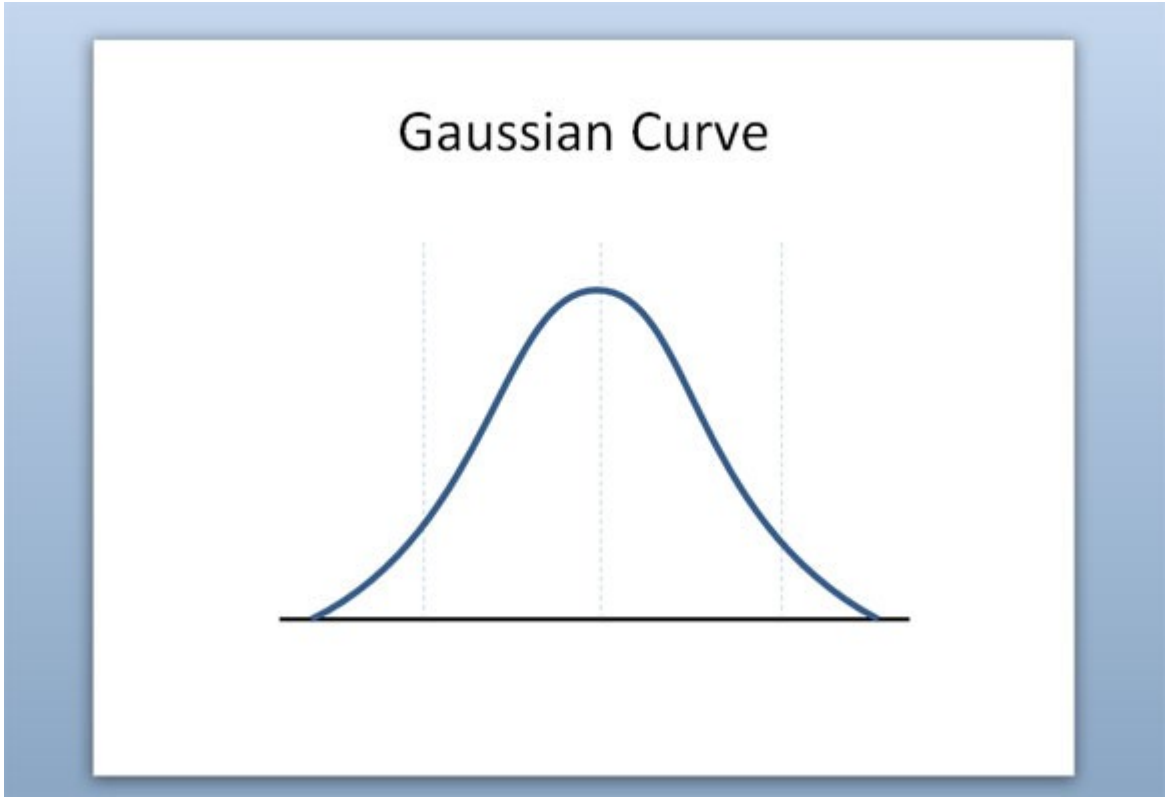
CV

Comparison of Coefficient of Variations

Procedure 1	Procedure 2
$\bar{X} = 16$	$\bar{X} = 12$
$SD = 1.67$	$SD = 1.25$
$CV = \frac{1.67}{16}(100)$	$CV = \frac{1.25}{12}*(100)$
$= 10.4\%$	$= 10.4\%$

Although the two procedures have different means and standard deviations, they have identical precision

Gaussian Distribution

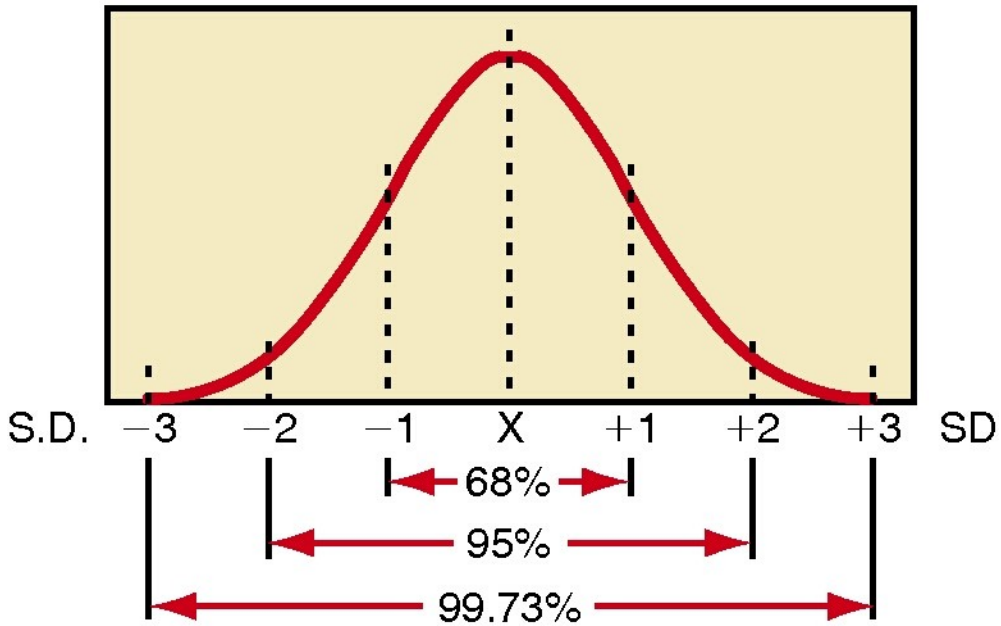


Relative Distribution of QC

- 68% of QC values will fall within ± 1 SD of the mean
- 95.5% QC of values will fall within ± 2 SD of the mean
- 99.7% of QC values will fall within ± 3 SD of the mean

- Only **0.3%** or 3 out of 1000 will fall outside of ± 3SD limits
- Any value outside of ± 3SD limits is considered to be associated with significant error and patient results should **not** be reported

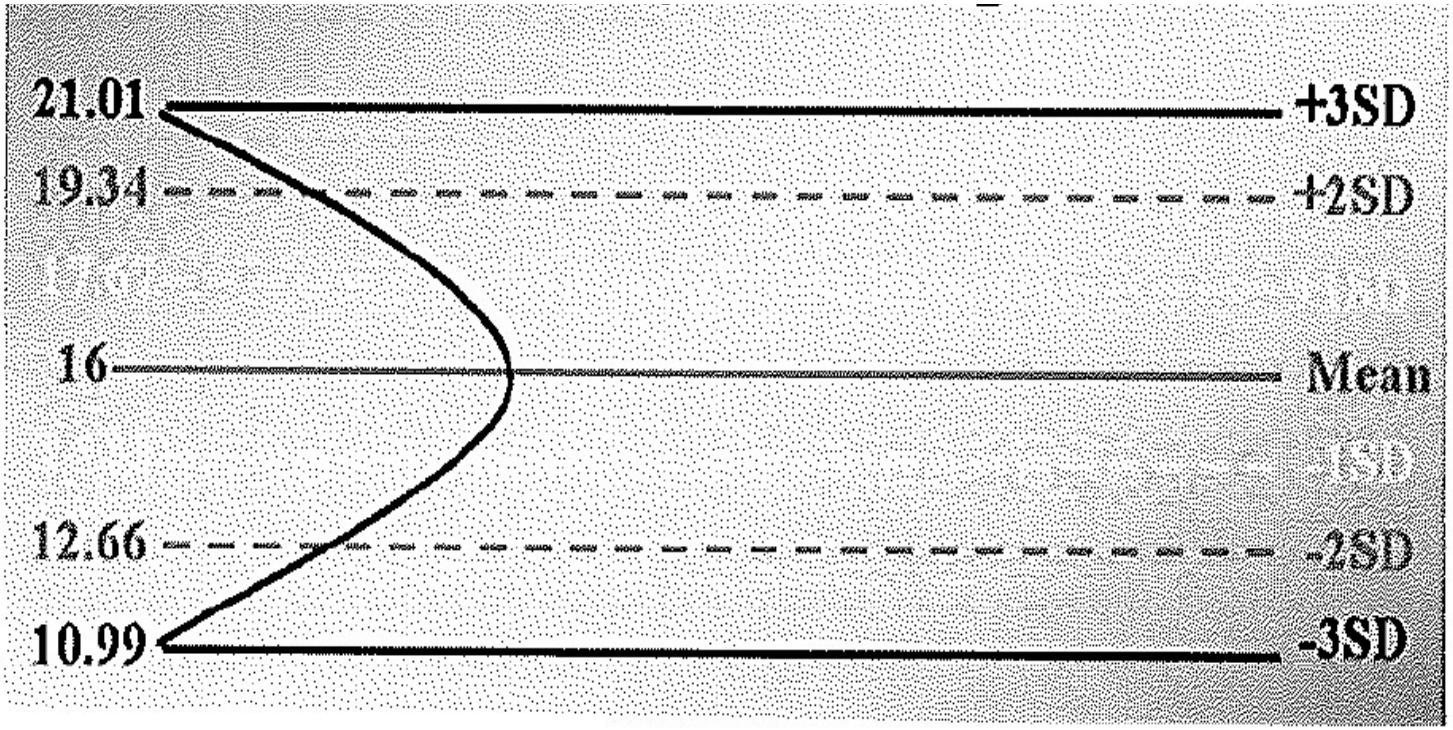
Quality Control Statistics



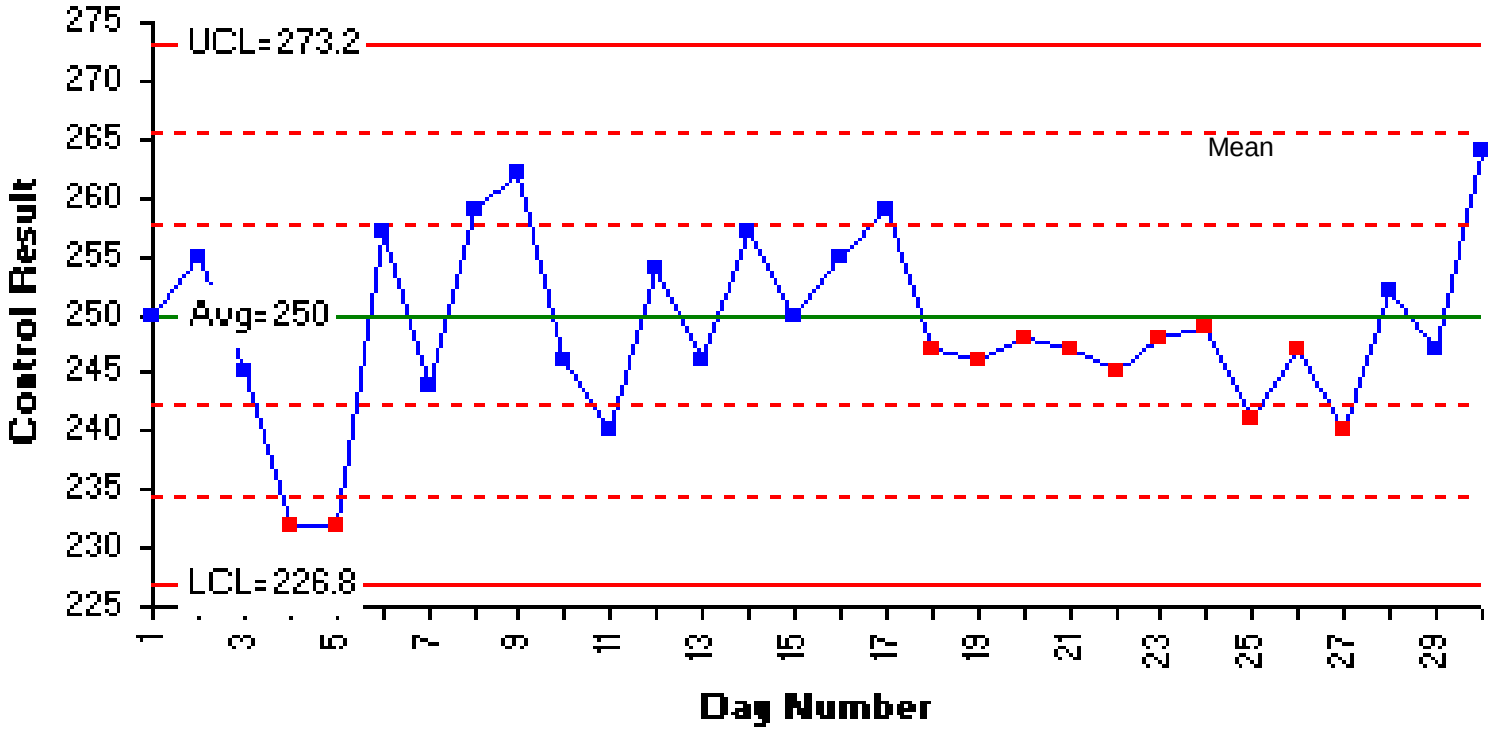
Levey Jennings (LJ) Chart

- Control results are easier to interpret when they are in chart form
- LJ chart is a graphical display of the degree of precision of a measurement
- LJ chart is based on the Gaussian distribution of values

LJ Chart



Levey Jennings Chart



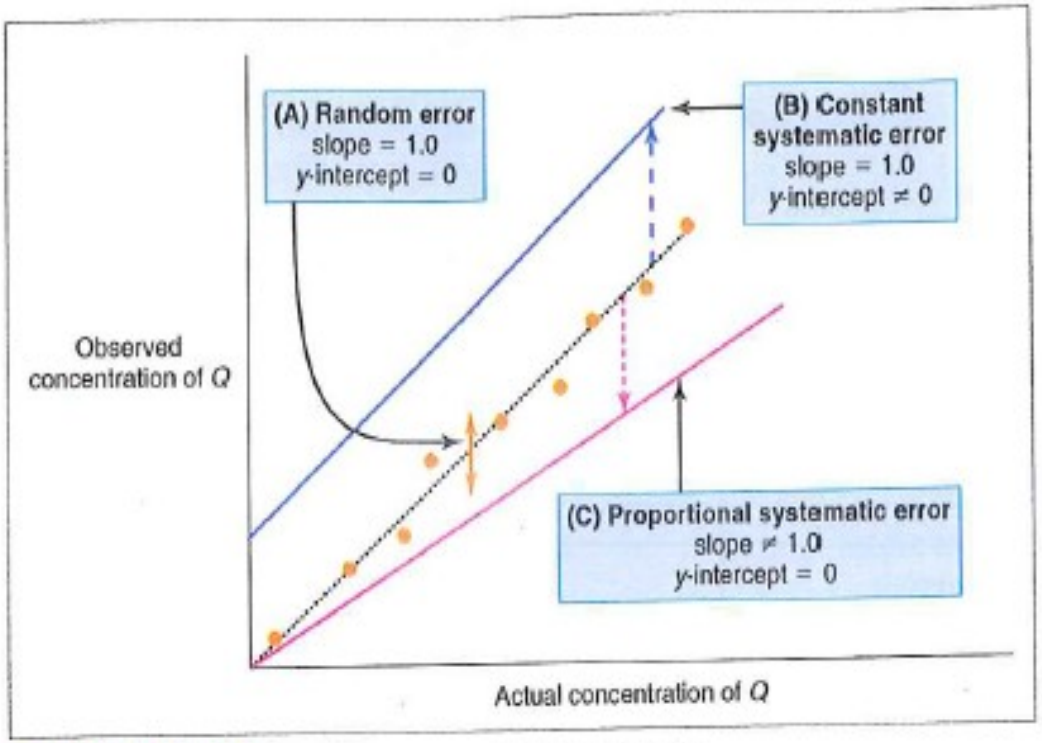
Random and Systematic Errors

- Primary function of QC is to alert the operator to a change in the analytical system

- ***Random error (RE)-*** inherent variations in analyzers causing variation in results above and below the mean.

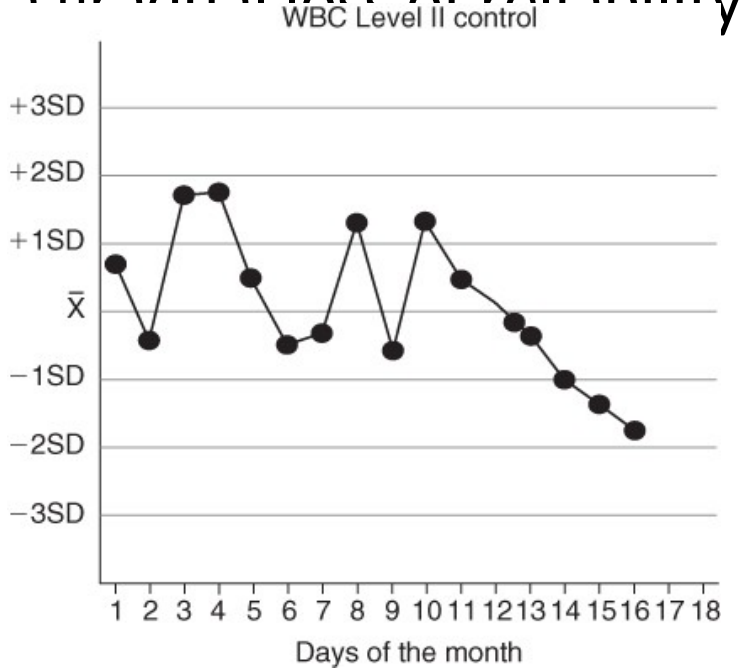
- ***Systematic error (SE)-*** a change that is always in **ONE** direction and is indicated by a shift in the mean.

Random versus Systematic Error



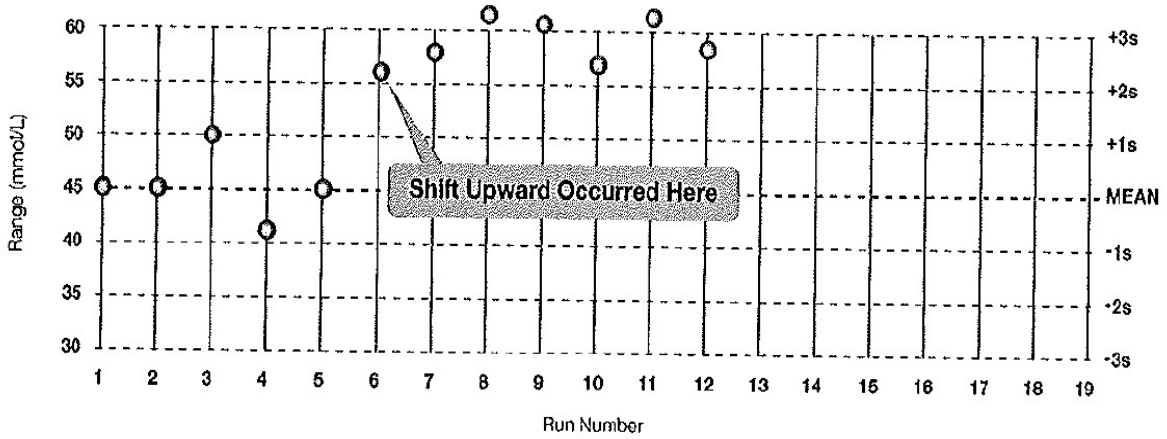
Trend

- series of controls consistently increasing or decreasing
- indicates a gradual loss of reliability in the test system



Shift

- an abrupt change of the mean for the control
- a sudden positive or negative change in the test system performance



Causes of Random Error

- fluctuations in temperature
- fluctuations in volume
- environmental conditions
- inconsistent handling of materials
- electrical interference
- bubble in sample or reagent

Causes of Systematic Error

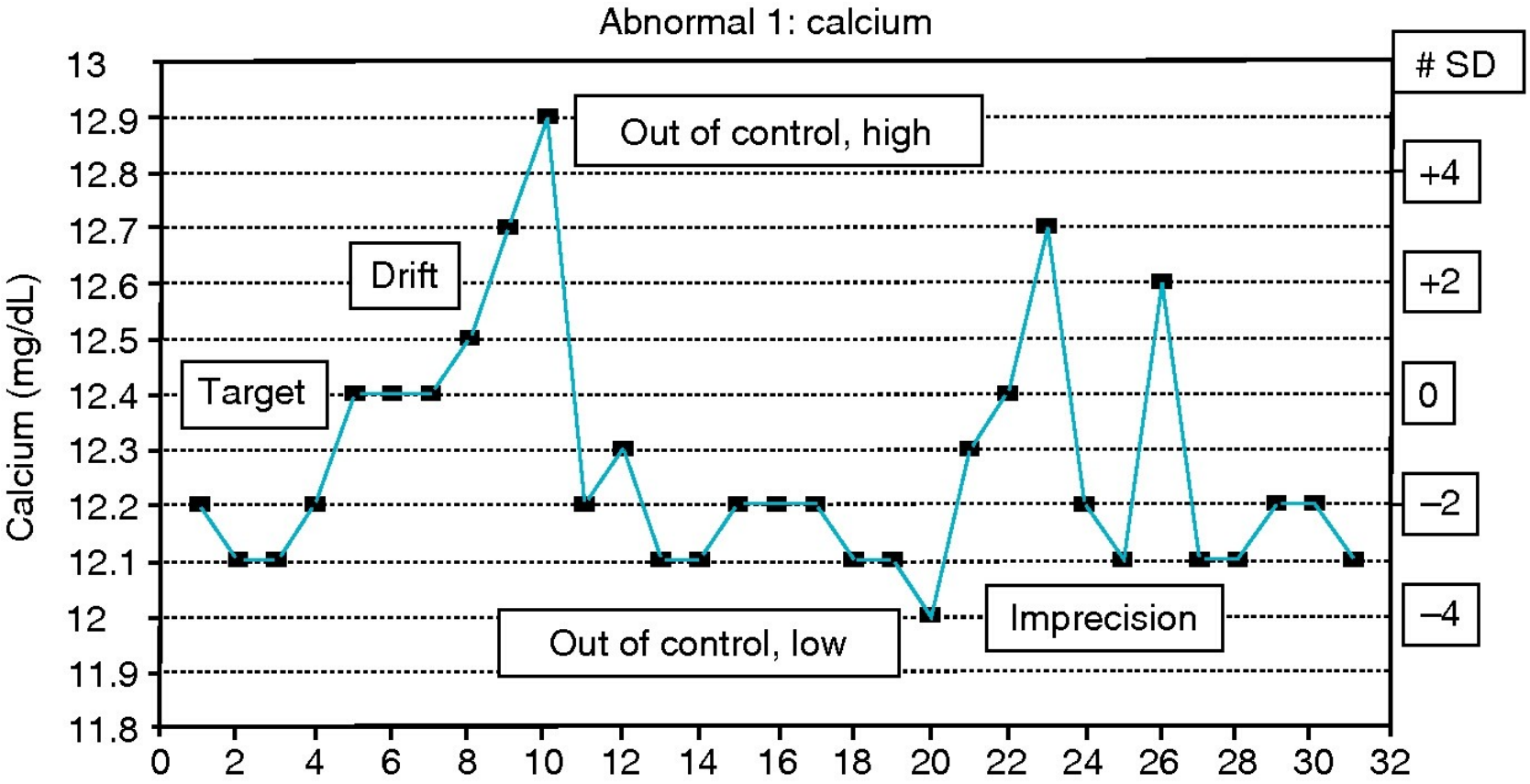
- Trend
  - Deterioration of light source
  - Debris
  - Aging/deteriorating reagents or QC
  - Deterioration of calibration

Causes of Systematic Error

- Shift
  - Sudden change in light source
  - Change in reagent formulation
  - Change in reagent lot #
  - Major instrument maintenance
  - Change in room temp/humidity
  - Inaccurate calibration
  - Failure of sampling system

Westgard Rules

- Set of criteria which one can monitor test performance and accept or reject the run
- Multirule QC- uses a combination of decision criteria to decide whether an analytical run is “in-control” or “out-of-control”
- Successful in determining if problem is random error or systematic error
- If all control values fall within 2s control limits, a run is judged to be “in-control”
- https://www.westgard.com/


Abnormal 1: calcium
Calcium (mg/dL)
13
12.9
12.8
12.7
12.6
12.5
12.4
12.3
12.2
12.1
12
11.9
11.8
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
SD
+4
+2
0
–2
–4
Out of control, high
Drift
Target
Out of control, low
Imprecision

Traditional Westgard Rules

- 1_{2S}, 1_{3S}, 2_{2S}, R_{4S}, 4_{1S}, 10_{x}
- Written as N_L

  N represents the number of control observations to be evaluated

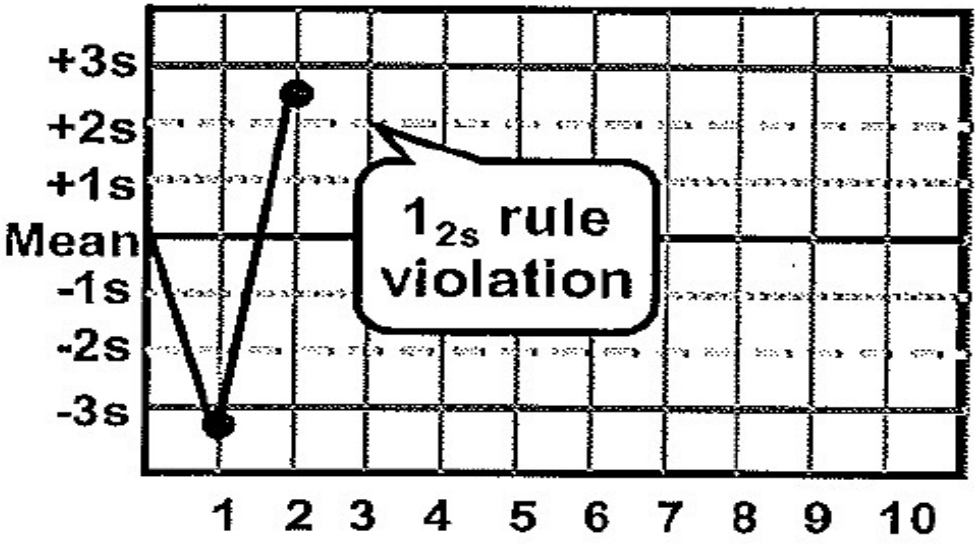
  L represents the statistical limit for evaluating control observations

  For example:

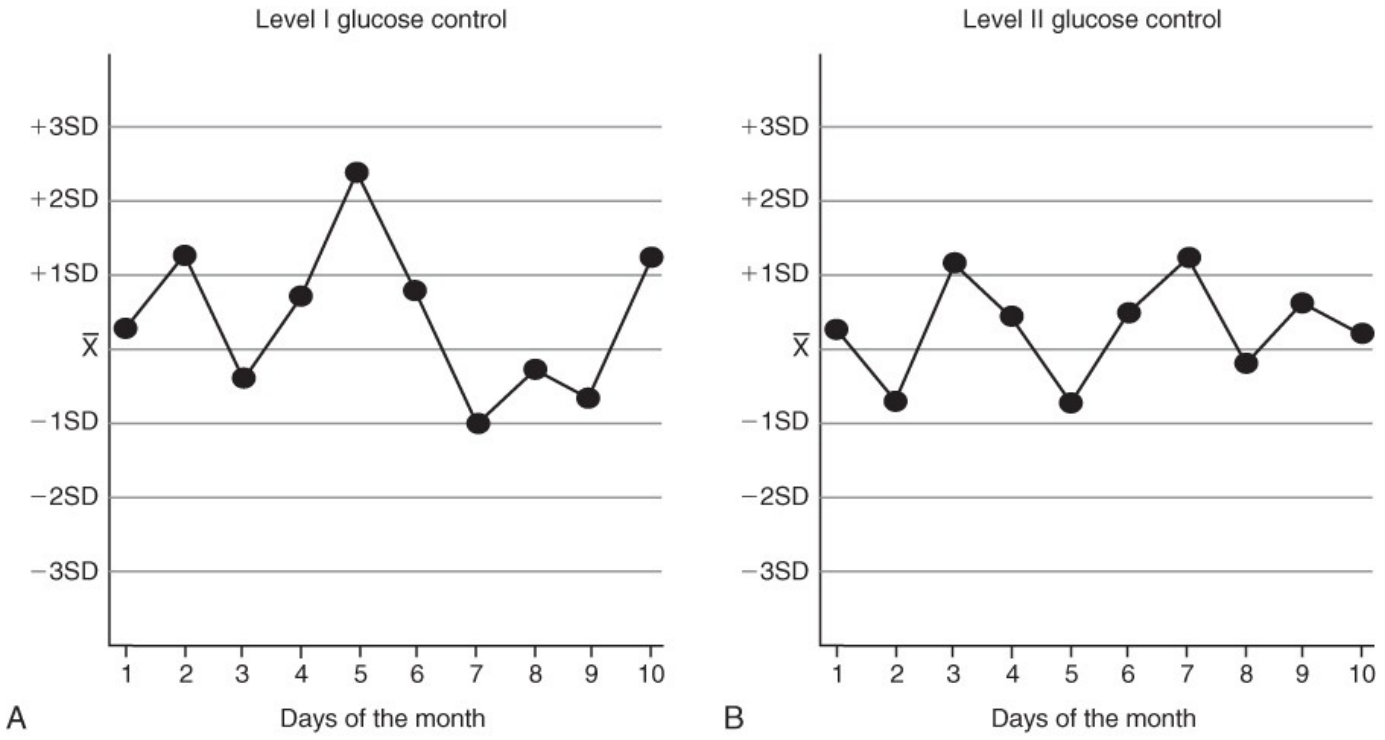
  - 1_{3S} represents a control rule that is violated when one control observation exceeds the ±3 SD control limits

1_{2s}

1_{2s}- one control values lies outside of the mean ± 2SD. Warning flag tells the technologist to check the other rules.

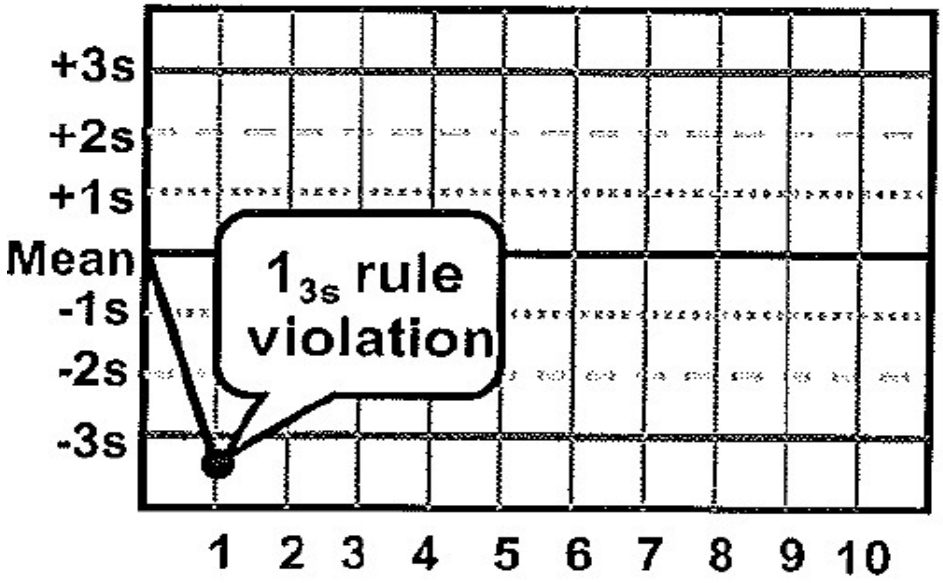


1_{2s}

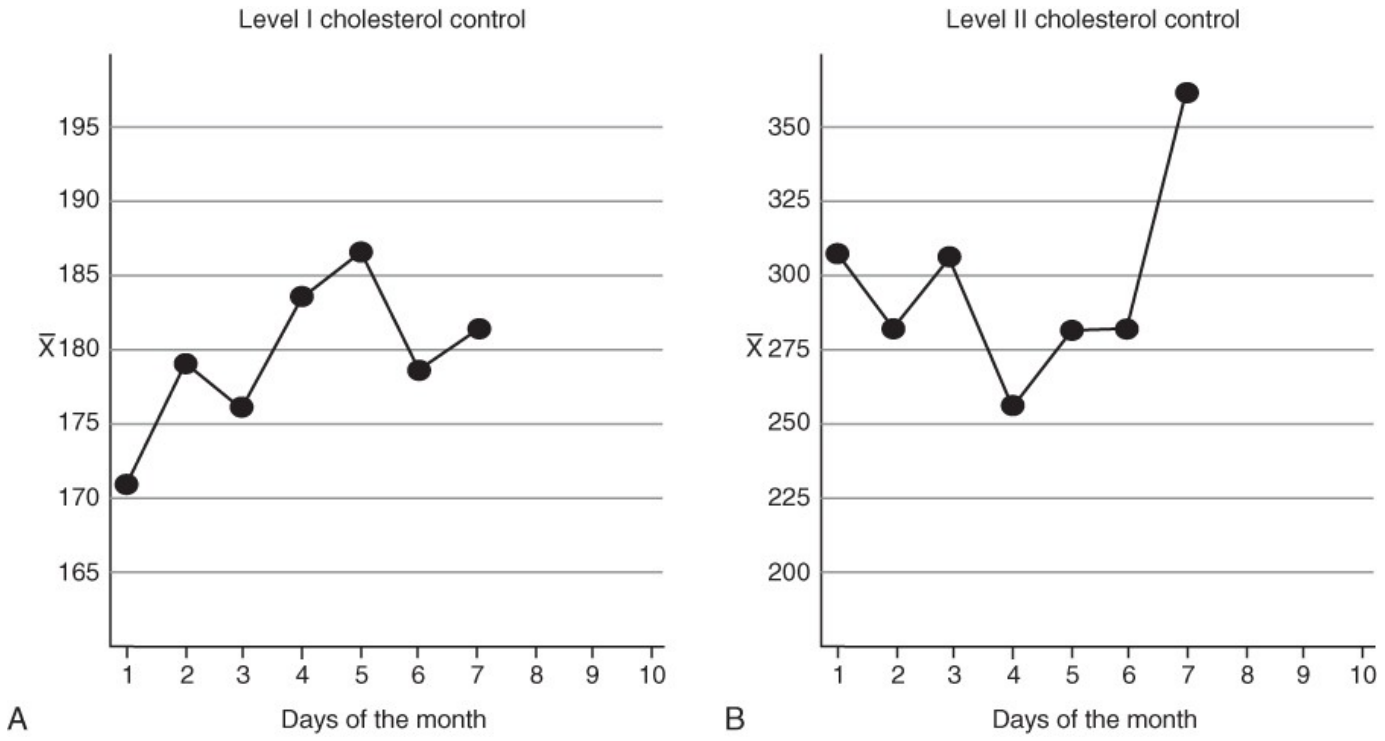

Level I glucose control
+3SD
+2SD
+1SD
X̄
−1SD
−2SD
−3SD
1 2 3 4 5 6 7 8 9 10
Days of the month
A
Level II glucose control
+3SD
+2SD
+1SD
X̄
−1SD
−2SD
−3SD
1 2 3 4 5 6 7 8 9 10
Days of the month
B

1_{3s}

1_{3s}-one control values lies outside of ± 3SD

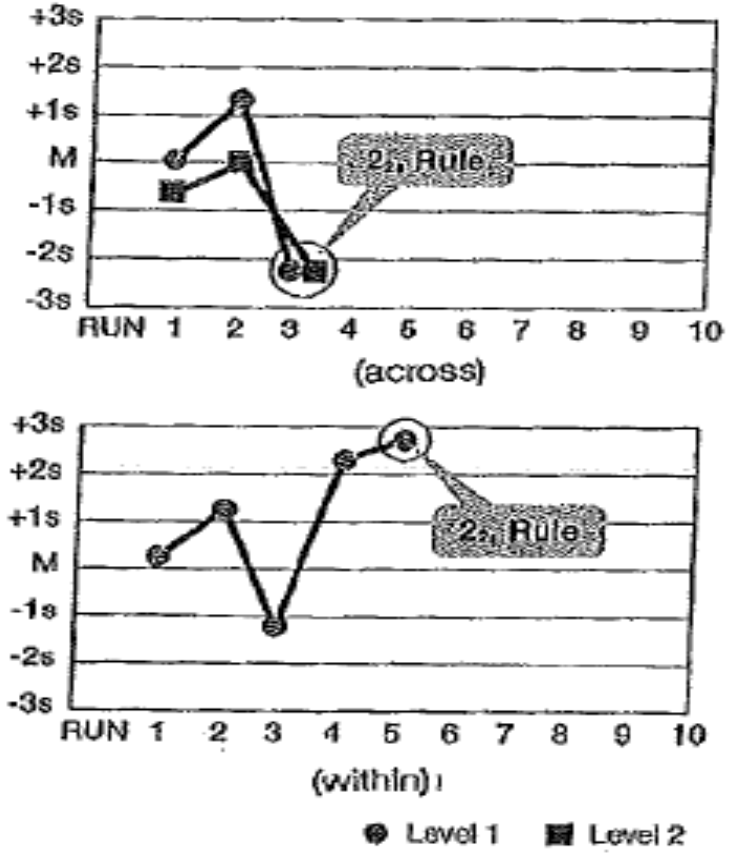


1_{3s}


Level I cholesterol control
195
190
185
X̄ 180
175
170
165
1 2 3 4 5 6 7 8 9 10
A
Days of the month
Level II cholesterol control
350
325
300
X̄ 275
250
225
200
1 2 3 4 5 6 7 8 9 10
B
Days of the month

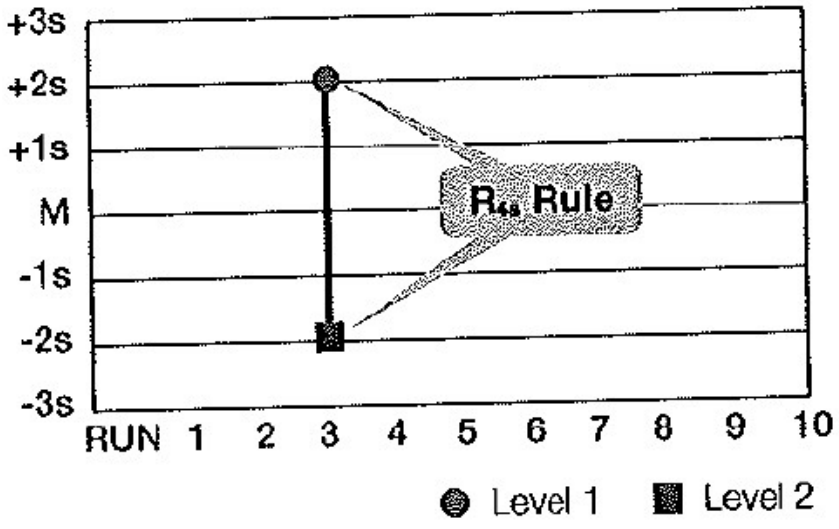
2_{2s}

2_{2s}- Two consecutive control values lie outside the mean +2SD or the mean -2SD(must be in the same direction).

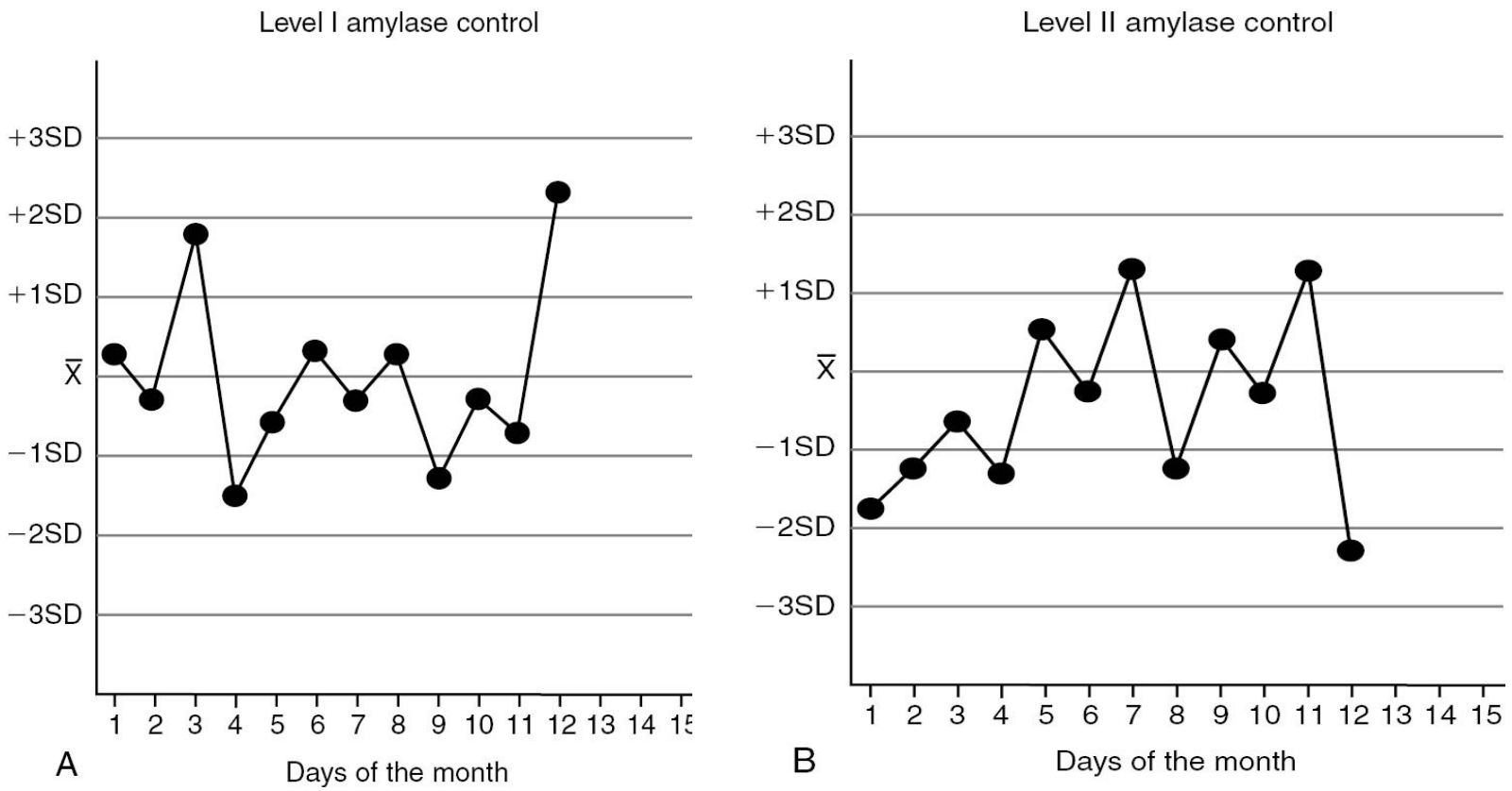


R_{4S}

R_{4S} one control value exceeds the mean +2SD and another control value exceeds the mean -2SD (they are more than 4SD apart from each other). **This rule is best applied within a single run.**

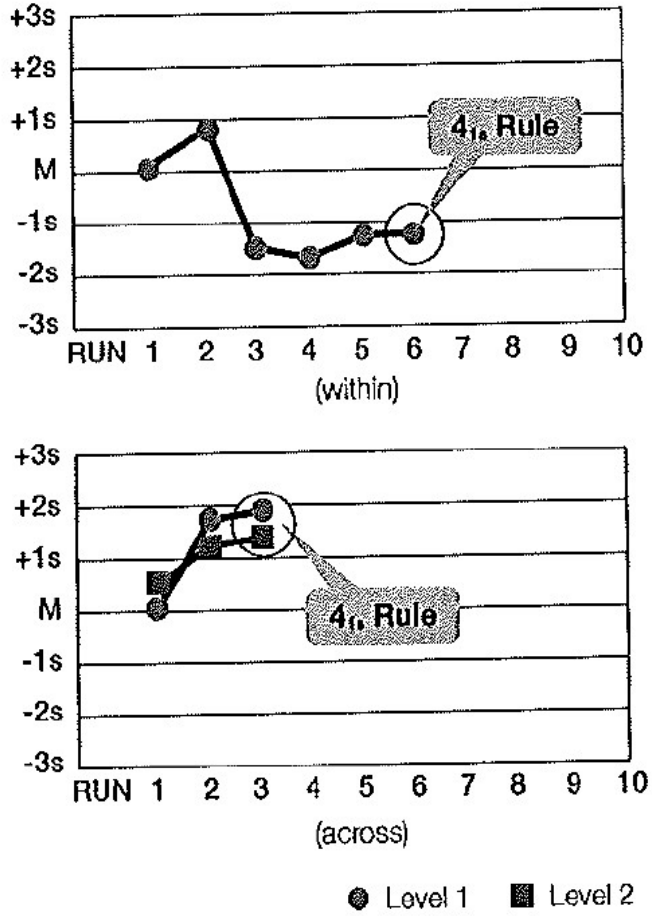


R_{4S}


Level I amylase control
+3SD
+2SD
+1SD
X̄
−1SD
−2SD
−3SD
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
A
Days of the month
Level II amylase control
+3SD
+2SD
+1SD
X̄
−1SD
−2SD
−3SD
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
B
Days of the month

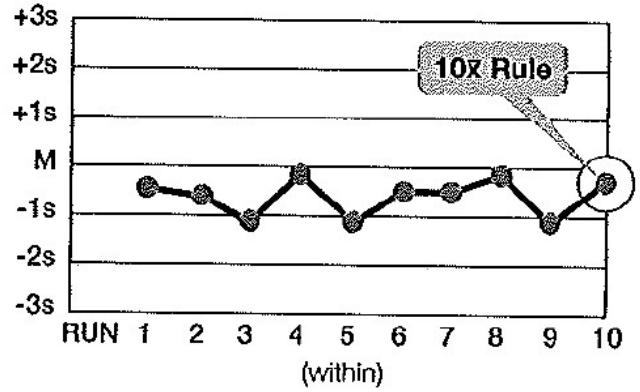
4_{1s}

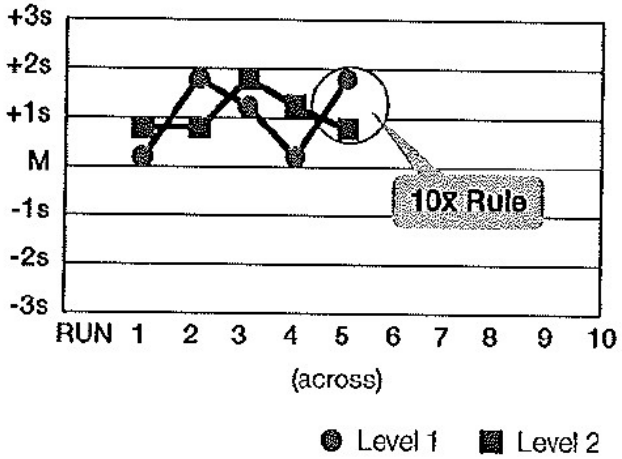
4_{1s} four consecutive control values lie outside the mean +1SD or the mean -1SD.



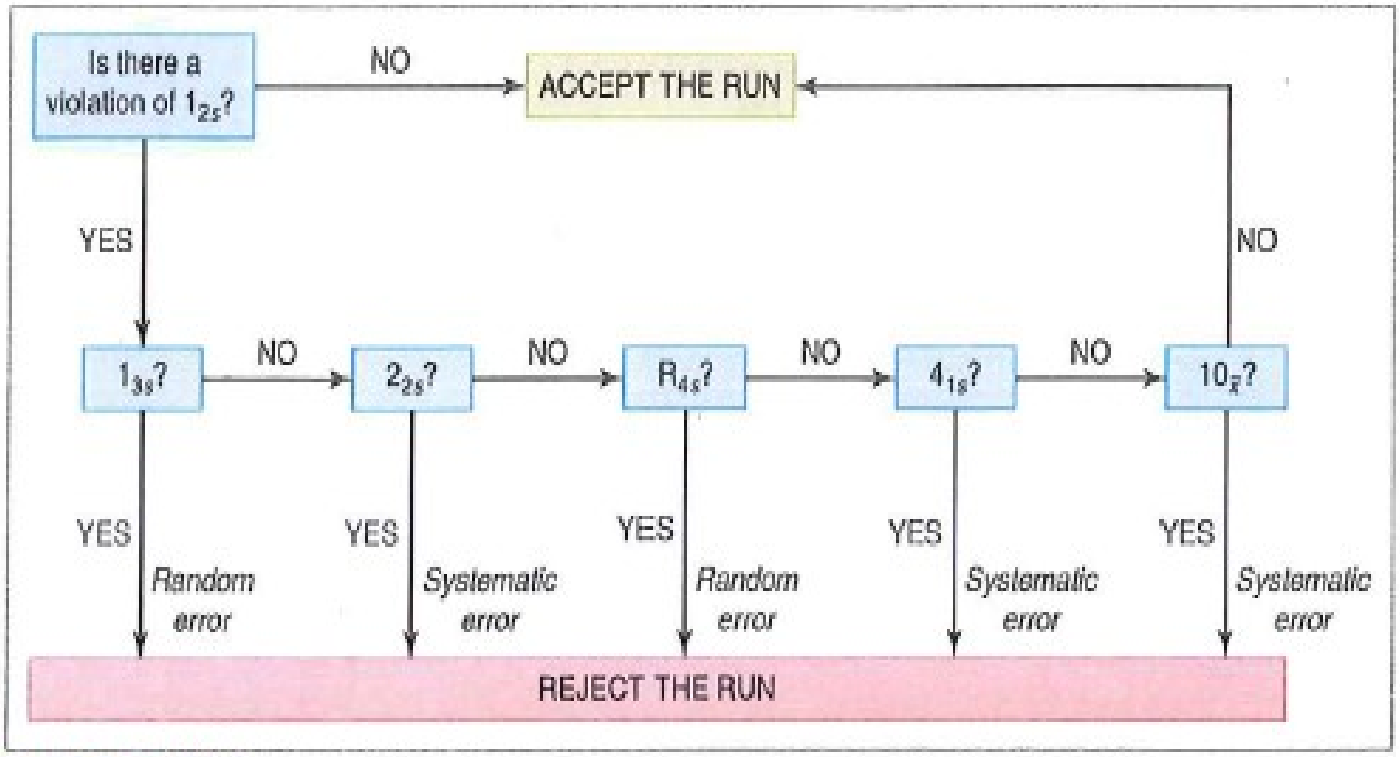
10_x

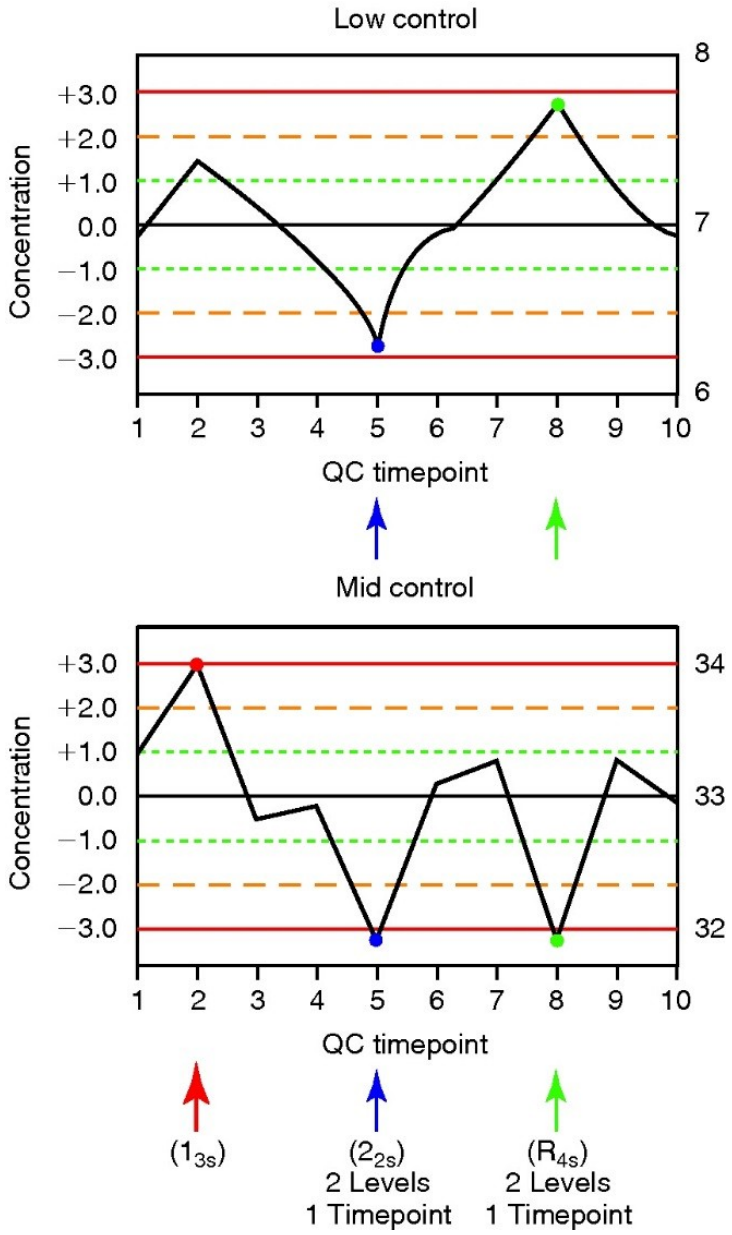
10_x ten consecutive control values lie on the same side of the mean.





Logic Diagram for Traditional Westgard Rules

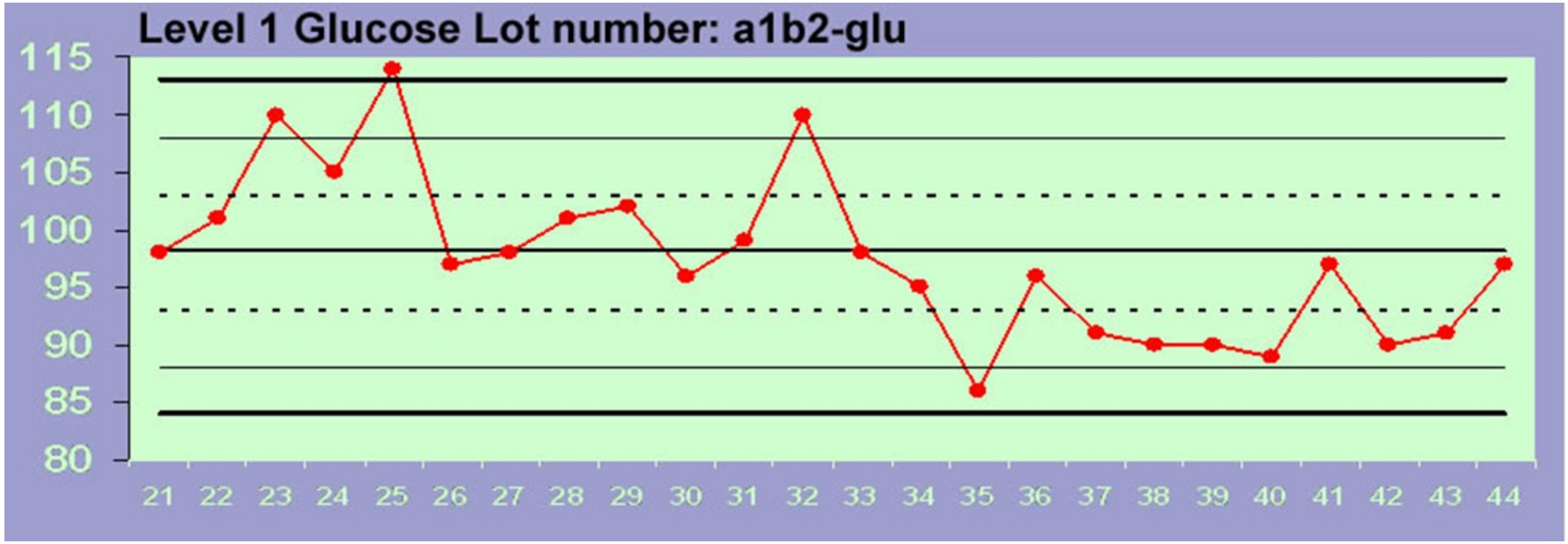


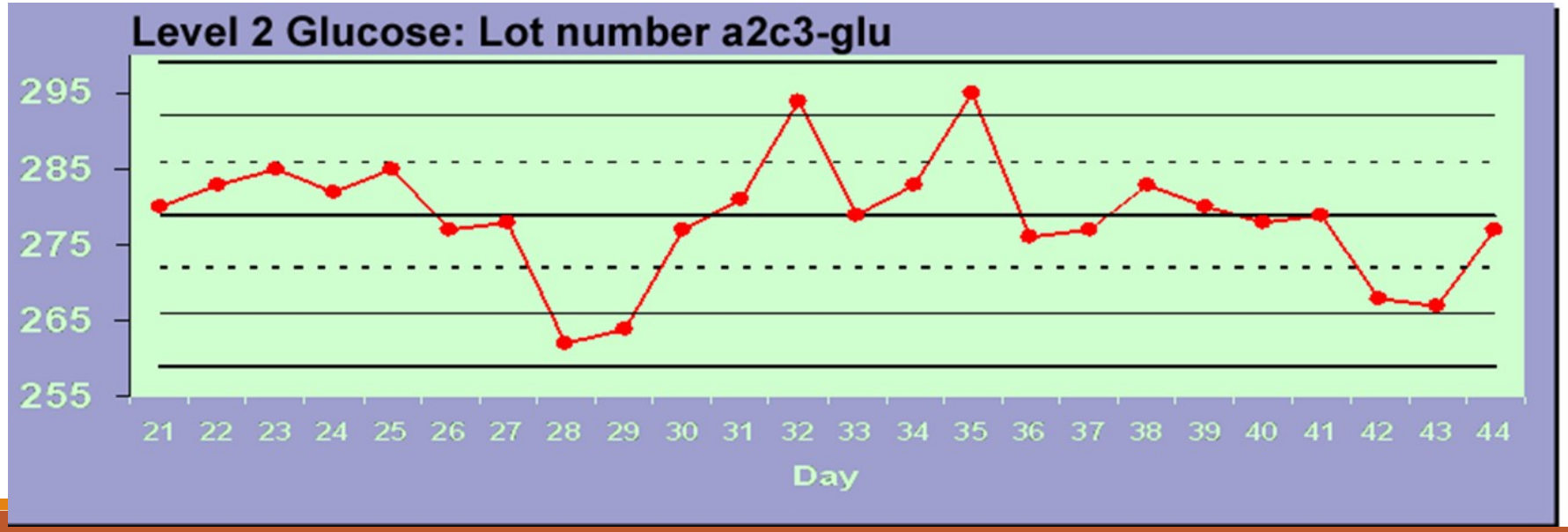

Low control
Concentration
+3.0
+2.0
+1.0
0.0
−1.0
−2.0
−3.0
8
7
6
1 2 3 4 5 6 7 8 9 10
QC timepoint
Mid control
Concentration
+3.0
+2.0
+1.0
0.0
−1.0
−2.0
−3.0
34
33
32
1 2 3 4 5 6 7 8 9 10
QC timepoint
(1 3s)
(2 2s)
2 Levels
1 Timepoint
(R 4s)
2 Levels
1 Timepoint

Multirules to use when 3 different QC materials are analyzed

2 of 3_{2S} – reject the run when 2 of 3 controls exceed the mean ± 2SD

3_{1S} – reject the run when 3 consecutive controls exceed the same mean ± 1SD


Level 1 Glucose Lot number: a1b2-glu
115
110
105
100
95
90
85
80
21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44


Level 2 Glucose: Lot number a2c3-glu
295
285
275
265
255
21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44
Day

Answers

Day 21, 22, 24, 26, 27, 30, 31, 33, 34, 36-44 – in control

Day 23, 28, 29 – 1_{2s}

Day 25 - 1_{3s}

Day 29 - 2_{2s} (across runs)

Day 32 – 2_{2s} (within run)

Day 35 - R_{4s}

Developing QC Criteria

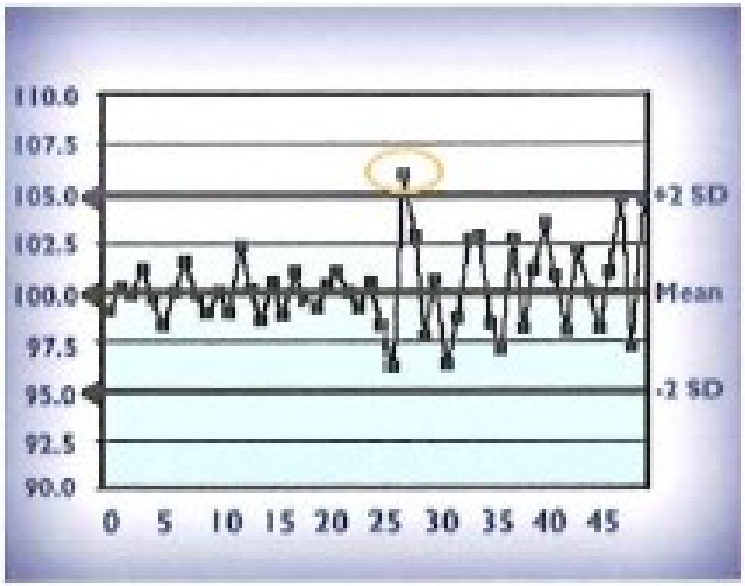
Determining Mean and SD of QC Material

- Collect at least 20 measurements over at least 10 days
- Analyze control materials for a long enough period to observe the variation expected in your laboratory
- Too short a period leads to too small an estimate of the standard deviation
- Calculate mean and SD for initial L-J charts
- Calculations of the mean, standard deviation, and CV are done monthly to evaluate test performance

Assigning SD

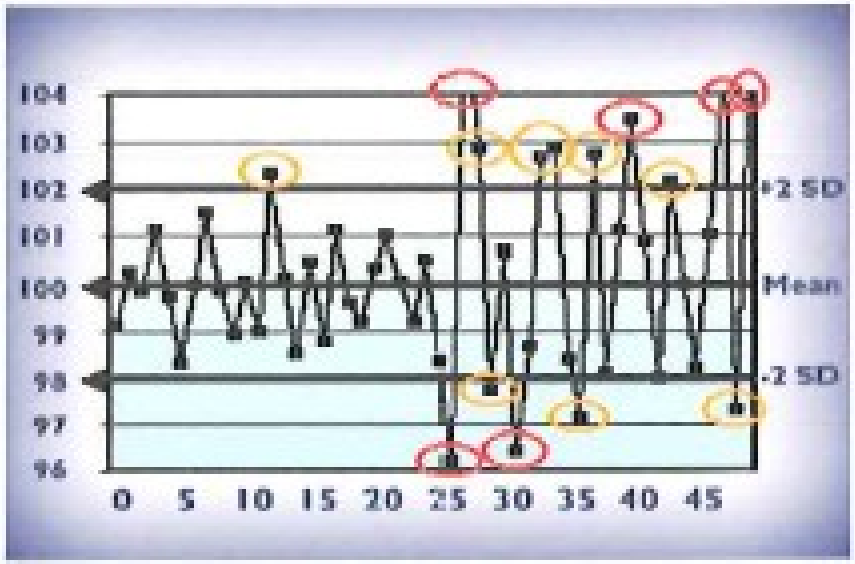
- If SD is assigned higher than actual, fewer results will fall outside of ± 2 SD
- A shift of 2 SD may go undetected
- No QC flags even when significant change in method precision occurs

Example: Assigned SD 2.5



A significant increase in random error does not generate a QC flag when the ASSIGNED SD is significantly higher then the ACTUAL value.

Actual SD 1.0



Increased random error is immediately apparent when the SD is ASSIGNED at an ACTUAL observed value.

Setting Target/True Value

- The target/true value for controls remains constant throughout the life of the control
- The target/true value can be established based on (in order of preference):

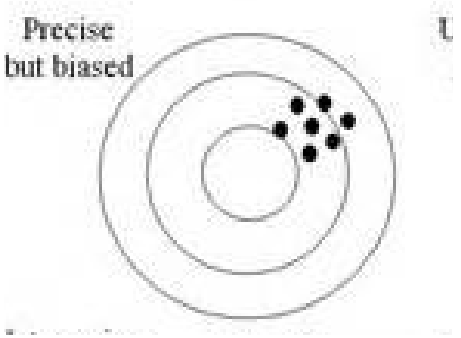
-average value obtained through inter-laboratory comparison program

-value published in the control package insert

-average of results from your lab's past months data

Bias

- Measured as the difference between the observed mean and the true value
- Bias causes all values to shift above or below the target/true value as reflected by the mean
- Bias = measured mean – true/target value
- l Bias l = absolute value of bias



Total Error (TE)

- TE is a combination of inaccuracy (systematic error) and imprecision (random error)
- TE = IBIASI + (2 x SD)
- TE as a % = (TE/Target mean) *100
- TE tells you how far 95% of results are reported from the target/true value

Total Allowable Error (Tea)

- The amount of error that is allowable without invalidating the interpretation of a test result

- Can be based on:

-CLIA guidelines (see handout)

-clinical/medical decision interval (D_{int})

-biological total

Example of Medical Decision Levels

Test	Units	Reference Interval	Decision Levels				
ELECTROLYTES			1	2	3	4	5
Calcium	mg/dL	9.0-10.6	7.0	11.0	13.5		
Chloride	mmol/L	98-109	90	112			
CO2 Content	mmol/L	23-30	6.0	20	33		
Magnesium	mEq/L	1.2-2.4	1.2	2.0	5.0		
	mmol/L	0.6-1.2	0.6	1.0	2.5		
Phosphorus	mg/dL	2.5-5.0	1.5	2.5	5.0		
Potassium	mmol/L	3.7-5.1	3.0	5.8	7.5		
Sodium	mmol/L	138-146	115	135	150		

Using Biological Variation to Determine Allowable Error

- Biological variation, the natural fluctuation of body fluid constituents around the homeostatic setting point
  - has two components: within and between-subject variation
- Derived figures for allowable bias and impression based on biological variation
- Determined by a review of over 140 articles in the scientific literature

Best Practices for Westgard Rules

- Define the quality that is needed for each test (Total allowable error- TEa)
- Know the performance of your method (CV and bias from method evaluation)
- Calculate the Sigma metric for testing process

Sigma = (TE_a - bias)/CV

- Determine whether to use single-rule or multi-rule QC procedures based on the performance of the method

QC Strategy Based on Sigma Score

Sigma Score	QC Frequency	Number of QC Samples	QC Rules
6 or more	Once per day	Each level of QC	1:3s
5	Once per day	Each level of QC	Multi-rule strategy
4	At least twice per day	Each level of QC	Multi-rule strategy
<4	At least four times per day	Each level of QC	Multi-rule strategy

Table 1. *Recommended QC strategy based on Sigma score*

https://www.mlo-online.com/using-sigma-metrics-measurement-uncertainty-qc

MU versus TE

- The TE approach:
  - includes bias in its calculations
- The measurement uncertainty (MU) approach:
  - if the bias is known and of importance, then the lab should eliminate or minimize it by recalibrating or adding a correction factor or constant to the result
- MU focuses on the imprecision of the measuring system only
- MU is most useful for manufacturers: Identify and eliminate sources of errors to produce better testing methodologies

Measurement Uncertainty (MU)

- Laboratories generally measure a patient sample once. MU focuses on identifying the dispersion of results that might have been obtained for an analyte if a sample had been measured repeatedly
- MU does not estimate error, but provides a quantitative estimate of where the true value of a measured analyte is believed by the laboratory to lie, with a stated confidence level
- MU is based on 2 SD of QC result

MU

Example: 2 SD for QC level 1 is 1.5 mmol/L (95% CI)

If patient result is 34.6 mmol/L, the lab is 95% confident that the true result lies between 33.1 – 36.1 mmol/L

- Provides quantitative evidence that lab results meet clinical requirements for reliability
- The clinician must be certain that any change identified in a patient's test result is not due to the laboratory system, but to a change in patient’s status

Monitoring Quality

Proficiency Testing

- Required by CLIA
- Is in addition to internal QC programs
- External to the program (subscription)
- Means of verification of laboratory accuracy

Monitoring Quality

IQAP

- Inter-laboratory quality assurance program
- Submit QC data to instrument manufacturer who compares your data to peer group (pool)
- Your lab's mean, SD, and CV are compared to your peer group
- Another way to ensure accuracy and precision of analyzer and quality results

IQAP

- ***CVI***- ratio of your CV to the Pool CV
- ***SDI***-compares the difference between your laboratory mean and the pool mean relative to the variability of all pool means

- CVI between 0.00 and 2.00 indicates good or precise performance
- SDI between 0.00 and 2.00 indicates good or accurate performance

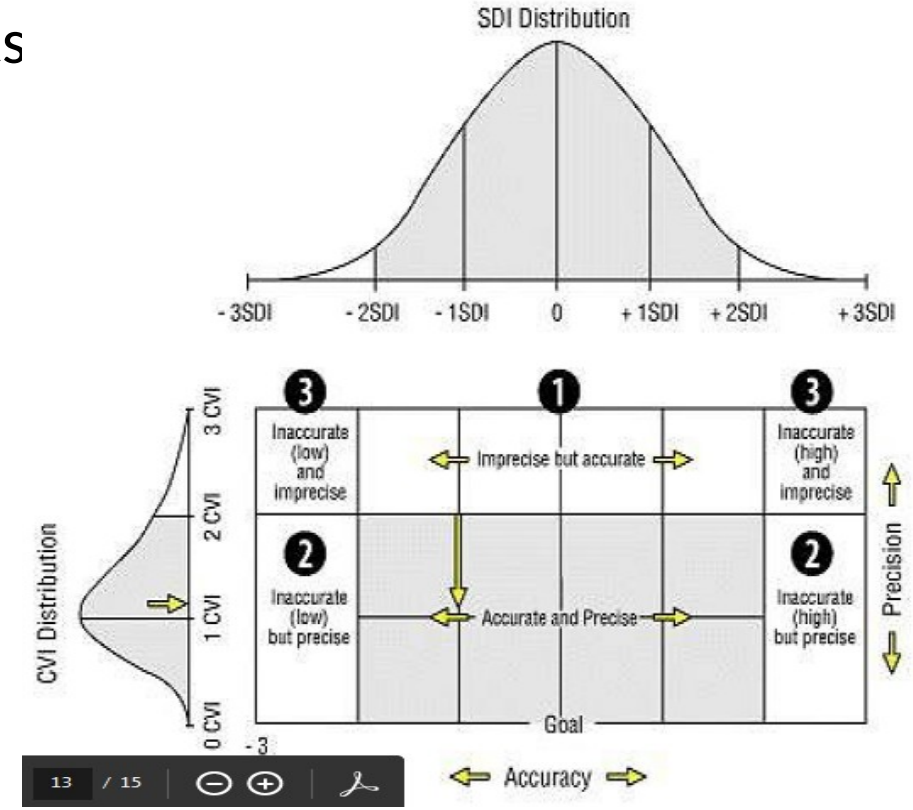
CVI and SDI

1) Accuracy is within limits, precision is not

2) Precision is within limits

accuracy is not

3) Neither is within limits



Interpretation of Lab Data

Sources of random variation in patient results

- Variations/inconsistencies in preanalytical sample collection and transportation
- Variations in the analytical process (accuracy, precision, and changes in bias)
- Biological variation

https://www.cdc.gov/nchs/data/nhsr/nhsr021.pdf

Biological Variation

- Naturally occurring variation within each individual
- CVI- Coefficient of Variation INDIVIDUAL
- Some analytes show cyclical variation:

- throughout the day

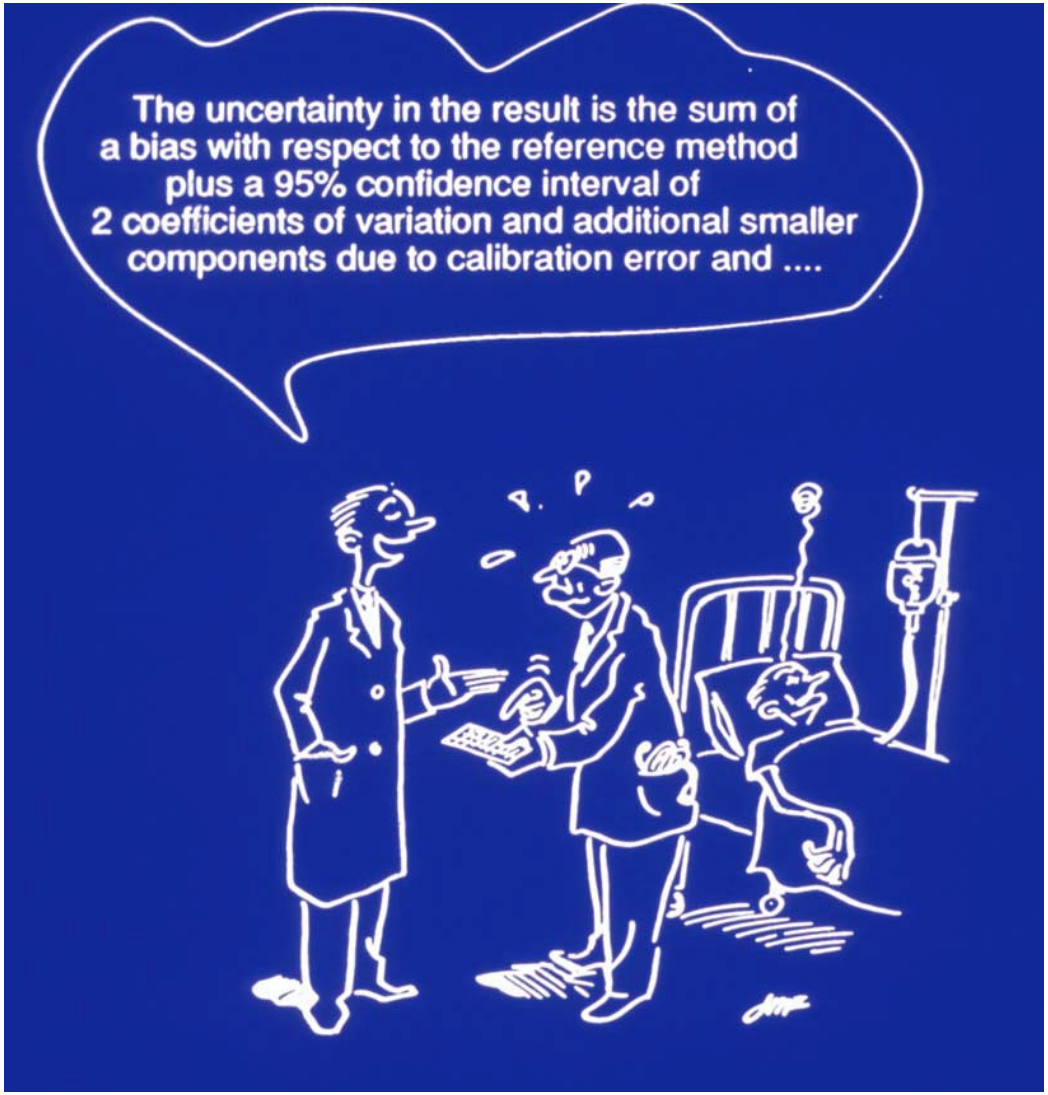
- throughout the month

- season to season

-over life span of individual

CV_I

- All analytes show random variation around a homeostatic set point
- CVI – is the CV% representing the amount of variation that can be expected with NO CHANGE in your clinical condition
- Biological Variation is **NOT** dependent on laboratory method or on geographical location of the population so laboratories **DO NOT** have to generate their own data on biological variation


The uncertainty in the result is the sum of
a bias with respect to the reference method
plus a 95% confidence interval of
2 coefficients of variation and additional smaller
components due to calibration error and ....