Future of Quality Control – Evidence Based QC

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Agenda

• The Repeat Issue
• Chasing Zero Bias
• What is Six Sigma
• Evidence Based Control Limits
• Customer Feedback
• Laboratory Benefits
• Additional Information

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The Repeat Issue

• Incorrect control limits cause
  – Desensitizing lab staff to true out-of-control errors
  • False alarms (cry wolf)
  – Repeat controls when out-of-limits
  • Becomes a repeat, repeat, open new vial, repeat
  – Practice becomes testing controls not the analyzer
  – Higher QC expense, reduced lab productivity
  • Stress to laboratory staff (anxiety running controls)
  • Repeating controls, documentation, increased TAT, review of past samples

CAP Q-Probe QC Practices

• 95% of labs repeat same vial when control is out-of-range
  – Changes a \( 1_{3SD} \) rule to \( 2_{3SD} \) or even \( 3_{3SD} \)
• Complex multirules yield no observed benefit
• Recommend simplifying QC system
• Study from 1994
Balanced Control Limits

• Control limits must be appropriately sensitive
  – such that significant accuracy changes are always detected.

• Recalibration is not required for minor accuracy variations of no clinical consequence.
  – In other words, there should be a high probability for error detection and a low probability for false rejection.

Is a 3SD Limit Quality?

• Analyzer A
  – HGB 13.6
  – 1SD .11
  – 3 SD rule +/- .33

• Analyzer B
  – HGB 13.8
  – 1SD .34
  – 3 SD rules +/-1.0
Chasing Zero Bias

- **RBC**
  - Mean 4.30 \((10^{12}/L)\)
  - CV = 1%
  - 2SDI = 0.06 \((10^{12}/L)\)
  - 1SD = 0.6%

Overall Patient Range

Increased Chasing 0 Bias

Sysmex Quality

- **RBC**
- **WBC**
- **HGB**
- **HCT**
- **PLT**

- = Insight 2SDI range
- = CLIA PT survey limits

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6 Sigma in the Lab

Common Method

- Measure test quality to determine sigma score
- Adjust control procedures for test quality
- Difficult for most labs to implement
- Different control limits per serial number
- TEa normally PT survey limits

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<tr>
<th>Sigma Score</th>
<th>Westgard Recommendation</th>
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<tr>
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<td>1.35s with 2 or 3 controls</td>
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<td>5</td>
<td>1.3s with 2 or 3 controls</td>
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<tr>
<td>4</td>
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<tr>
<td>3</td>
<td>Multirule with at least 6 controls</td>
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<th>Sigma Score</th>
<th>Clinical opinion leaders Recommendation</th>
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<td>1.35s with 1 control per day</td>
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<td>Multirule, 2 levels, 2 times a day</td>
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<td>3</td>
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Sysmex Quality

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TEa</th>
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<th>CV</th>
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<td>PT</td>
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<td>2</td>
<td>10.2</td>
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- Analyzer quality supports reduced QC effort
- Analyzer tested using multiple parameters per level of qc
- Automatic internal checks
- QC limits supported by many studies

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What is Six Sigma?

6 Sigma Quality = 3 DPM
0% out-of-range

1 Sigma Quality = 691,462 DPM
69% out-of-range

Sigma method well suited for control and monitoring of analyzer
- Tool to set performance goal
- Great for monitoring quality
- Calculates balance between error detection and false rejection
- Uses more than SD

Sigma Error QC Limits

Performance Goal (TEa)

\[ \text{Sigma} = \frac{(\text{TEa} - \text{Bias})}{\text{CV}} \]
Evidence Based Control Limits

• Sysmex Evidence Based Control Limits are:
  – Control limits that provide appropriate error detection with minimal false rejection.

• Sysmex Evidence Based Control Limits are not:
  – Standalone control rules
  – Multirules
  – Quality Control procedure

Evidence Based Limits

• Sigma control rules
  – Common industry quality measure
  – Rule built using performance goal, bias, and precision of test method
  – Formula to balance error detection with low false rejection rate
    • Predicts defects per million (DPM)
  – Common measure and performance goal by parameter independent of manufacturer
New Recommendations

Evidence Based Limits

- Sysmex did the work for the lab
- Balanced Error Detection with Low False Rejection Rate
- Control limits based on 6 Sigma methods
  - Calculated for each control level and model
- Monitors true analyzer performance
  - Calculated using tens of thousands of data points

Evidence Based Limits

\[ \text{Sigma} = \frac{\text{Performance Goal} - \text{Bias}}{\text{CV}} \]

Balanced Error Detection with low False Rejection

Performance Goal (TEa)

Precision (CV) cannot be adjusted
**Sigma Control Limit**

- **Analyzer A**
  - Performance goal 2.8%
    - Control limit 13.2 – 14.0
    - 5.6 Sigma quality
  - 3 SD rule 13.3 -13.9

- **Analyzer B**
  - Performance goal 2.8%
    - Control limit 13.4 – 14.2
    - 1.9 Sigma quality
  - 3 SD rule 12.8 -14.8

Sigma = (Performance Goal – Bias)/CV

**Performance Goal**

- Used 6 cumulative Insight reports for each model
  - Over 500 days of control data in calculation
  - Control performance throughout lot life
  - Analyzer and reagent performance

- Performance goal calculated using 4 Sigma quality goal
  - 4 Sigma limit = (performance goal – bias)/CV
  - 3% false positive rate
Performance Goal

- Performance goal calculated using 4 Sigma quality goal

\[ 4 \text{ Sigma limit} = \frac{(\text{performance goal} - \text{bias})}{\text{CV}} \]

- Set to 4Sigma
  - 3% false rejection rate

- Measured
  - 1 and 2 SDI bias

- Calculated
  - TEa control limit to balance error detection and low false rejection

- Measured
  - True analytical performance
    - >600 serial # data
      - Many different reagent lots
    - 6 cumulative reports
      - >500 days of data

Customer Feedback

- IHN study
  - 20% reduction in false control rejections without any loss of error detection
  - Using new limits they report 3% false rejection rate (perfect performance)
  - Lab manual now instructs to repeat controls only after investigation
    - Fixed repeat issues
    - Saved Tech time
    - Reduced control material
Customer Feedback

- Fixed repeat issue and false control rejection issues
- Staff now investigates out-of-limit events

From: Ann
Subject: QC Feedback

Hey Scott,

I was able to visit an XN customer yesterday and got some very positive feedback about the QC limits. This was a legacy customer that struggled significantly with getting historical limits pinned down and always fought with false flagging and numerous unnecessary repeats. She said that once she got the new NRBC limits on her XN, it has been smooth sailing. She specifically said that now if something is out, they all gather around to see what's wrong because it is such a rare occurrence. Great comments that I wanted to pass along, thanks for doing what you do! We all appreciate it.

Have a good day,

~Ann

Laboratory Benefit

- Improve lab satisfaction with control products and processes
- Easily identify changes in analyzer performance
  - Appropriate error detection with low false rejections
- Reduce laboratory cost
- Increase overall productivity
  - Increased analyzer uptime
  - Reduce labor cost for QC processes
Quality

• Narrow control limits do not improve result quality
  – Error detection without corrective action desensitizes QA processes
• Only improvements to sample preparation or test systems can improve result quality
  – Control limits are to identify if there has been a clinical change to the test system

Additional Information

• Customer communication 63-1100 02/2014
  – Located in CRC
• Insight Guide
  – Insight/User Manuals/Participant Overview Guide
• CAP q-probe 94-08 QC Exceptions
• International Journal of Laboratory Hematology
  – Rationale for using insensitive quality control rules for today's hematology analyzers
THANK YOU