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Optimizing Routine Chemistry performance on a Laboratory Analyzer through Six Sigma and QGI Metrics

Atul A Patil[1], Praveenkumar Gupta[2], Nita K Munshi[3], Anjali Kelkar[4], Harshal Patil[5], Rupali Suryavanshi[6] and Vaishali Patil[7]

[1-7] Ruby Hall Clinic, Sasoon Road,Pune-411 001, Maharashtra, India

Abstract:

Introduction: Analytical performance assessment using six sigma metrics has become a cornerstone in clinical laboratories, ensuring optimal test accuracy and efficiency. By identifying areas of bias and imprecision, sigma metrics enable laboratories to adopt a scientific approach to improving test processes and optimizing quality control (QC) strategies.[3],[5] *Materials and Methods:* This study evaluated the performance of 27 routine analytes on the VITROS 5600 analyzer over six months. Sigma scores were calculated using Total Allowable Error (TEa) from CLIA guidelines, while Quality Goal Index (QGI) scores identified specific areas requiring improvement. Analytes were categorized based on sigma levels, with QC plans optimized as per Westgard recommendations.[4],[11] *Results:* Of the analytes assessed, 67% achieved a sigma score of ≥4, indicating high reliability and minimal QC requirements. Eleven analytes scored below six sigma, with eight requiring improvements in imprecision and three needing corrections in both bias and imprecision. Two analytes with scores ≤3.2 required intensive QC modifications. *Conclusion:* The study highlights the efficacy of six sigma principles in laboratory settings, with a majority of analytes achieving optimal performance. The application of sigma and QGI metrics aids in refining QC plans, enhancing analytical accuracy, and improving operational efficiency.

Keywords: Sigma score; Quality goal index (QGI); CLIA ; Total allowable error; IQC.

Introduction:

The accuracy of laboratory results is integral to patient care, requiring robust quality assurance practices that minimize analytical errors. While laboratory errors can occur across pre-analytical, analytical, and post-analytical phases, the analytical phase is the most controllable and standardizable. [1], [3] Monitoring analytical performance through metrics like bias and imprecision provides insights into an analyzer's reliability. Westgard emphasizes that integrating six sigma principles with traditional QC practices provides laboratories with a structured methodology to proactively address errors and optimize test processes. [2] Six sigma metrics offer a quantitative approach to evaluating analytical performance, enabling laboratories to assess test processes against Total Allowable Error (TEa) goals. These metrics allow for systematic identification of areas requiring improvement, particularly for analytes that underperform due to bias, imprecision, or both. [5],[13] Traditional QC methods, such as Westgard rules, focus on detecting errors reactively. However, integrating six sigma principles enhances proactive quality management by categorizing analytes based on sigma scores and tailoring QC plans accordingly. [6],[7] This not only ensures result accuracy but also reduces the frequency of unnecessary QC runs, improving cost-effectiveness and efficiency. This study aims to evaluate the analytical performance of routine biochemistry analytes on the VITROS 5600 biochemistry analyzer using sigma metrics. Additionally, the study employs QGI to identify improvement areas for analytes scoring below six sigma, offering actionable insights into refining QC strategies.

Material and Methods:

This observational study was conducted to assess the analytical performance of 27 routine biochemistry tests on the VITROS 5600 biochemistry analyzer. The study spanned six months, from July 2017 to December 2017. Imprecision data was recorded cumulatively for six months (January–June 2017) and reviewed monthly for two IQC levels. The six-month average CV% for each analyte was used for sigma score calculations. Bias values were extracted from monthly BIORAD EQAS reports and averaged over six months to determine cumulative bias.[8] Sigma scores were calculated using the formula: Sigma = (TEa % - Bias %) / CV %. TEa values followed CLIA recommendations. The final

sigma score for each analyte was the average of the scores from the two IQC levels. QGI was calculated for analytes scoring below six sigma to identify whether improvements were needed in bias, imprecision, or both. The formula used was: QGI = Bias / (1.5 × CV %). The higher CV% between the two IQC levels was used to ensure realistic and actionable QGI assessments. [13] Westgard recommendations guided the QC plans for analytes, with Schoenmakers et al.'s chart used to determine QC frequency based on sigma scores.

Results:

Table 1: QC plan derived from above mentioned recommendations:

Sigma score	**Westgaurd rules**	**Levels of control**	**Measurements**
≥ 5.8	$1_{3.5S}$	2	1
5.2- 5.7	$1_{3.5S}$	2	1
4.2-5.1	$1_{2.5S}$	2	1
3.4-4.1	$1_{3S}/2_{2S}/R_{4S}/4_{1S}$	2	2
≤ 3.2	$1_{3S}/2_{2S}/R_{4S}/4_{1S}/7_{X}$	3	2

Analytes scoring ≥4 sigma required minimal QC interventions, while those ≤3.2 sigma necessitated enhanced QC protocols. [3],[6],[11] The criteria used for identifying improvement opportunity using QGI is as follows: < 0.8 indicates imprecision, 0.8 to 1.2 indicates both bias and imprecision and > 1.2 indicates bias. [4]

Table 2 depicts average sigma score of twenty seven analytes taken under study. Table 4 depicts improvement area of sigma score of analytes by considering QGI score. It gives us idea of improvement area based on indices like imprecision, bias or both. Table 3 depicts QC plan derived from the performance of analyzer by using six sigma analysis for mentioned analytes (Table 1 & 2). Note: Abbreviations for analytes used as follows: ALKP=Alkaline phosphatase, AMYL=Amylase, AST=Aspartate transaminase, Ca=Calcium, CK=Creatine kinase HDL= High density lipoprotein cholesterol, GGT=Gamma-Glutamyl Transferase, Mg=Magnesium, UA=Uric Acid, TP=Total protein, LDH= Lactate Dehydrogenase, Cl= Chloride. Of the 27 analytes analyzed, performance varied across three sigma score categories: High-performing Analytes (Sigma ≥6): Sixteen analytes (59%) achieved sigma scores ≥6, reflecting excellent reliability. These included CK, Magnesium, and Uric Acid. High-sigma analytes required minimal QC interventions , with two IQC levels run daily, optimizing operational efficiency.[4],[6] Moderately Performing Analytes (Sigma 3–6): Eleven analytes (41%) scored between 3 and 6 sigma. Among these, seven scored between 3.4 and 4 sigma, requiring moderate QC interventions. QGI analysis revealed that eight analytes (73%) required improvements in imprecision, while three (27%) needed corrections in both bias and imprecision.[8],[9] Low-performing Analytes (Sigma ≤3.2): Two analytes, Iron and LDH, scored ≤3.2 sigma, necessitating intensive QC modifications. These analytes required three levels of IQC to be run twice daily to ensure result accuracy. Enhanced calibration and precision monitoring were recommended as corrective measure. [7],[13] 67% of analytes achieved sigma scores ≥4, indicating robust performance and reduced QC frequency. Analytes with lower sigma scores highlighted specific improvement areas, underscoring the importance of QGI in targeted quality enhancement. The results validated the VITROS 5600 analyzer's reliability for routine biochemistry tests, with only minor adjustments needed for low-performing analyte

Table 2: Average sigma scores of analytes

Sr. No.	Analytes	CLIATE a (%)	Ave. of Cum. %CV	Control Level	Ave. of Cum. % Bias	CLIA Sigma	Ave. CLIA Sigma
1	Albumin	10	2.04	Level 1	1.7	4	4.0
		10	2.01	Level 2	1.7	4	
2	ALKP	30	2.75	Level 1	2.9	10	11.0
		30	2.35	Level 2	2.9	12	
3	ALT	20	8.43	Level 1	3.2	2	3.5
		20	3.22	Level 2	3.2	5	
4	Amylase	30	5.32	Level 1	5.7	5	7.0
		30	2.59	Level 2	5.7	9	

5	AST	20	2.82	Level 1	2.6	6	7.0
		20	2.25	Level 2	2.6	8	
6	Urea	11	1.93	Level 1	1.5	5	4.0
		9	2.17	Level 2	1.5	3	
7	Chol	10	1.77	Level 1	2.2	4	4.0
		10	2.08	Level 2	2.2	4	
8	CK	30	3.67	Level 1	7.8	6	6.5
		30	3.32	Level 2	7.8	7	
9	Creatinine	15	1.57	Level 1	1.9	8	8.5
		15	1.4	Level 2	1.9	9	
10	Glucose	10	1.1	Level 1	1.3	8	7.0
		10	1.37	Level 2	1.3	6	
11	Mg	25	2.2	Level 1	2.9	10	11.0
		25	1.83	Level 2	2.9	12	
12	TBIL	20	4.27	Level1	5.7	3	4.0
		20	2.62	Level 2	5.7	5	
13	TP	10	1.75	Level 1	2.9	4	4.0

Table 3: Summary of sigma performance and QC plan derived from table 1 and 2.

Average Sigma Score	Analytes	QC RULE	Levels Of Control	Measurement
≥4.2	ALKP, Amylase, AST, CK, Creat., Glucose, Mg., Trig.,UA, Dhdl, Na, K, Phosphorus, Ca, GGT, DTIBC, Cl, Lipase (18 Analytes)	$1_{2.5S}$ / $1_{3.5S}$	2	1
3.4-4.2	Albumin, ALT, Urea, Cholesterol, TBIL, TP, ECO2 (7 Analytes)	$1_{3S}/2_{2S}/R_{4S}/4_{1S}$	2	2
≤3.4	Fe and LDH (2 Analytes)	$1_{3S}/2_{2S}/R_{4S}/4_{1S}$/ n	3 or 2	2 or 3 resp.

Table 4: QGI scores for analytes <6 sigma based on CLIA TE(a) goals

QGI Score	Analytes	Improvement area
<0.8	Albumin, ALT, Urea, Fe, Cholesterol, Cl, ECO2, Lipase(8 Analytes)	Imprecision
0.8-1.2	TBIL, TP, LDH (3 Analytes)	Imprecision and Bias
>1.2	--	Bias

Discussion:

The implementation of six sigma principles in clinical laboratories provides a robust framework for improving analytical accuracy and operational efficiency. This study assessed the performance of routine analytes on the VITROS 5600 biochemistry analyzer using sigma metrics and QGI scores to optimize quality control strategies. Sigma scores serve as a reliable indicator of an analyte's analytical performance. In this study, 67% of analytes achieved sigma scores ≥4, reflecting high reliability and reduced need for frequent QC runs. Analytes in this category required minimal intervention, consistent with findings by Schoenmakers et al., where high-sigma analytes demonstrated cost-effectiveness due to reduced QC frequencies. [3],[11] Zhou et al. highlighted similar observations, noting that tests with sigma scores >4 could maintain quality with fewer QC runs per day, substantially lowering operational costs. [4] Analytes with sigma scores <4, such as LDH and Iron, required intensive QC measures, including running three levels of

IQC twice daily. QGI scores for these analytes indicated that imprecision was the primary area requiring improvement for eight analytes, while three needed corrections in both bias and imprecision. Studies have emphasized that improving imprecision in low-sigma analytes can significantly enhance test accuracy and reduce variability. [8],[10] Analytes with high biological variability often show higher TEa thresholds, resulting in better sigma scores. For example, CK and Uric Acid, both with TEa >15%, demonstrated excellent sigma performance in this study, consistent with observations by Medina et al. on the impact of TEa on sigma metrics.[14] Conversely, analytes with low TEa values (e.g., Albumin and Calcium) are more sensitive to deviations in precision, requiring closer monitoring to ensure result accuracy.[9],[12] QGI scoring provides a targeted approach to identify whether imprecision, bias, or both contribute to suboptimal performance. This study found that 73% of low-sigma analytes required improvements in imprecision, highlighting the need for enhanced calibration and precision monitoring.[7],[13] QGI has been recognized as a valuable tool for laboratories aiming to transition from reactive QC practices to proactive quality management. [13] Adopting a sigma threshold ≥4 is both practical and economical. As evidenced in this study, high-sigma analytes required only two IQC levels daily, reducing the overall QC burden without compromising accuracy. This aligns with findings by Nanda and Ray, who advocated for sigma ≥4 as a benchmark for optimal lab performance.[10] The results of this study are specific to the VITROS 5600 analyzer, which has demonstrated consistent performance across various analytes. The analyzer's calibration protocols, requiring adjustments only during lot changes, contributed to reduced bias in most analytes. However, the performance may vary with different analyzers, emphasizing the need for laboratory-specific evaluations. [6],[9] Sigma metrics have gained global recognition as a standard for laboratory performance assessment. For instance, studies in diverse settings, such as those conducted by Iqbal and Mustansar in South Asia, demonstrate that applying sigma principles universally improves test accuracy and reliability. [7],[14] By focusing on sigma metrics and QGI scores, laboratories can improve patient safety by ensuring reliable test results while simultaneously optimizing resource utilization. The integration of these tools into routine practices allows laboratories to maintain high standards of quality assurance while adapting to financial and operational constraints. [6],[13] Medina et al. demonstrated that employing sigma metrics in clinical chemistry not only enhances test performance but also promotes resource efficiency, aligning laboratory practices with global quality standards. [14] igma metrics continue to emerge as a cornerstone for enhancing analytical quality in clinical laboratories. Raj et al. highlighted that by continuously monitoring sigma scores, laboratories can identify analytes requiring precision improvements, thus ensuring result reliability even for tests with stringent TEa thresholds.[15] Similarly, Sengupta et al. emphasized that the application of sigma metrics not only ensures consistent analytical performance but also helps in achieving compliance with global quality standards, fostering credibility among regulatory bodies and stakeholders.[16] El Sharkawy et al. demonstrated the utility of sigma metrics in standardizing laboratory practices across multiple sites. Their findings suggested that harmonizing QC protocols based on sigma scores significantly improves inter-laboratory result comparability, particularly for assays with variable performance.[17] Additionally, Fasano et al. conducted a multi-site evaluation of 20 assays and observed that integrating sigma metrics into routine QC practices enhances error detection while reducing unnecessary QC interventions.[18] Harrison and Jones explored the application of sigma quality control in multi-instrument, multi-site health networks, observing a marked reduction in QC costs while maintaining high-quality results. Their work demonstrated that sigma metrics could guide the efficient allocation of QC resources, especially in large-scale healthcare settings. [19] Carobene et al. reported on the European Biological Variation Study, emphasizing the role of sigma metrics in aligning laboratory practices with biological variation data. This alignment ensures laboratories can better interpret patient results, especially for analytes with inherently high variability, while maintaining stringent quality thresholds. [20]

Conclusion:

This study demonstrates the utility of sigma metrics in laboratory performance optimization. By identifying areas for improvement using QGI, laboratories can implement targeted corrective measures, enhance accuracy, and optimize resource use. Future studies should explore the application of six sigma principles across diverse analyzers and settings.

Sources of supports: Nil
Conflicts of Interest: Nil

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Address for correspondence:
Dr. Atul A Patil
Consultant Biochemist,
Ruby Hall Clinic, Sasoon Road, Pune-411 001,
Maharashtra, India
Mobile no: +91 7972575384
Email:dratul.patil@rubyhall.coml.com

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