Clinical Chemistry

Quality Control Policies, Processes, & Procedures

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What is Quality Control?

- The statistical process used to monitor and evaluate the *analytical process* that produces patient results.
QC Product Storage & Handling

• All QC products are to be handled and stored strictly in accordance with the accompanying product insert
• DO NOT use QC products beyond the expiration date
• DO NOT use fans or other heat sources to thaw frozen QC products
• DO NOT use mechanical mixers to mix thawed or reconstituted QC products
• Promptly re-cap each vial and return to 2°C to 8°C storage after each use
QC Testing Frequency

• QC testing should be performed any time an event occurs that has the potential to adversely affect the analytical process. These events include, but are not limited to:
  • Daily, Weekly or Monthly Maintenance
  • Corrective or Preventive Maintenance
  • Reagent lot change, or for some assays, reagent pack change
  • Assay calibration

• Outside of these events:
  • < 200 analyses per shift – once at the commencement of each shift
  • > 200 analyses per shift – once every 200 analyses
QC Testing Frequency

- The *minimum* QC testing frequency is listed in Appendix 5 of STD-CH-8 Clinical Chemistry QC Manual
Basic QC Statistics

- **Mean** – the mean or average is a laboratory’s best estimate of an analyte’s true value for a specified level of control; the mean is calculated as the sum of all values divided by the number of values.

- **Standard Deviation (SD)** – the SD is a statistic which quantifies the dispersion of values within a specified set of values; a measure of precision.

- **Coefficient of Variation (CV)** – the CV is the ratio of the standard deviation to the mean expressed as a percentage.
Normal (Gaussian) Distribution

99.7%
95.5%
68.2%
Normal (Gaussian) Distribution

- Assumption: QC data exhibits a normally distributed (Gaussian) population
- 68.2% of QC values will fall between ± 1 SD
- 95.5% of QC values will fall between ± 2 SDs
- 99.7% of QC values will fall between ± 3 SDs
- In other words, only 3 in 1000 normal QC values will fall outside ± 3SDs. Therefore, statistically, it is highly likely that any QC value falling outside ± 3 SDs will be abnormal, indicating a problem with the analytical process
Westgard Rules

• A set of statistical process control (SPC) rules developed by James O. Westgard, PhD, *et al*
$1_{2s}$ Rule

![Graph showing $1_{2s}$ Rule with data points and a line plot indicating the rule for Level 1.](image-url)
12s Rule

• The 12s rule is violated when a single control observation is outside the ± 2 SD limit

• When used as a rejection rule, the 12s rule yields a high proportion of false rejections

• The 12s rule should only be used as a rejection rule where performance of the assay indicates that a 12s rejection rule is warranted
1_{3s} Rule

[Graph showing the 1_{3s} Rule over 10 RUNs with levels from -3s to +3s]
$1_{3s}$ Rule

• The $1_{3s}$ rule is violated when a single control observation is outside the ± 3 SD limit

• While a value outside ± 3 SD may be statistically significant, it may not be clinically significant
$2_{2s} \& 2 \text{ of } 3_{2s}$
$2_2s$ & $2$ of $3_2s$

- The $2_2s$ rule is violated within a run when two consecutive QC results are outside the ± 2 SD limit on the same side of the mean.

- The $2_2s$ rule is violated across runs when the previous value for a particular control level exceeds the same ± 2 SD limit.

- The 2 of $3_2s$ rule is a variation of the $2_2s$ rule used when testing three levels of QC, and is violated when two of three levels of control within the same run exceed ± 2 SD on the same side of the mean.
$R_{4s}$ Rule

- The $R_{4s}$ rule is violated when there is at least a 4 SD difference between control values in a single run.
4_{1s} Rule
**4₁s Rule**

- Used for bi-level controls

- The $4₁s$ rule is violated within the control material if the last 4 values of the same control material are within the same mean ± 1s limit

- The $4₁s$ rule is violated across control material if the last 4 consecutive control values for different control levels are within the same mean ± 1s limit
$3_{1s}$ Rule
3_{1s} Rule

- Used for tri-level controls

- The $3_{1s}$ rule is violated within the control material if the last 3 values of the same control material are within the same mean $\pm 1s$ limit

- The $3_{1s}$ rule is violated across control material if the last 3 consecutive control values for different control levels are within the same mean $\pm 1s$ limit
QC Troubleshooting

- **Random Error** – any deviation away from an expected result
- **Systematic Error** – a trend or shift away from an expected result

<table>
<thead>
<tr>
<th>Westgard Rule</th>
<th>Error Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>$1_{2s}$</td>
<td>Random or Systematic</td>
</tr>
<tr>
<td>$1_{3s}$</td>
<td>Random, or beginning of a large Systematic error</td>
</tr>
<tr>
<td>$2_{2s}$, 2 of $3_{2s}$</td>
<td>Systematic</td>
</tr>
<tr>
<td>$R_{4s}$</td>
<td>Random</td>
</tr>
<tr>
<td>$4_{1s}$</td>
<td>Systematic</td>
</tr>
<tr>
<td>$3_{1s}$</td>
<td>Systematic</td>
</tr>
</tbody>
</table>
Random Error

- Random error is any deviation away from an expected result. Possible sources of random error include, but are not limited to:
  - Sample or reagent pipetting errors
  - Air bubbles in reagents or reagent lines
  - Inadequately mixed reagents
  - Air bubbles in water supply
  - Unstable incubation temperatures (enzymes)
  - Unstable electrical supply
  - Misplacement of control samples within run
  - Incorrect handling of control products
  - Inappropriate storage of control products
  - Operator technique
Systematic Error

• Systematic error is a trend or shift away from an expected result
Systematic Error - Trend
Systematic Error - Trend

- A trend indicates a gradual loss of reliability in a test system.
  Possible causes of trending include, but are not limited to:
  - Gradual accumulation of debris in sample and/or reagent tubing
  - Gradual accumulation of debris on electrode surfaces
  - Gradual deterioration of reagent whilst in use, storage or shipment
  - Gradual deterioration of control product while in use, storage or shipment
  - Gradual deterioration of incubation chamber temperature (enzymes)
  - Gradual deterioration of light filter integrity
  - Gradual deterioration of calibration
  - Gradual deterioration of the instrument light source
Systematic Error - Shift
Systematic Error - Shift

- A shift is an abrupt change in the control mean. Possible causes of shifts include, but are not limited to:
  - Change of reagent lot
  - Change in reagent formulation
  - Change of calibrator lot
  - Incorrect calibrator values
  - Inaccurate calibration or re-calibration
  - Major instrument maintenance
  - Sudden change in incubation temperature (enzymes)
  - Change in room temperature or humidity
  - Failure in the sampling system
  - Failure in the reagent dispense system
  - Sudden failure or change in light source
QC Corrective Action

- When performing QC corrective action, avoid:
  - Blindly repeating controls
  - Blindly re-calibrating the assay
  - Blindly trying fresh control aliquots or vials
QC Corrective Action

• Inspect QC charts and rules violated to determine the type of error and identify any shifts or trends in recent QC data

• Relate the type of error to potential causes

• Relate causes to recent changes in the analytical system – reagent, calibration, maintenance, etc

• Verify the resolution by repeating QC and document the corrective action
QC Corrective Action

• IS-CH-7 Clinical Chemistry QC Troubleshooting Guide

• STD-CH-8 Clinical Chemistry QC Manual, Chapter 5
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