Improving the Sensitivity of QC Monitoring: Taking the leap from manufacturer's to established QC ranges

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Objectives

- To determine when and why to establish new quality control (QC) ranges
- To explain the importance of historical (cumulative) Coefficient of Variation (CV_H)
- To evaluate the quality of historical CV

Objectives continued...

- To calculate the CV of External Quality Assurance (EQA)
- To utilize historical CV, EQA CV and Manufacturer's CV in order to develop useful quality control ranges

Mean = average of data = $\bar{X}$

Sum of all data divided by the total number of data points

$$\bar{X} = (X_1+X_2+X_3+....X_N)/N$$

Example:

8+9+7+7+9+8 =48 (Sum)

$\bar{X}$ = Sum/number of data points = 48/6 =8

MEAN = 8

Standard Deviation (SD)

Standard Deviation (SD) = is a measure of how much the data varies around the MEAN

$$SD = \sqrt{\frac{\Sigma(X - \bar{X})^2}{(n - 1)}}$$

where:

X = each score
$\bar{X}$ = the mean or average
n = the number of values
Σ means we sum across the values

Coefficient of Variation (CV)

CV is SD expressed as a proportion of the mean

CV = (SD / Mean) x 100

CV is expressed as a percent (**%**)

Utilizing CV allows you to change the SD in proportion to any MEAN value

QC Material CV types discussed

- CV_H –Historical CV accumulated over time
- CV_{EQA} –CV derived from EQA peer data
- CV_{REF} –CV used to set QC SD ranges
- CV_{MAN} –Manufacturer's CV from QC material package insert

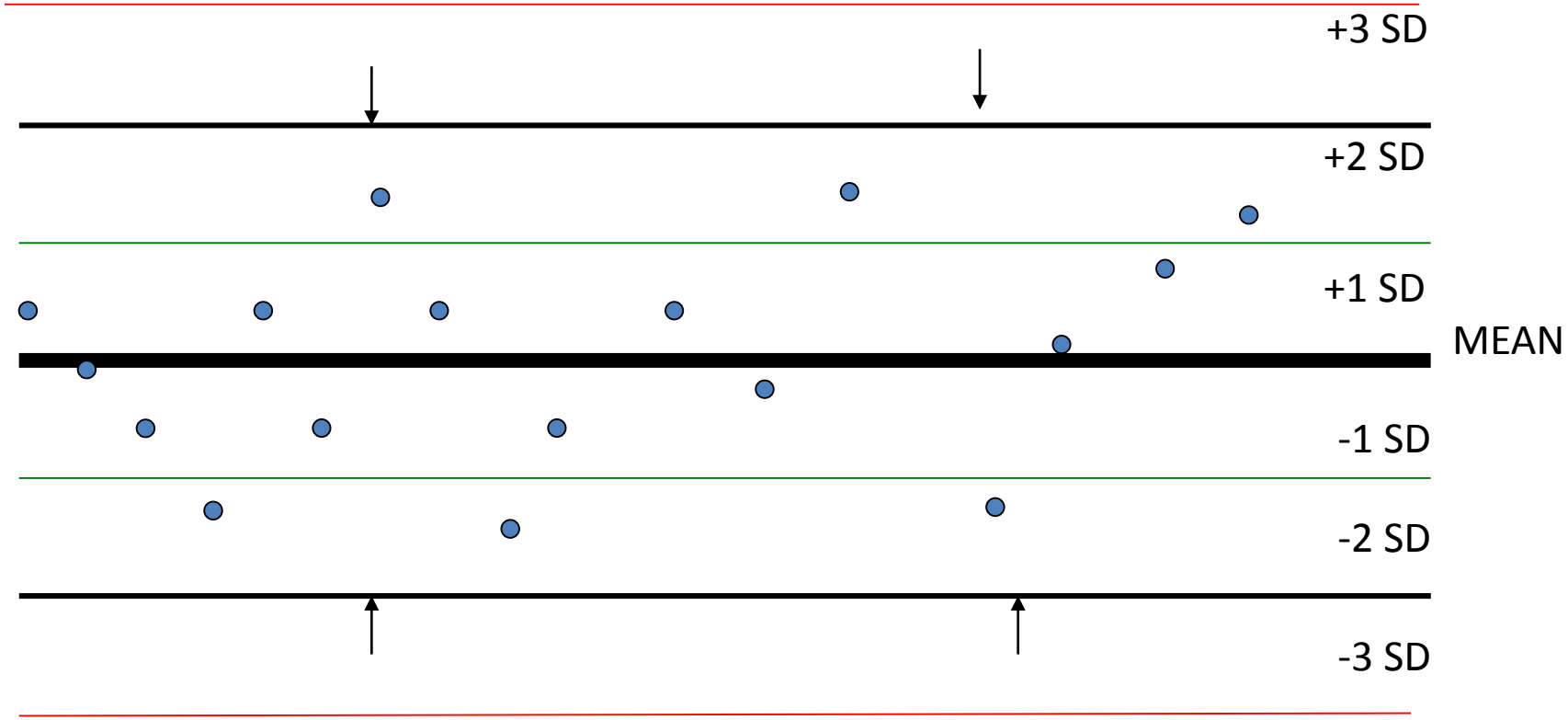
When to establish new QC ranges

- When receiving a new lot of QC samples
- When receiving a new lot of reagent that significantly changes results from the old lot (reference ranges also need to be adjusted)
- As QC samples age

Defining QC ranges

- QC range limits are defined by SD values
- Typically an acceptable range is established using +/- 2 Standard Deviations (SD) around the MEAN
- Statistically this covers 95% of the expected values

A well running QC system

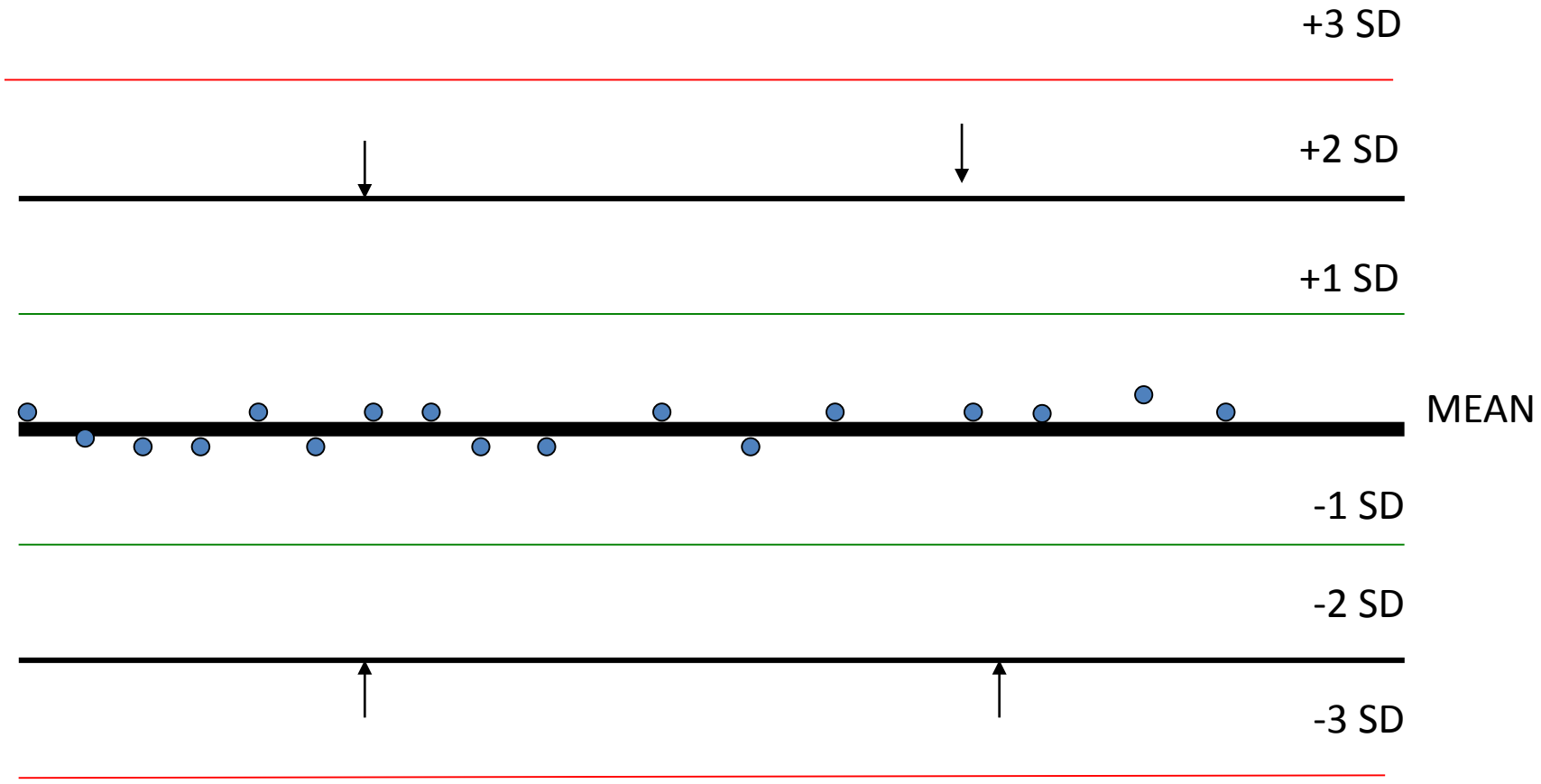


SD limits too large!

- All QC results pass --even unacceptable ones
- Low sensitivity –the QC will **not** let you know when something is wrong in the system
- The acceptable range for QC is **not** a sensitive indicator of result quality & provides little value

SD limits too large!

↓↓ QC failures

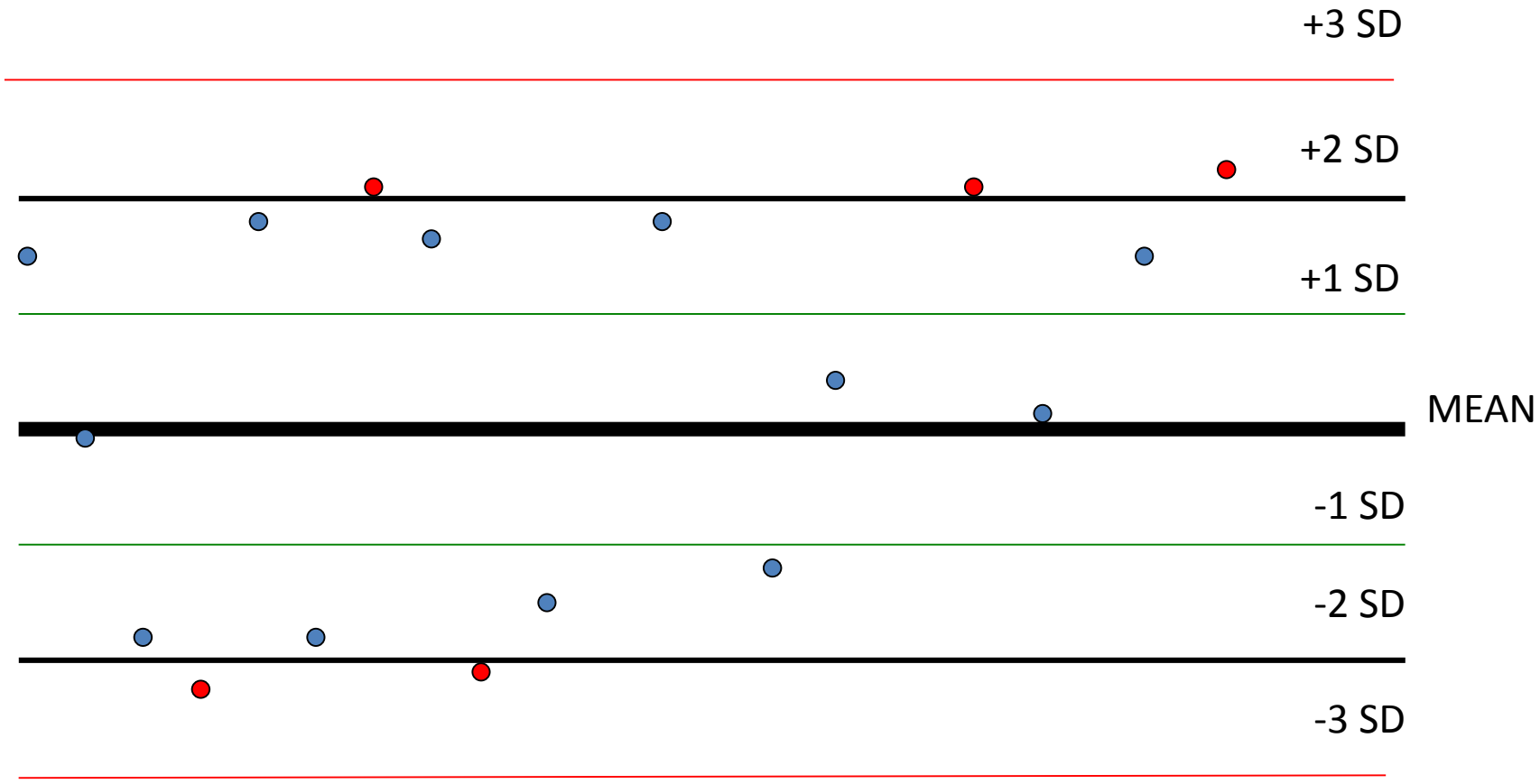


SD limits too small !!

- Few QC results pass --even values that are OK
- Sensitivity too high --You are stopped from releasing acceptable patient results
- Wasting QC material and time

SD limits too small !!

↑↑ QC failures



What are acceptable QC Values?

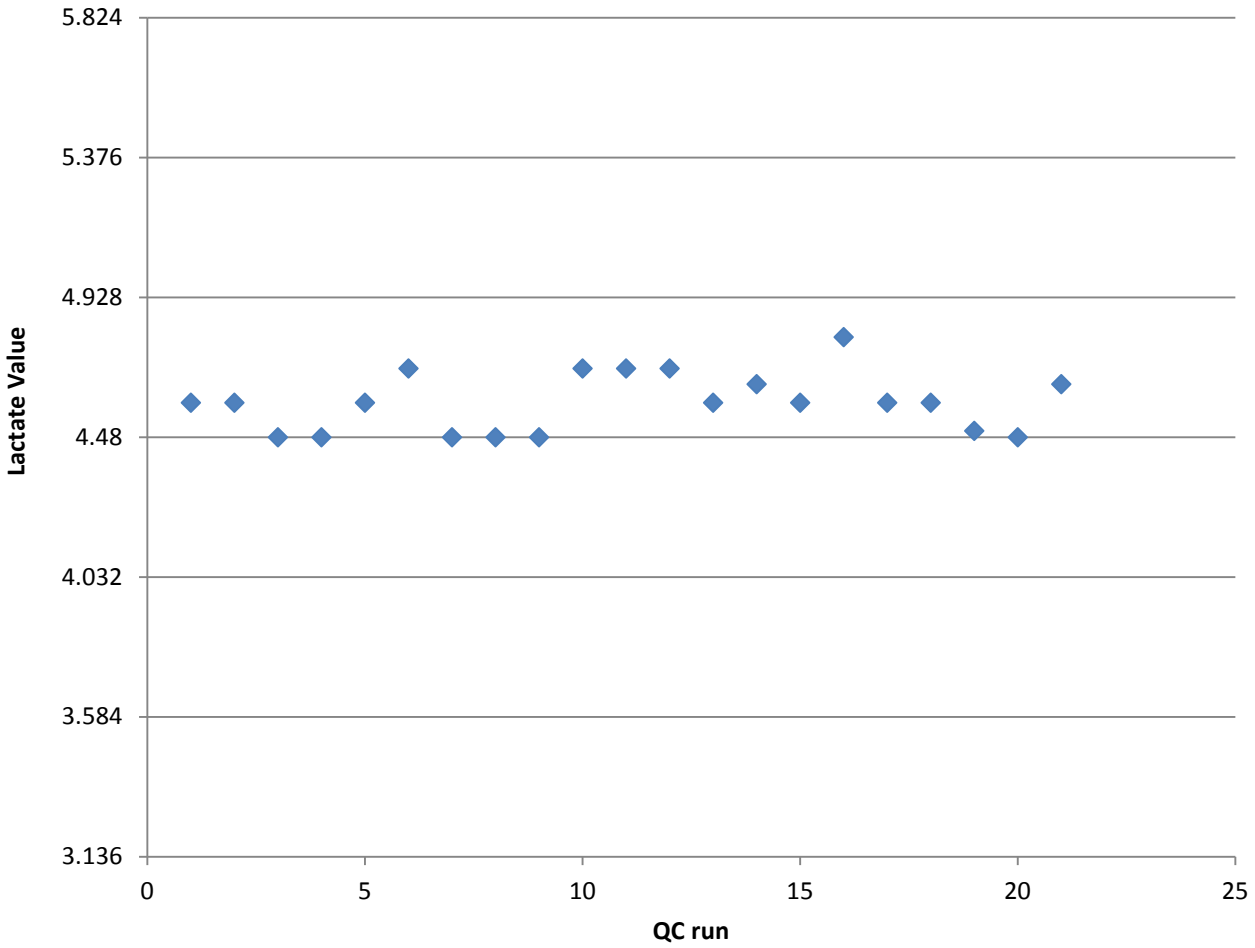
- The laboratory must establish it's own limits of acceptable QC values
- The correct SD value is what makes the QC material a sensitive indicator of acceptability
- We will use Historical (Cumulative) CV ($CV_{H)}$ to establish sensitive SD limits and QC ranges

Why not use the manufacturer's QC limits?

- Manufacturer's limits are often 2-3 times too large –Not sensitive to your laboratory conditions
- They are general guidelines that include several different instrument/method types
- If the QC range is too large you will not find problems

	Lactate U/L Roche Cobas C700						
	Your result	Mean	SD	Lower	Upper	SDI	Your Grade
6	4.14	3.85	0.19	3.28	4.42	1.5	Acceptable
7	3.52	3.20	0.19	2.63	3.77	1.7	Acceptable
8	4.48	3.84	0.20	3.24	4.44	3.2	Unacceptable
9	6.59	6.12	0.36	5.04	7.20	1.3	Acceptable
10	4.91	4.26	0.21	3.63	4.89	3.1	Unacceptable

Mean = 4.48
SD = 0.448
CV = 10%



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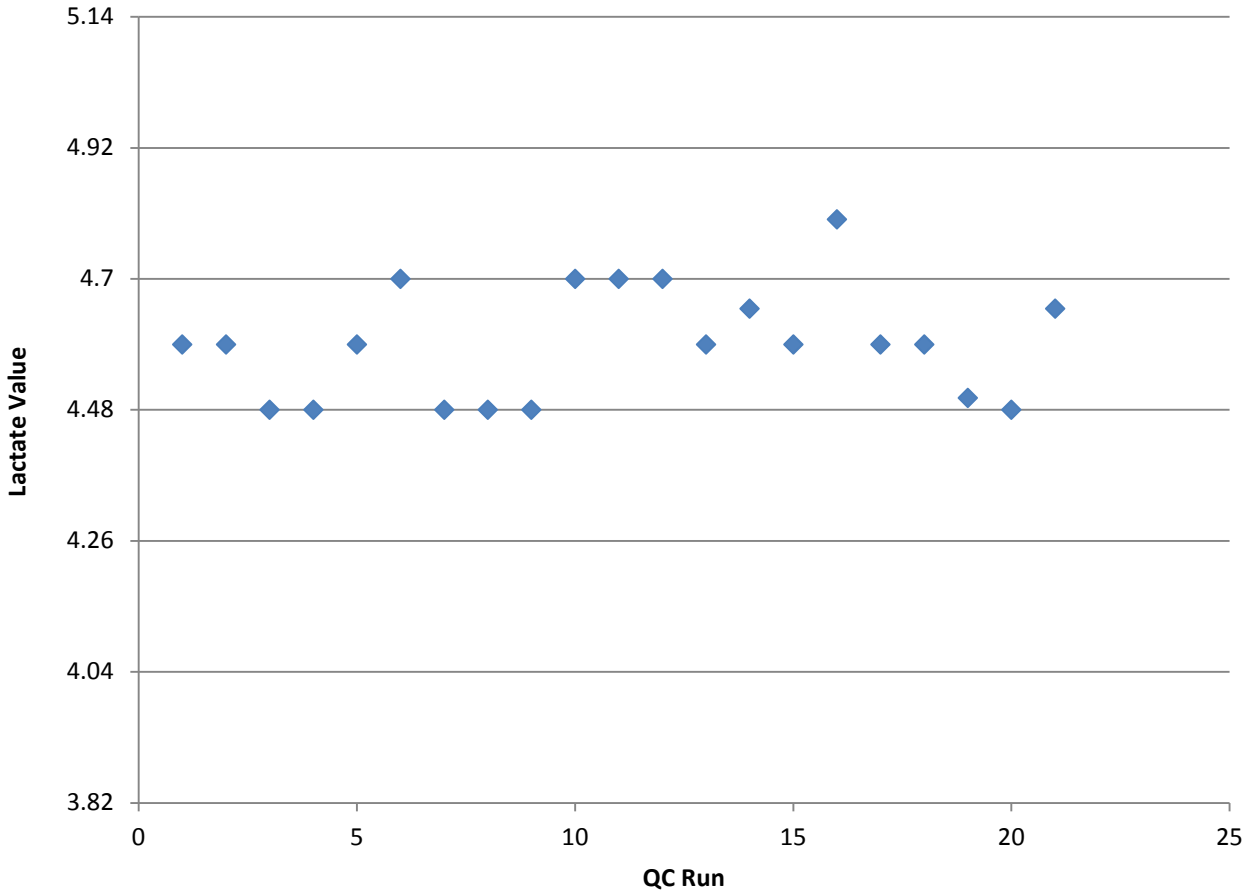
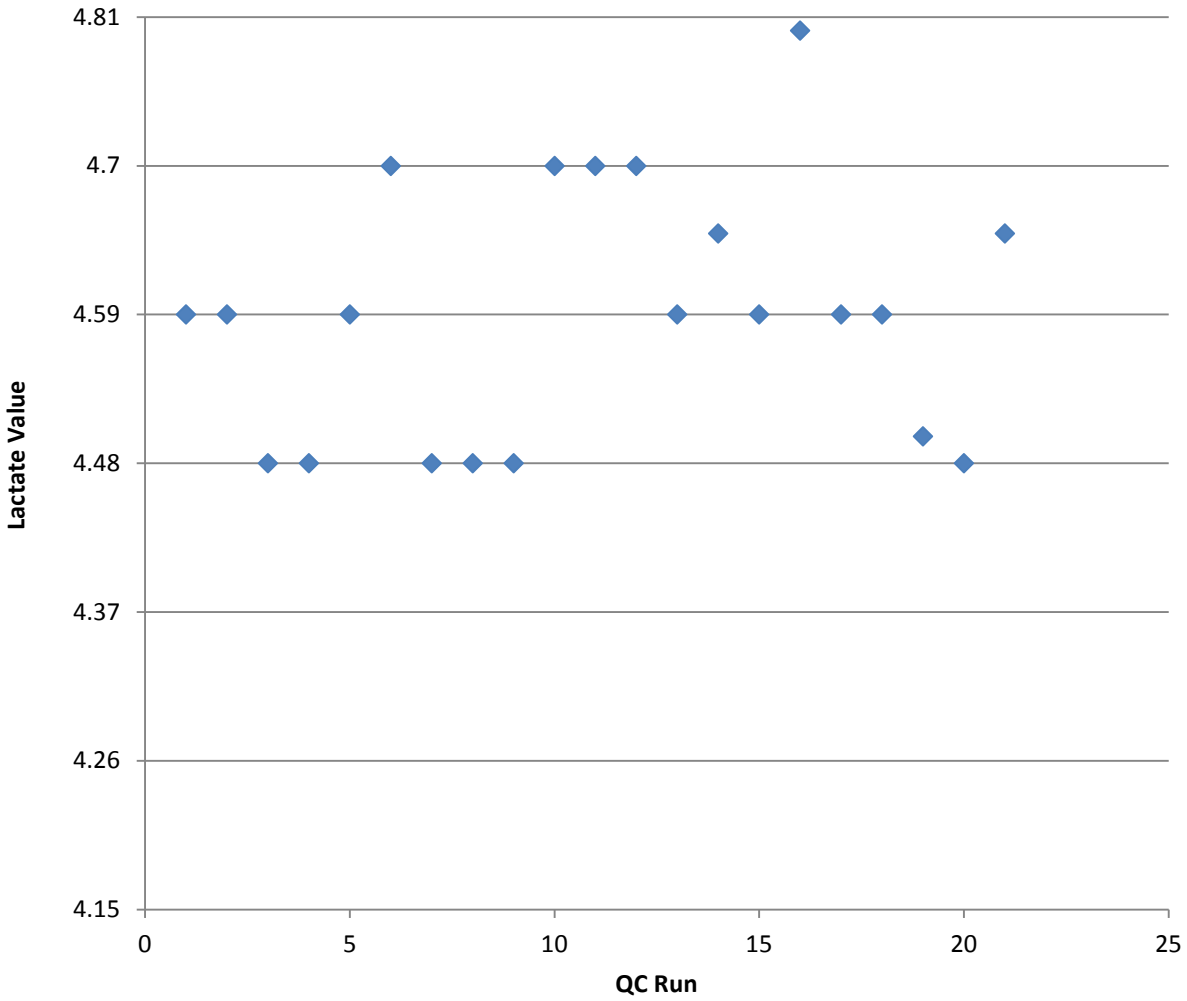
0.20 / 3.84 = 5.2%

0.21 / 4.26 = 4.9%

Mean = 4.48
SD = 0.22
CV = 4.9%



Mean = 4.48
SD = 0.11
CV = 2.5%



How do I determine the SD limits that are correct?

Utilizing CV_H allows you to set your QC limits based on the capability of your instrument according to its precision

An important form of CV is CV_H

It is extremely useful for the laboratory to track the CV_H of QC data for each quantitative analyte over time

CV_H is cumulative precision data

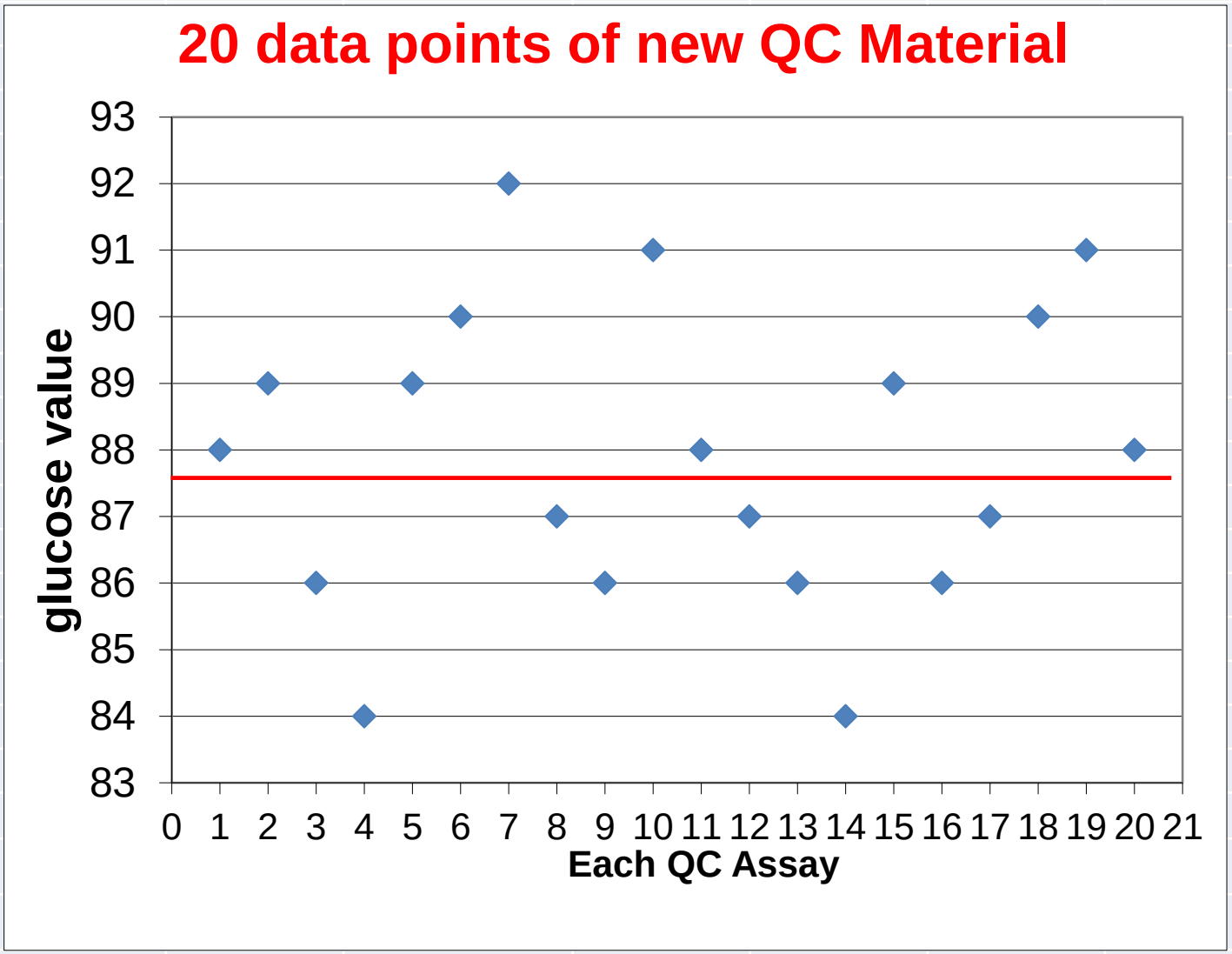
- Gather all QC data accumulated over time
  - Across different reagent lots
  - Across different employees
  - Across different “normal” conditions
- Each QC level/analyte/instrument combination has a unique CV_H

Establishing CV_H

1. Gather each analyte QC data for each type of instrument/method/QC material
2. Remove any data that is greater than 4 SD from the MEAN
3. Calculate the MEAN, SD and CV for the month and on an on-going basis for the life of the QC material

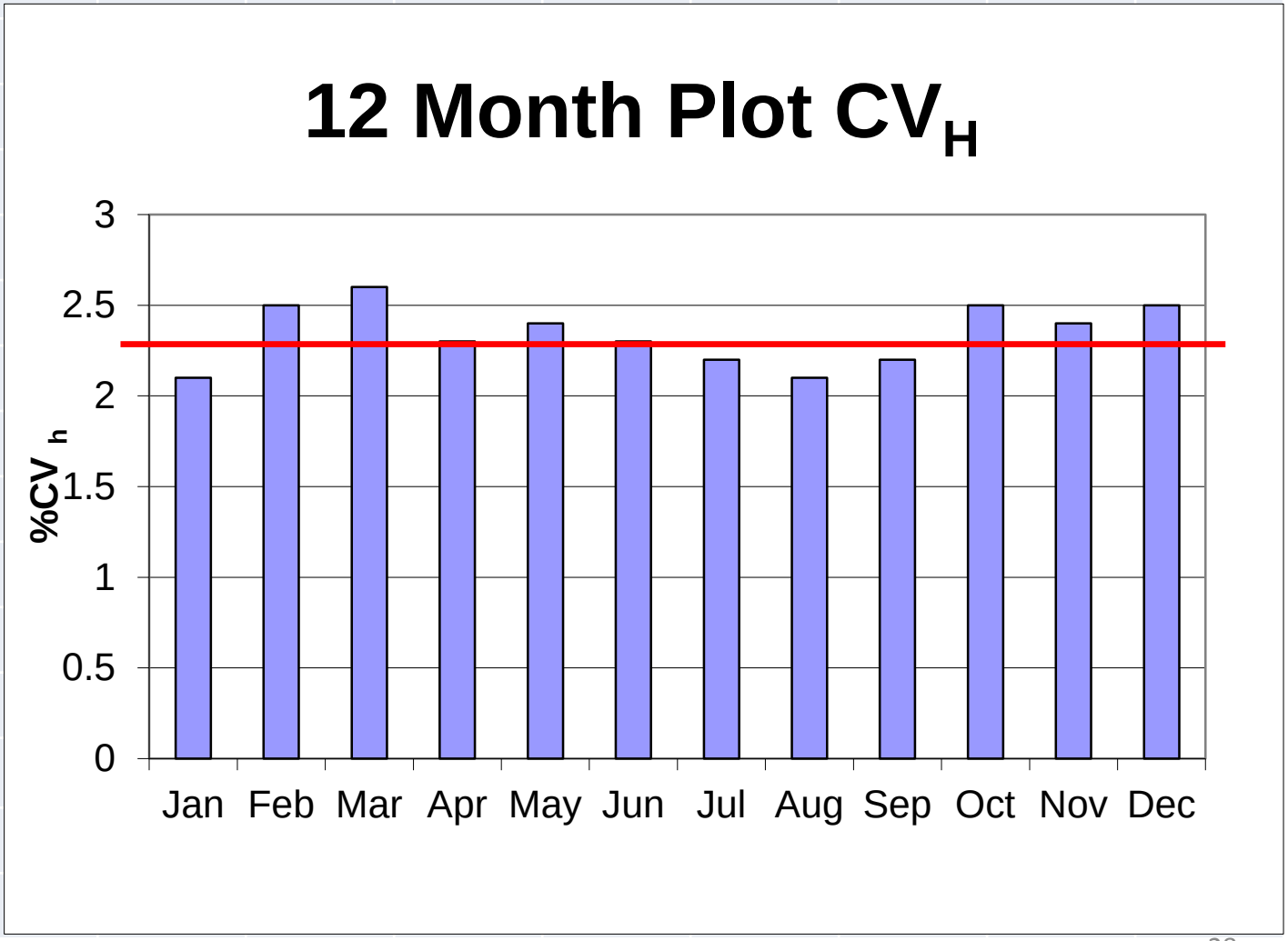
Example of 1 month glucose QC data

	Glucose
1	88
2	89
3	86
4	84
5	89
6	90
7	92
8	87
9	86
10	91
11	88
12	87
13	86
14	84
15	89
16	86
17	87
18	90
19	91
20	88
Average	87.9
SD	2.2
CV	2.49



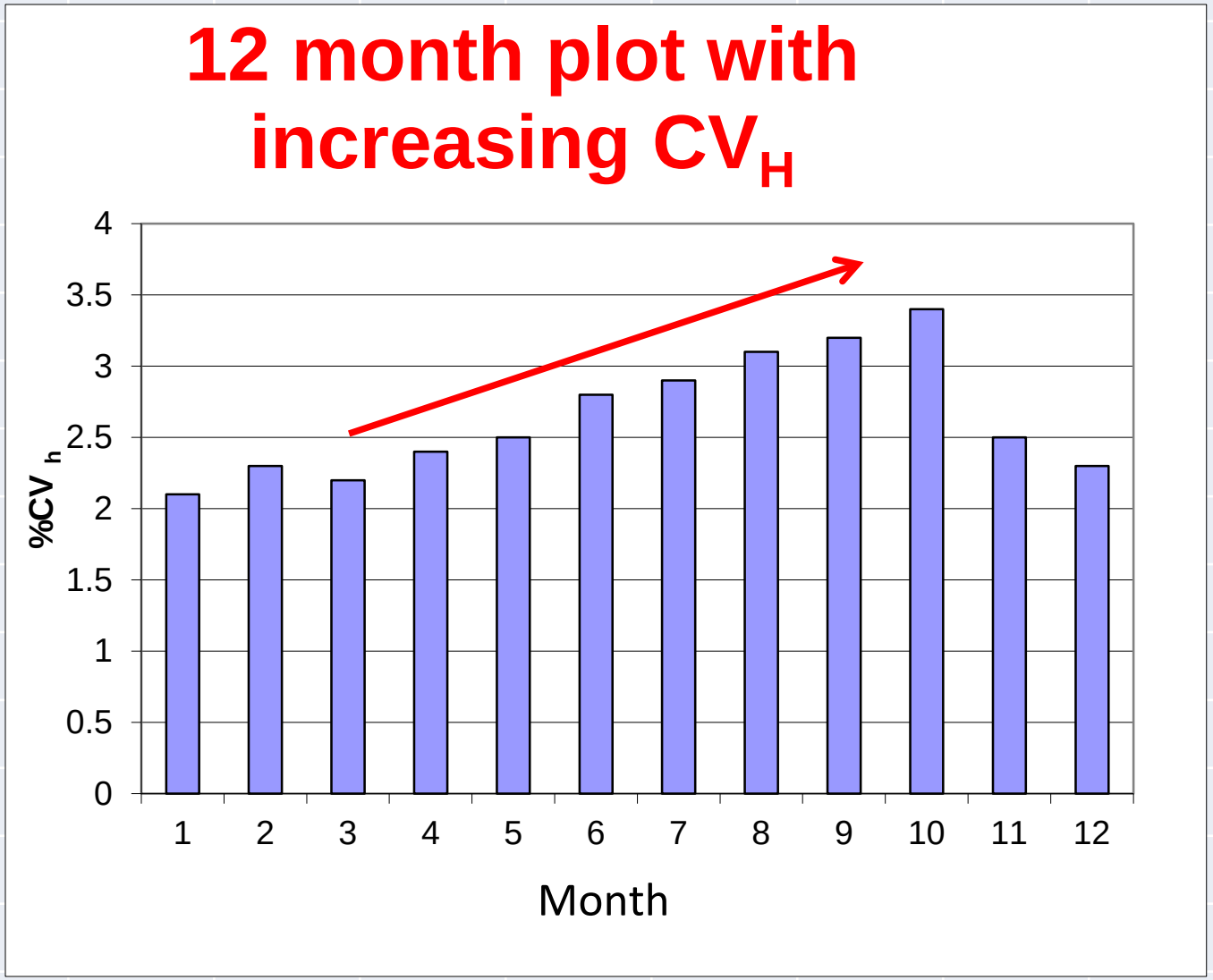
Track CV_H over time

	Normal
Jan	2.1
Feb	2.5
Mar	2.6
Apr	2.3
May	2.4
Jun	2.3
Jul	2.2
Aug	2.1
Sep	2.2
Oct	2.5
Nov	2.4
Dec	2.5
CV_H	2.34



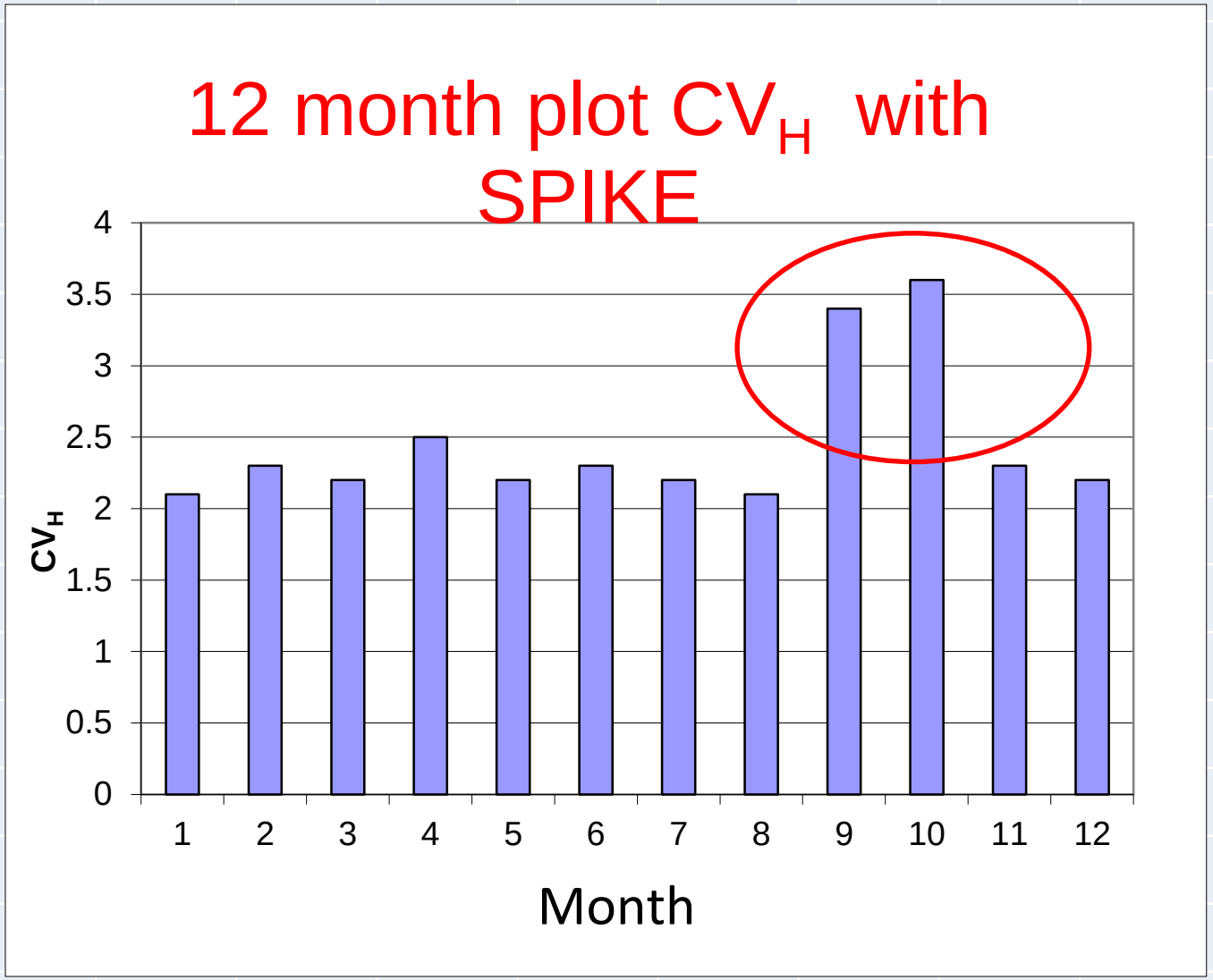
Monitor CV_H to alert for problems

	Increasing CV
Jan	2.1
Feb	2.3
Mar	2.2
Apr	2.4
May	2.5
Jun	2.8
Jul	2.9
Aug	3.1
Sep	3.2
Oct	3.4
Nov	2.5
Dec	2.3
CV_H	2.64



Monitor CV_H to alert for problems

	Random CV
Jan	2.1
Feb	2.3
Mar	2.2
Apr	2.5
May	2.2
Jun	2.3
Jul	2.2
Aug	2.1
Sep	3.4
Oct	3.6
Nov	2.3
Dec	2.2
CV_H	2.45



Things that increase your CV_H

- Day to day instrument differences
- Electrical and power quality
- Different persons operating the instrument
- Different reagent lots
- QC material preparation
- Reagent Quality

How do you determine if your CV_H is an acceptable value?

COMPARE your value to some standard

Standard 1:

Instrument/Method manufacturer's value

- The instrument manufacturer determines and publishes the instrument/reagent method CV (precision)
- If you can not achieve the precision (CV) that the manufacturer claims on your instrument, contact the manufacturer for service

Standard 2:

The External Quality Control (EQA) survey method CV

- CAP & Accutest (OWA) materials are considered an External Quality Assurance (EQA) quality indicator. (Between labs)
- This is not the same as internal QC (Within Labs)
- EQA providers publish instrument/method peer CV data with survey results. Your lab CV_H should be lower than the CV_{EQA} published

Calculating CV_{EQA}

EVALUATION
ORIGINAL

st Unit of Measure Peer Group	Evaluation and Comparative Method Statistic						
	Specimen	Your Result	Mean	S.D.	No. of Labs	S.D.I	Limits of Lower
a Nitrogen (BUN)	CHM-01	19.1	18.94	0.71	236	+0.2	16.5
g/dL	CHM-02	36.9	36.14	1.07	237	+0.7	32.8
UREASE WITH GLDH	CHM-03	11.2	11.18	0.58	233	0.0	9.1
ROCHE MODULAR	CHM-04	45.3	44.36	1.27	233	+0.7	40.1
	CHM-05	36.4	36.19	1.11	237	+0.2	32.5

CV = (0.71 ÷ 18.94) • 100 = 3.7%

CV = (1.07÷ 36.14) • 100 = 3.0%

CV = (0.58÷ 11.18) • 100 = 5.2%

CV = (1.27 ÷ 44.36) • 100 = 2.9%

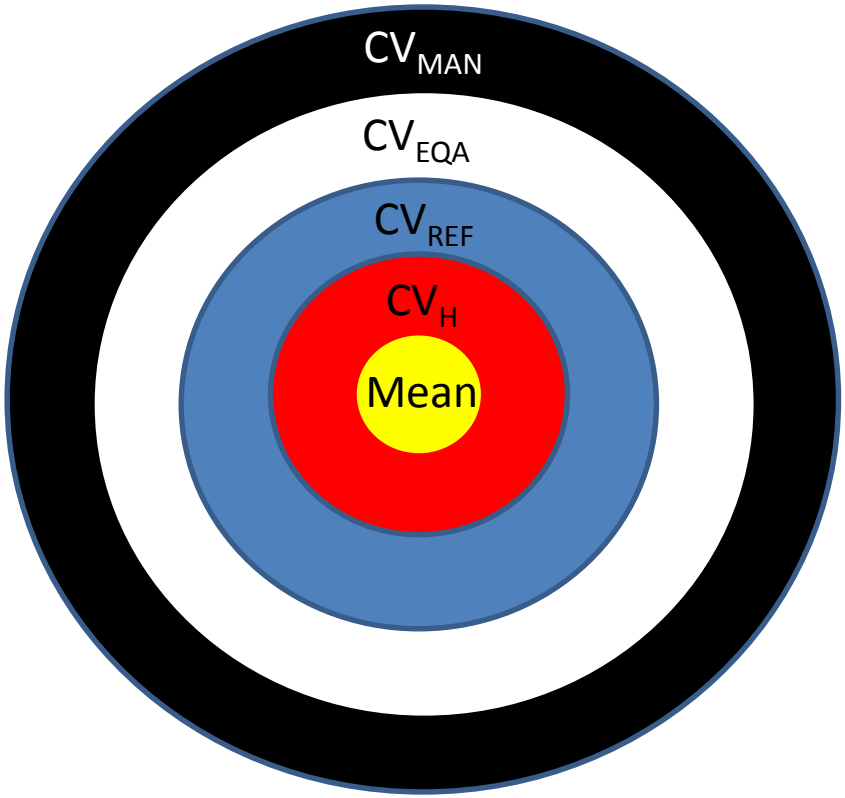
CV = (1.11 ÷ 36.19) • 100 = 3.1%

CV = (SD ÷ Mean) X 100

CV relationships

QC analyte SD should be set using a reference CV_{REF} less than both manufacturer's CV_{MAN} and CV_{EQA}

$CV_H < CV_{REF} < CV_{EQA} < CV_{MAN}$



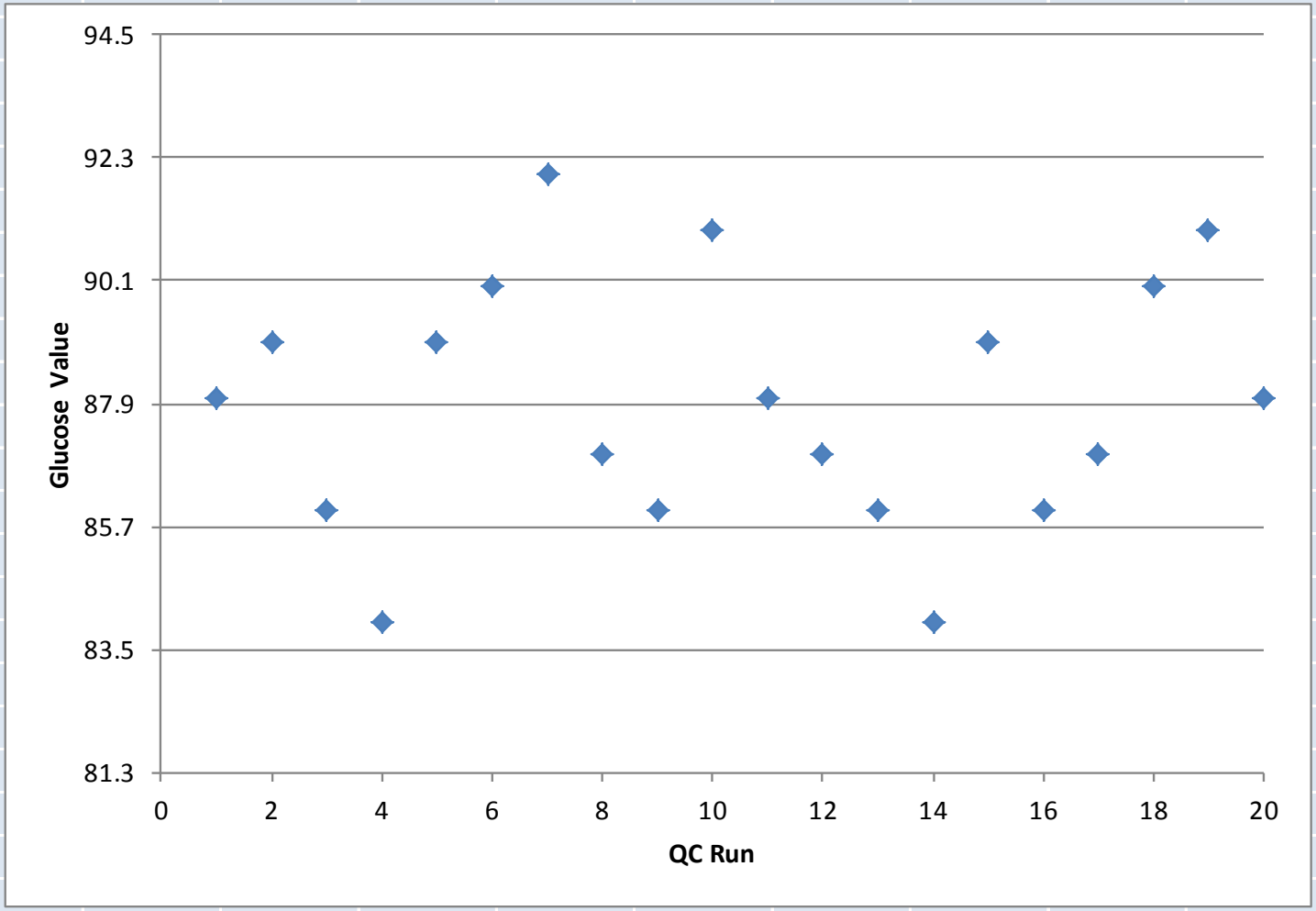
Demonstration of establishing sensitive SD limits using CV_H

Establishing your new mean

1. Ensure that your old lot of QC material is running inside of your current range with no bias, shifts or trends
2. Run new normal QC material for at least 20 data points with old QC material for at least 5 days. Ensure that your old QC material is within acceptable range for each run.
3. Calculate SD, MEAN & CV from data
4. Is the CV ≤ CV_H and CV_{MAN}?

20 data points of Normal QC data -Glucose

1	88
2	89
3	86
4	84
5	89
6	90
7	92
8	87
9	86
10	91
11	88
12	87
13	86
14	84
15	89
16	86
17	87
18	90
19	91
20	88
MEAN	87.9
SD	2.2
CV	2.55%



Example normal glucose QC data

MEAN = 87.9

SD = 2.2

CV = 2.55 from new precision data

Compare – CV to other CV values…

>CV_H = 2.7 accumulated over time

>CV_{EQA} = 3.3 from EQA peer group

>CV_{MAN} = 3.6 from package insert

Example normal glucose QC data

To calculate SD for sensitive QC limits use a CV_{REF} between CV_H and CV_{EQA}

$CV_H = 2.7 < \mathbf{3.0} < CV_{EQA} = 3.3 < CV_{MAN} = 3.6$

Reference $CV_{\mathbf{REF}}$ is 3.0%

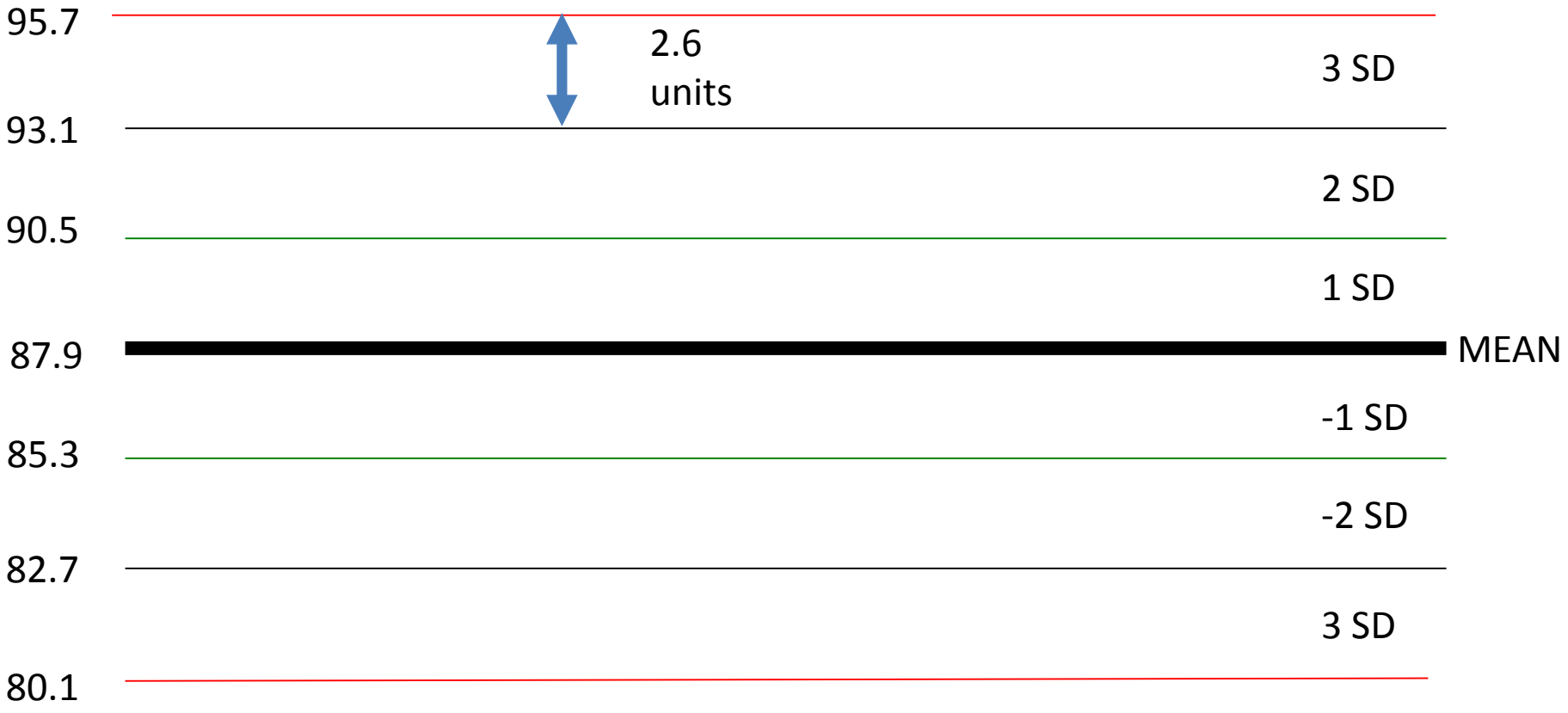
Use CV_{REF} to calculate SD limits

$$SD = MEAN \times (CV_{REF}/100)$$

$$SD = 87.9 \times (3.0/100)$$

$$SD = 2.6$$

QC range limits are defined by CV_{REF}



Questions?

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Thank You

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