Applying Sigma Metrics to Reduce Outliers

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KEYWORDS

• Six sigma • Sigma metrics • Instrumentation assessment • Quality control
• Laboratory standardization • QC rules failure rates

KEY POINTS

- Sigma metrics can be used to aid in the evaluation and selection of clinical laboratory instrumentation.
- A Six Sigma–designed quality control (QC) program can be used in monitoring the performance of assays, resulting in cost savings in reagents, supplies, and labor, especially if most of the assays are of 5 sigma or better.
- QC rules failure rates increase dramatically as the sigma metric of the method decreases.
- Reproducibility of results between laboratories is much better with methods of 5-sigma or 6-sigma metrics.

Over the last several decades, laboratory testing results have improved in both accuracy and precision. This improvement has mostly been caused by changing technology of instrumentation and the quality of the assays developed with that instrumentation. With this improved assay quality, the following questions need to be asked: how does this quality relate to acceptable quality goals set forth by the laboratory, what accuracy and precision are required by the method to achieve these quality goals, and how is this determined? It is necessary to answer these questions to assess the quality of the laboratory results being generated by the laboratory. Without this knowledge, the laboratory cannot accurately determine whether or not their results are within allowable clinical error.

ASSESSMENT OF NEW INSTRUMENTATION

When evaluating new instrumentation, there are numerous factors to consider; most of these factors are related to costs. These factors include, but are not limited to:

- Cost of instrumentation, including automation, middleware, and service costs
- Cost of reagents and supplies

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- Reliability of the instruments
- Ease of use
- Instrument throughput
- Specimen requirements
- Test menu (consolidation of workstations)
- Middleware capabilities
- Turnaround times
- Vendor support

All of these factors affect the overall cost of the operation of the instrumentation. However, one important factor that is too often overlooked is assay quality. Quality measures such as accuracy and reproducibility affect physician decisions, which in turn can affect patient outcomes. Assay quality also affects the laboratory. Poor assay quality can affect the efficiency of the QC program used to monitor the assays, and this can translate into time and cost and may also affect proficiency testing.

SIGMA-METRIC ANALYSIS

In our laboratory, we conducted a quality comparison of the different vendor instruments, performing a sigma-metric analysis for each instrument. The Six Sigma approach is a universal benchmark that describes the number of defects per million of a process or system. For laboratory assays, a defect is defined as an event that is outside the tolerance limits of an assay. The sigma metric is measured on a scale of 0 to 6, with 6 being world class (3.4 defects per million) and 3 being the minimum level of performance for a system (about 66,800 defects per million). It uses basic laboratory quality measures, bias and imprecision, and can be used to compare assay quality across multiple instrument systems, or to evaluate the assay performance of a given instrument system and to set the appropriate QC rules required to effectively monitor the assays.[1] The sigma metric is calculated using the following equation:

$$\text{Sigma metric} = (\text{TEa} - \text{Bias}_{\text{observed}})/\text{CV(coefficient of variation)}_{\text{observed}}$$

where *TEa* is total allowable error. For the purposes of comparing estimated sigma metrics for different vendor systems during the instrument assessment phase, bias and imprecision values are available from several sources, such as external proficiency testing programs, quality control (QC) programs, information from the vendor, and literature sources. TEa can be taken from several different analytical or clinical benchmarks, such as proficiency testing criteria, external quality assessment standards, RiliBAK guidelines (Guidelines for Quality Assurance of Medical Laboratory Examinations of the German Medical Association), desirable biological variation database,[2] and ISO (International Standards Organization) 15189.

Once the instrumentation is in place, the same quality measures can be used to evaluate the true assay performance and to set the appropriate QC rules required to effectively monitor an assay. Imprecision data from the laboratory replication study and the measured bias against a reference method or peer group can be used along with the TEa to generate a sigma metric. These values can also be correlated with Westgard Sigma Rules to set the QC procedures. Five-sigma and 6-sigma methods only require a simple QC rule to monitor the method with fewer controls per run. Three-sigma and 4-sigma methods require multiple QC rules to monitor the method with a higher number of controls per run. Methods with a sigma metric of less than 3 are difficult to monitor even with multiple QC rules and many controls per run; these methods should be avoided.