Letter to the Editor

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How to evaluate fixed clinical QC limits vs. risk-based SQC strategies

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To the Editor,

There are two schools of thought on how to design Statistical quality control (SQC) procedures. The traditional approach has been based on the total error model and a structured planning process, as described in the CLSI C24-Ed4 guideline for SQC [1]. Now in the era of metrology, there is a new approach to set fixed clinical control limits based on an "acceptability range" calculated as 2*APS_u, i.e., a 95% limit based on the Analytical Performance Specification for Standard Measurement Uncertainty, u [2].

The use of an "acceptability range" is operationally similar to an earlier proposal for use of "fixed clinical limits" in the mid-1990s [3]. The mechanics are the same, just draw the lines that represent the performance specification directly on the control charts, in this case ±2*APS_u.

For example, consider that APS_u for HbA_{1c} is 3.0% [4], so the acceptability range of 2*APS_u would be TV ± 6.0%. Based on the stable imprecision of the method, these control limits can also be described in terms of the number of SDs from the mean, for example, if the stable imprecision is 2.0% and bias is 0.0%, the control limit corresponds to 3s (6.0%/2.0%); if stable imprecision is 1.0% and bias is 0.0%, the control limit corresponds to 6s (6.0%/1.0%). If the out-of-control condition is defined as 1 control result exceeding a control limit, then the control rule is 1:3 s N=1 for the first example and 1:6 s N=1 for the 2nd example. Here N represents the total number of control measurements in a QC event.

In contrast, a risk-based SQC strategy is determined using a structured planning process having the following steps:

1. Define the quality specifications for the test.
2. Select appropriate control materials and levels.
3. Determine the stable (in control) performance of the measurement procedure.
4. Identify candidate quality control strategies.
5. Specify desirable goals for the QC performance characteristics.
6. Select a quality control strategy (control rules, number of control measurements) whose predicted performance meets or exceeds the quality control performance goals.

In practice, the quality specification and stable imprecision are used to calculate a Sigma-metric (steps 1–3).

$$\text{Sigma} = (\%\text{TEa} - |\%\text{Bias}|)/\%\text{CV or } \%\text{TEa}/\%\text{CV when Bias is zero}$$

Candidate QC procedures are identified (step 4) using a Sigma-metric Run Size Nomogram [5]. The desired performance goal is set as a maximum of 1 erroneous test result for detection of the error condition (step 5, based on Parvin's MaxE (Nuf) patient risk model, [6]). Then the risk-based SQC strategy is identified from the Nomogram by drawing a vertical line corresponding to the Sigma-metric, inspecting the control rules, Ns, and run sizes at the intersections with the lines to identify an appropriate SQC strategy. For example, Figure 1 shows the results for a 4-Sigma testing process, where a 1:3s/2:2s/R:4s/4:1s multirule procedure having 4 control measurements (MR4) and a run size of 190 patient samples would be an appropriate risk-based SQC strategy.

It is possible to assess the performance of fixed clinical limits in a similar way, i.e., calculate a Sigma-metric using 2*% APS_u as a 95% tolerance limit, bias as 0.0, and the observed SD or CV, i.e., Sigma = 2*% APSu/% CV or 2*APSu/SD. For example, a HbA_{1c} method having an APSu of 3.0%, stable imprecision of 1.5% and bias of 0.0, would also have a Sigma of 4.0. However, it may be more

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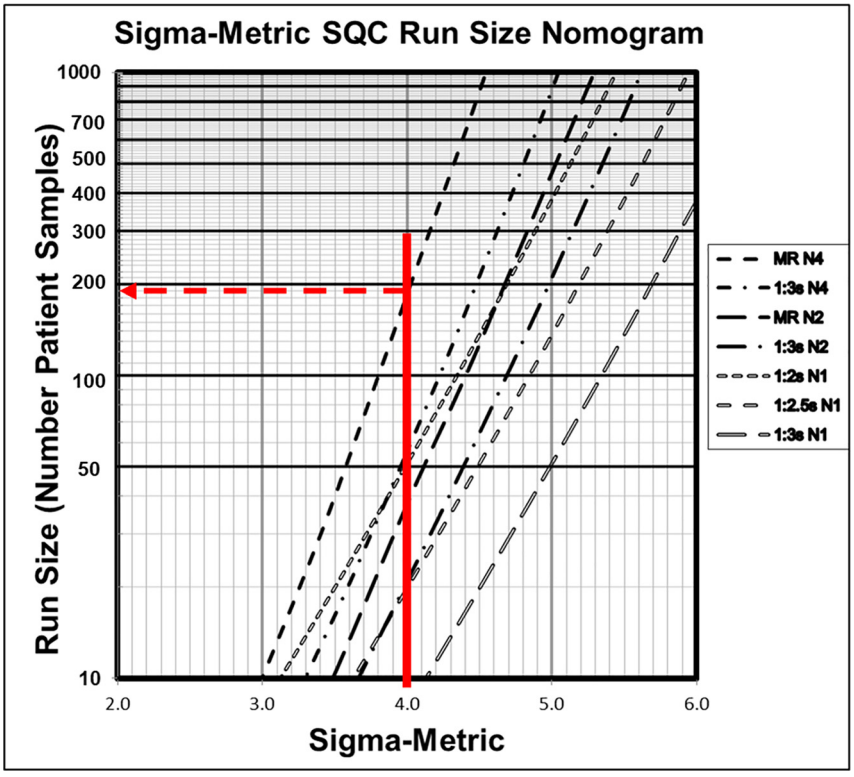

Figure 1: A Sigma-metric run size Nomogram that shows run size on the y-axis (logarithmic scale) and the Sigma-metric on the x-axis.
The angled lines represent the QC procedures shown in the key at the right. The vertical line represents a method with 4.0 Sigma quality. A maximum run size of 190 patient samples can be achieved using a 1:3s/2:2s/R:4s/4:1s multirule procedure with 4 control measurements.

convincing to consider an empirical validation where the stable imprecision data is used as a baseline to which systematic errors are added and run rejection determined. For example, additions of SEs equal to +1SD, +2SD, +3SD, and +4SD would be appropriate for assessing how often rejections are observed over a range of realistic sizes of systematic errors. It would be useful to calculate the ratios of runs rejected to the total runs, which gives an estimate of the probability for rejection that can be presented in the form of a power curve or power function graph [7] and therefore can be compared to the theoretical expectation for the actual control rule defined by the clinical fixed limit.

Based on the traditional Total Error framework, an SQC strategy is the outcome from a planning process, not a simple matter of drawing acceptability limits on a control chart. CLSI C24-Ed4 provides a consensus "road map" for developing such a planning process that minimizes the risk of producing erroneous test results that would go undetected by the QC procedure. By setting a limit to the maximum number of erroneous test results that might be reported, the laboratory can optimize the control rules, number of control measurements, and the frequency of QC events (in terms of run size) for bracketed operation of continuous production processes. New tools continue to simplify the calculations and support applications in medical laboratories [8–10]. Thus, the new construct for making improvements in QC practices should be a risk-based SQC strategy, not using an acceptability range as control limits. However, the quality requirement for deriving the risk-based SQC strategy could indeed be a tolerance range based on the desired APS for MU.

A risk-based SQC planning provides "individualized" SQC strategies appropriate for different levels of observed quality to assure the same risk for patients (e.g., ≤1 erroneous results in a run). In contrast, using fixed clinical QC limits leads to a "one size" SQC that won't fit all different levels of observed quality, i.e., the same SQC will yield different levels of patient risk when Sigma varies.

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