Quality Control

As promised, let's dive deeper into QC!

- Quality Control (QC) is the process by which one monitors analytical procedures in order to ensure the accuracy and precision of test results and thus the validity of patient results prior to their reporting.
- Accomplished by monitoring QC materials such as serum, urine, and CSF alongside with patient samples.

Internal QC

- Internal QC involves the following:
  - Establishing mean and SD for the QC material, verifying the accuracy and precision of the control material, and establishing acceptable statistical limits for each analytical method using that control material.
  - Assaying the QC material alongside patient samples and verifying that the control material results fall within the acceptable limits prior to accepting or rejecting a given assay run.
Internal QC continued

- Internal QC involves the following:
  - Monitoring control results over time for changes in precision (random error) or accuracy (systematic error) using prescribed methods and then addressing the problem, when one exists, by finding and correcting the source of error and reanalyzing the patient and control samples.

External QC

- External QC involves the following:
  - The comparison of a lab’s assay results from unknown test samples with the mean results of those obtained on the same samples by other labs.
  - The comparison of a lab’s assay results from unknown test samples with those obtained by an external agency using reference method. This is often part of a proficiency testing program.

QC Materials

- QC material is prepared by pooling either human or animal source body fluids.
- Usually serum and urine.
- Others include: whole blood, plasma, and CSF.
- Can be liquid, frozen, and lyophilized.
- Must pay attention to storage temps.
- Typically 2-3 levels (low, normal, high).
- Should be free of diseases (HIV, HBV, etc).
- Either Assayed (Measured) or Unassayed (not measured).
Lot Switch

- It is good practice to assay an old lot number of control alongside a new lot number of control when first using it.
- Likewise, controls should be assayed with every manual test and at regular intervals on automated instruments to ensure the reliability (accuracy and precision) of the test results and therefore the validity of patient test results.
- Hospitals run levels of controls per shift change, per instrument or batch run.

Definitions

- **Accuracy**: a measure of how closely a test result agrees with the "true" value for that sample.
- **Precision**: A measure of how closely repeated measurement of a sample (replicates) agree with each other.
- **Imprecision**: Measurements do not closely replicate, and the SD will be larger.

**Precision and Accuracy**

- Precise and inaccurate
- Precise and accurate
Imprecise and inaccurate

Definitions

- **Reliability** – A measure of both the accuracy and precision of a method.
- **Central Tendency** – Represents a large group of data points that are equal to or very nearly the same as one data point (cluster of data points) and are represented by a peak on a frequency diagram.
- **Normal or Gaussian Distribution** – Implies that there are approximately the same number and distribution of data points to either side of the peak (bell-shaped curve). Mean, median, and mode are approximately equal values.

Normal Distribution

![Normal Distribution Graph](image)
Definitions

**Mode** – the most frequent number or value found in a data set.

**Range** – the difference between the high and low values of data in a data set.

**Variance** – A mathematical representation of the dispersion or degree of tightness of data points around the mean or peak in a data set. It is the square of the SD and is calculated as follows:

\[
\text{SD}^2 = \frac{\sum (\text{individual value} - \text{mean})^2}{\text{number of values or data points} - 1}
\]

**Standard Deviation** – the mathematical representation of the dispersion or degree of tightness of data points around the mean or peak in a data set. It is easily calculated by taking the square root of the variance.

**Confidence Interval (CI)** – refers to the limits (high and low) between which a specified proportion of the data points in a data set will fall.

- 68% CI = mean +/- 1 SD
- 95% CI = mean +/- 2 SD
- 99% CI = mean +/- 3 SD
CV

- **Coefficient of Variation** – the SD divided by the mean and multiplied by 100 to obtain a percentage.
  - \( \% \text{ CV} = \frac{\text{SD}}{\text{mean}} \times 100 \)

Levey-Jennings Charts

- An approach to monitoring method performance for precision and long term accuracy
- Involves Plotting control values on a Levey-Jennings chart which consists of a solid line representing the target mean value and dashed lines that represent plus and minus 1, 2, and 3 SD from the mean.
- Values are plotted against time
Trend

- A small but steady and continuous change of the control values on one direction.
- Often indicate reagent or calibrator deterioration or gradual instrumental failure
Shift
• A change of the mean for the control material.
• New mean is continuous but different from the original mean
• Can be caused by resetting an instrument, a small but consistent flaw in the instrument, or a change of lot number of control

Findings Over Time
• Ideally should have control values clustered about the mean (+/- 2SD) 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

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"
- A set of criteria by which one can monitor test performance and accept or reject the run
- Useful in determining if the problem is random error or systematic errors

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 $\pm 2$SD
- Alerts tech to possible problems
- Not cause for rejecting a run
**12S Rule** = A warning to trigger careful inspection of the control data

Westgard – 13S Rule
- If either of the two control results falls outside of ±3SD, rule is violated
- Run must be rejected
- Reject the run when a single control measurement exceeds the +3SD or -3SD control limit

**13S Rule** = Reject Run
Westgard – $2_2$S 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

22S Rule = Reject the run when 2 consecutive control measurements exceed the same +2SD or -2SD control limit

Westgard R₄S

- One control value exceeds the mean + 2SD and another control value exceeds the mean – 2SD.
- They are more than 4SD apart from one another and were assayed consecutively
- Reject the analysis/run
Westgard $4_{\text{IS}}$
- Four consecutive control values lie outside the mean $+1\text{S}$ or the mean $-1\text{SD}$.
- Reject the analysis/run

Westgard $10_{\bar{X}}$
- Ten consecutive control values lie on the same side of the mean.
- Reject the analysis/run

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
Random Error versus Systematic Error

- **Random error** - occurs on a unique sample without any defined pattern.
  - 13 and R13 are examples
- **Systematic error** - is present in all samples and effects those samples approximately equally.
  - 241, 41, and 10 are examples

Solving “out-of-control” problems

- Policies and procedures for remedial action
- Troubleshooting

Summary: 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