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Research Article

Six Sigma Approach for Performance Analysis of Hematology Analyzers in a Clinical Laboratory

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Abstract

Background: Accurate laboratory results are crucial for patient care, necessitating rigorous performance monitoring. Sigma metrics, a statistical method, can be used for performance evaluation of analytical methods in a diagnostic laboratory.

Objective: This study aimed to evaluate performance and recommend customized quality control design for an automated blood count analyzer by application of Six sigma methodology.

Methods: Internal Quality control and peer group evaluation data were used to calculate average imprecision and bias observed for the analytical instrument under study. CLIA (Clinical Laboratory Improvement Amendments) goals for analytical performance (Total allowable error) were applied to derive the 'sigma value' for the key measured parameters- Hemoglobin (Hb), Red Blood Cell count (RBC), Hematocrit (HCT), White Blood Cell count (WBC) and Platelet count to rate the performance based upon sigma scale and recommend tailored quality control strategies for each parameter.

Results: The analyzer showed acceptable performance (above 3 sigma) for all parameters evaluated, with some parameters like Platelets showing beyond world class performance. While the overall analyzer performance was observed to be acceptable, a potential for further optimization was realized, especially for parameters like RBC and Hematocrit.

Conclusion: Six sigma is an invaluable statistical tool available to diagnostic laboratories to ascertain analytical performances of its testing methods and optimize quality control processes, by utilizing readily available internal and external quality assurance data.

Keywords: Total Allowable Error; Bias; CV (Coefficient of Variation); Sigma

Introduction

Quality Improvement strategies are increasingly important for health care laboratories in today's competitive marketplace [1]. The quality of laboratory results is paramount for effective patient care, making it essential for clinical laboratories to engage in continuous and rigorous performance monitoring of testing methods including the analytical instruments.

A blood count (Complete blood count), is one of the most frequently requested laboratory tests by clinicians [2]. Rigorous performance monitoring of automated blood count analyzers is thus crucial to ensure high quality of test results released by any laboratory. Clinical laboratories traditionally rely on use on internal quality controls and participation in external quality assurance programs for monitoring test quality. Traditional QC rejection rules are commonly employed for monitoring internal quality control outcomes [3]. The implementation of statistical methodologies like Sigma metrics can significantly enhance performance evaluation and QC rule development, ensuring that laboratory results meet the highest standards.

The Sigma (σ) value for any method represents the standard deviation (SD) associated with it. Six sigma is a methodology for quality measurement and process improvement that was initially developed by Motorola in the early 1980s [4]. Application of Sigma methodology can be extended to any process that has a measurable outcome. A poor outcome is counted as an error or defect. This is further quantified in terms of total number of defects per million opportunities (DPMO). Six sigma provides a quantitative frame work for evaluating process performance with evidence for process improvement and describes how many 'Sigmas' will fit within the tolerance limits [5]. Quality is assessed on the sigma (σ) scale with a criterion of 3 σ as the minimum requirement for acceptable performance and 6 σ, being the goal for world-class quality [6].

The "Sigma" in Six Sigma refers to the benchmarking scale upon which the process or method performance is judged [6]. Defects can be counted or estimated and then converted to a defects-per-million (DPM) ratio (Table 1).

Sigma value	Reference Level	Defect per million opportunities
6	World class	3.4
5	Excellent	233
4	Good	6210
3	Marginal	66,807
2	Poor	308,537
1	Unacceptable	690,000

Table 1: Sigma performance table [6].

Table 1 outlines the sigma values and their corresponding quality levels, ranging from "World Class" to "Unacceptable," along with the associated defects per million opportunities (DPMO). It provides a clear reference for assessing the performance quality based on sigma levels.

Sigma metrics is being routinely practiced by many clinical biochemistry laboratories and various studies and literatures are also available for the same [7,8], but when it comes to clinical hematology laboratory, six sigma implementation is relatively still in its early stages.

The present study was undertaken to evaluate the quality of the analytical performance of the DXH900 blood count analyzer in a hematology laboratory on sigma scale. Quality Control data and peer group evaluation data were used to derive observed bias and imprecision for the parameters Hemoglobin, RBC count, WBC count, hematocrit and Platelet count. The sigma value was then calculated at each level of control to ascertain the analytical performance and the number of defects per million for the parameters.

Methods and Findings

Study design

The performance of the DXH900 hematology analyzer was evaluated using internal quality control data and the peer group evaluation data received from inter laboratory Quality Assurance Programs (IQAP). Parameters assessed included Hemoglobin (Hb), Red Blood Cells (RBC), Hematocrit (HCT), White Blood Cells (WBC), and Platelets. Quality control and peer group performance data were used to calculate each parameter's bias and imprecision, which were then analyzed using sigma metrics.

Methodology

Data collection

Data from four different Lots of commercial Internal quality control materials was collected at three different levels of concentration for each parameter. Outcomes of multiple runs conducted over several days and by different operators were utilized to ascertain the mean and standard deviation (SD) for each parameter at different concentration levels. The IQAP peer group quality assurance program was used to record the observed laboratory mean and the peer group means for each parameter at different concentration levels in order to calculate bias. Total allowable error (TEa) values for the parameters were taken from the Clinical Laboratories Improvement Act (CLIA) goals for analytical performance [9].

Calculations

Calculation 1: For each level of control, coefficient of variation (CV) was calculated from observed mean and Standard deviation (SD) and all calculations done as per given equations for each of the four control Lots (Tables 2,3,4 and 5):

CV% = SD/mean x 100

Calculation 2: Bias was calculated from Peer review provided in the IQAP evaluation report for the control lot (Tables 2,3,4 and 5).

Bias = [(laboratory mean–peer group mean)/peer group mean] ×100

Calculation 3: Average Bias (%) and CV (%) for each parameter were calculated from the four Quality control lot data (Table 6).

Calculation 4: Sigma metrics for the various analytes was calculated by the following equation at different concentrations of controls and as an average sigma for each parameter (Table 7):

Sigma (σ) = (TEa- Avg Bias%)/Avg CV%

Where;

TEa = total allowable error -CLIA analytical performance goals [9]

CV = coefficient of variation

SD = Standard Deviation

Results

Data Summary

Following performance data was gathered for various hematological parameters.

Table 2: Internal Quality control data analysis for Lot-1.

PARAMETER	CONTROL	PEER GROUP MEAN	LAB MEAN	SD	CV	TEA(CLIA 2024)	BIAS
Hb (g/dL)	LEVEL 1	4.2	4.2	0.01	0.24	4.00	0.00
	LEVEL 2	11.2	11.2	0.05	0.40	4.00	0.00
	LEVEL 3	15.7	15.7	0.06	0.38	4.00	0.00
RBC (106/uL)	LEVEL 1	1.57	1.58	0.01	0.63	4.00	0.64
	LEVEL 2	3.63	3.65	0.05	1.23	4.00	0.55
	LEVEL 3	5.28	5.3	0.06	1.13	4.00	0.38
HEMATOCRIT (%)	LEVEL 1	12.9	13	0.15	1.12	4.00	0.78
	LEVEL 2	33.2	33.4	0.35	1.04	4.00	0.60
	LEVEL 3	47.8	47.9	0.48	1.00	4.00	0.21
WBC (103/uL)	LEVEL 1	3.2	3.2	0.05	1.56	10.00	0.00
	LEVEL 2	18.8	19.4	0.25	1.29	10.00	3.19
	LEVEL 3	8.9	8.9	0.15	1.69	10.00	0.00
PLATELET (103/uL	LEVEL 1	71	70	1.01	1.45	25.00	-1.41
	LEVEL 2	406	402	8.26	2.05	25.00	-0.99
	LEVEL 3	213	209	3.23	1.55	25.00	-1.88

The above table (Table 2) shows internal quality control data for Lot 1 of control material, collected over a month. Three levels of quality control materials (LEVEL 1, LEVEL 2, LEVEL 3) were run daily and the data collected was analyzed to calculate laboratory mean, standard deviation (SD), coefficient of variation (CV) for parameters hemoglobin (Hb), Red Blood cell (RBC) count, Hematocrit, White blood cell (WBC) count and Platelet count at the three levels. Also shown are the peer group mean values for each parameter obtained from the respective monthly inter laboratory quality assurance program, the observed Bias % and the CLIA TEA (Total allowable error goals) for each of these CBC parameters.

Table 3: Internal Quality control data analysis for Lot-2.

PARAMETER	CONTROL	PEER GROUP MEAN	LAB MEAN	SD	CV	TEA(CLIA 2024)	BIAS
Hb (g/dL)	LEVEL 1	4.3	4.32	0.04	0.86	4.00	0.47
	LEVEL 2	11.4	11.35	0.06	0.49	4.00	-0.44
	LEVEL 3	15.9	15.78	0.10	0.61	4.00	-0.75
RBC (106/uL)	LEVEL 1	1.6	1.61	0.02	0.93	4.00	0.63
	LEVEL 2	3.65	3.68	0.04	1.09	4.00	0.82
	LEVEL 3	5.24	5.27	0.06	1.14	4.00	0.57
HEMATOCRIT (%)	LEVEL 1	13.2	13.26	0.11	0.84	4.00	0.45
	LEVEL 2	33.2	33.38	0.31	0.93	4.00	0.54
	LEVEL 3	47.4	47.41	0.51	1.08	4.00	0.02
WBC (103/uL)	LEVEL 1	3.2	3.2	0.05	1.56	10.00	0.00
	LEVEL 2	18.3	18.5	0.30	1.62	10.00	1.09
	LEVEL 3	8.6	8.5	0.15	1.76	10.00	-1.16
PLATELET (103/uL	LEVEL 1	68	67	1.00	1.49	25.00	-1.47
	LEVEL 2	418	413	6.50	1.57	25.00	-1.20
	LEVEL 3	207	204	4.00	1.96	25.00	-1.45

Table 3 presents the internal quality control data for Lot 2 of control material, also collected over a one-month period. The data, which includes measurements for hemoglobin (Hb), red blood cell (RBC) count, hematocrit, white blood cell (WBC) count, and platelet count at three control levels, were analyzed to compute the mean, standard deviation (SD), and coefficient of variation (CV). Additionally, peer group mean values from the monthly inter-laboratory quality assurance program, the observed Bias percentage, and the CLIA Total Allowable Error (TEA) goals for each of the CBC parameters are presented.

Table 4: Internal Quality control data analysis for Lot-3.

PARAMETER	CONTROL	PEER GROUP MEAN	LAB MEAN	SD	CV	TEA (CLIA 2024)	BIAS
Hb (g/dL)	LEVEL 1	4.4	4.3	0.05	1.16	4.00	-2.27
	LEVEL 2	11.4	11.3	0.05	0.44	4.00	-0.88
	LEVEL 3	15.7	15.8	0.10	0.63	4.00	0.64
RBC (106/uL)	LEVEL 1	1.59	1.59	0.01	0.63	4.00	0.00
	LEVEL 2	3.68	3.68	0.04	0.95	4.00	0.00
	LEVEL 3	5.26	5.26	0.04	0.67	4.00	0.00
HEMATOCRIT (%)	LEVEL 1	13.1	13	0.11	0.85	4.00	-0.76
	LEVEL 2	33.8	33.8	0.31	0.91	4.00	0.00
	LEVEL 3	47.5	47.4	0.51	1.08	4.00	-0.21
WBC (103/uL)	LEVEL 1	3.4	3.3	0.05	1.52	10.00	-2.94
	LEVEL 2	18	18	0.20	1.11	10.00	0.00
	LEVEL 3	8.7	8.6	0.10	1.16	10.00	-1.15
PLATELET (103/uL	LEVEL 1	69	69	1.00	1.45	25.00	0.00
	LEVEL 2	404	397	6.00	1.51	25.00	-1.73
	LEVEL 3	217	214	3.00	1.40	25.00	-1.38

Table 4 displays the monthly internal quality control data for Lot 3 of control material. Quality control testing was performed daily using three different levels of control material. The results for hemoglobin (Hb), RBC count, hematocrit, WBC count, and platelet count were analyzed to determine the mean, standard deviation (SD), and coefficient of variation (CV) at each level. Also included are the peer group mean values from the monthly inter-laboratory quality assurance program, the observed Bias percentage for each parameter, and the CLIA Total Allowable Error (TEA) goals for the respective CBC parameters.

Table 5: Internal Quality control data analysis for Lot-4.

PARAMETER	CONTROL	PEER GROUP MEAN	LAB MEAN	SD	CV	TEA(CLIA 2024)	BIAS
Hb (g/dL)	LEVEL 1	4.4	4.4	0.05	1.14	4.00	0.00
	LEVEL 2	11.2	11.1	0.05	0.45	4.00	-0.89
	LEVEL 3	15.7	15.7	0.10	0.64	4.00	0.00
RBC (106/uL)	LEVEL 1	1.6	1.61	0.01	0.62	4.00	0.63
	LEVEL 2	3.64	3.63	0.04	1.10	4.00	-0.27
	LEVEL 3	5.25	5.26	0.04	0.76	4.00	0.19
HEMATOCRIT (%)	LEVEL 1	13	13.1	0.16	1.19	4.00	0.77
	LEVEL 2	32.9	33	0.45	1.35	4.00	0.30
	LEVEL 3	47	47.4	0.33	0.69	4.00	0.85
WBC (103/uL)	LEVEL 1	3.2	3.1	0.05	1.61	10.00	-3.13
	LEVEL 2	18.7	18.7	0.25	1.34	10.00	0.00
	LEVEL 3	9	8.8	0.10	1.14	10.00	-2.22
PLATELET (103/uL	LEVEL 1	70	69	1.00	1.45	25.00	-1.43
	LEVEL 2	409	400	7.50	1.88	25.00	-2.20
	LEVEL 3	212	208	3.50	1.68	25.00	-1.89

In Table 5, the internal quality control data for Lot 4 of control material is presented, covering a period of one month. The observed laboratory means, standard deviations (SD), and coefficients of variation (CV) for parameters -hemoglobin (Hb), RBC count, hematocrit, WBC count, and platelet count values are presented along with the peer group mean values from the monthly inter-laboratory quality assurance program, the observed Bias percentage for each parameter, and the CLIA Total Allowable Error (TEA) goals for each parameter.

Table 6 presents the observed bias and CV for each lot (Lot 1, Lot 2, Lot 3, Lot 4) along with the average bias and CV observed across the four lots for each parameter under study.

Table 7 displays the average bias, average CV, total allowable error and the sigma value at each control level along with the overall average Sigma value for hemoglobin (Hb), red blood cell (RBC) count, hematocrit, white blood cell (WBC) count, and platelet count based on the entire QC data collected.

Table 6: Calculation of Average Bias and Imprecision observed across four Lots of control data for different parameters.

PARAMETER	CONTROL	BIAS (LOT1)	BIAS (LOT2)	BIAS (LOT3)	BIAS (LOT4)	AVG BIAS	CV (LOT1)	CV (LOT2)	CV (LOT3)	CV(LOT4)	AVG CV%
Hb (g/dL)	LEVEL 1	0.00	0.47	2.27	0.00	0.68	0.24	0.86	1.16	1.14	0.85
	LEVEL 2	0.00	0.44	0.88	0.89	0.55	0.40	0.49	0.44	1.14	0.45
	LEVEL 3	0.00	0.75	0.64	0.00	0.35	0.38	0.61	0.63	1.14	0.54
RBC (106/uL)	LEVEL 1	0.64	0.63	0.00	0.63	0.47	0.63	0.93	0.63	1.14	0.73
	LEVEL 2	0.55	0.82	0.00	0.27	0.41	1.23	1.09	0.95	1.14	1.09
	LEVEL 3	0.38	0.57	0.00	0.19	0.29	1.13	1.14	0.67	1.14	0.98
HEMATOCRIT (%	LEVEL 1	0.78	0.45	0.76	0.77	0.69	1.12	0.84	0.85	1.14	0.94
	LEVEL 2	0.60	0.54	0.00	0.30	0.36	1.04	0.93	0.91	1.14	0.96
	LEVEL 3	0.21	0.02	0.21	0.85	0.32	1.00	1.08	1.08	1.14	1.05
WBC (103/uL)	LEVEL 1	0.00	0.00	2.94	3.13	1.52	1.56	1.56	1.52	1.14	1.55
	LEVEL 2	3.19	1.09	0.00	0.00	1.07	1.29	1.62	1.11	1.14	1.34
	LEVEL 3	0.00	1.16	1.15	2.22	1.13	1.69	1.76	1.16	1.14	1.54
PLATELET (103/u	LEVEL 1	1.41	1.47	0.00	1.43	1.08	1.45	1.49	1.45	1.14	1.46
	LEVEL 2	0.99	1.20	1.73	2.20	1.53	2.05	1.57	1.51	1.14	1.71
	LEVEL 3	1.88	1.45	1.38	1.89	1.65	1.55	1.96	1.40	1.14	1.64

Table 7: Calculation of Sigma value (at different concentrations/levels and average value for each parameter).

PARAMETER	CONTROL	AVG BIAS	AVG CV%	TEa	SIGMA	AVG SIGMA
Hb (g/dL)	LEVEL 1	0.68	0.85	4	3.91	
	LEVEL 2	0.55	0.45	4	7.73	**6.12**
	LEVEL 3	0.35	0.54	4	6.72	
RBC (106/uL)	LEVEL 1	0.47	0.73	4	4.83	
	LEVEL 2	0.41	1.09	4	3.29	**3.97**
	LEVEL 3	0.29	0.98	4	3.80	
HEMATOCRIT (%	LEVEL 1	0.69	0.94	4	3.54	
	LEVEL 2	0.36	0.96	4	3.78	**3.60**
	LEVEL 3	0.32	1.05	4	3.49	
WBC (103/uL)	LEVEL 1	1.52	1.55	10	5.48	
	LEVEL 2	1.07	1.34	10	6.66	**5.97**
	LEVEL 3	1.13	1.54	10	5.77	
PLATELET (103/u	LEVEL 1	1.08	1.46	25	16.36	
	LEVEL 2	1.53	1.71	25	13.70	**14.78**
	LEVEL 3	1.65	1.64	25	14.27	

Observations:

- Hb (Hemoglobin, g/dL)
  - Sigma Values:
    - LEVEL 1: 3.91
    - LEVEL 2: 7.73
    - LEVEL 3: 6.72
  - Average Sigma: 6.12
  - The average sigma value for Hemoglobin is 6.12, which places it in the World Class performance category. This implies that Hemoglobin measurement demonstrates consistent results with a low defect rate of 3.4 DPMO, signifying near-perfect perfromance.
- RBC (Red Blood Cells, 10^6/uL)
  - Sigma values:
    - LEVEL 1: 4.83
    - LEVEL 2: 3.29
    - LEVEL 3: 3.80
  - Average Sigma: 3.97.
  - Interpretation: The average sigma for RBC is 3.97, indicating marginal but nearly reaching good performance category reflecting potential for performance improvement.
- Hematocrit (%)
  - Sigma values
    - LEVEL 1: 3.54
    - LEVEL 2: 3.78
    - LEVEL 3: 3.49
  - Average Sigma: 3.60.
  - Interpretation: The average sigma value of 3.60 for Hematocrit suggests above marginal but below good level of performance needing further optimization of method.

- WBC (White Blood Cells, 10^3/uL)
  - Sigma Values:
    - LEVEL 1: 5.48
    - LEVEL 2: 6.66
    - LEVEL 3: 5.77
  - Average Sigma: 5.97
  - Interpretation: With an average sigma of 5.97, WBC performance is categorized as Excellent, corresponding to a defect rate of 233 DPMO suggesting very low variability and a high level of consistency in measurements.
  - Platelet (10^3/uL):
    - Sigma Values:
      - LEVEL 1: 16.36
      - LEVEL 2: 13.70
      - LEVEL 3: 14.27
    - Average Sigma: 14.78
    - Interpretation: The extremely high sigma value of 14.78 places Platelet performance above the World Class performance category, with a defect rate of less than 3.4 DPMO. This indicates virtually flawless performance with minimal defects across all levels.

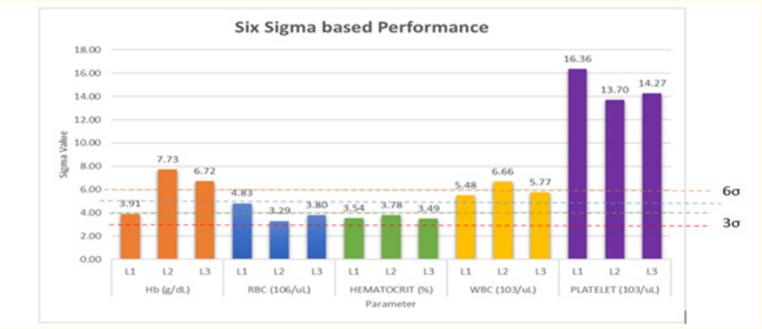

Figure 1: Sigma values observed for the key parameters at three different concentration levels L1(Level1), L2 (Level 2) and L3(Level 3).

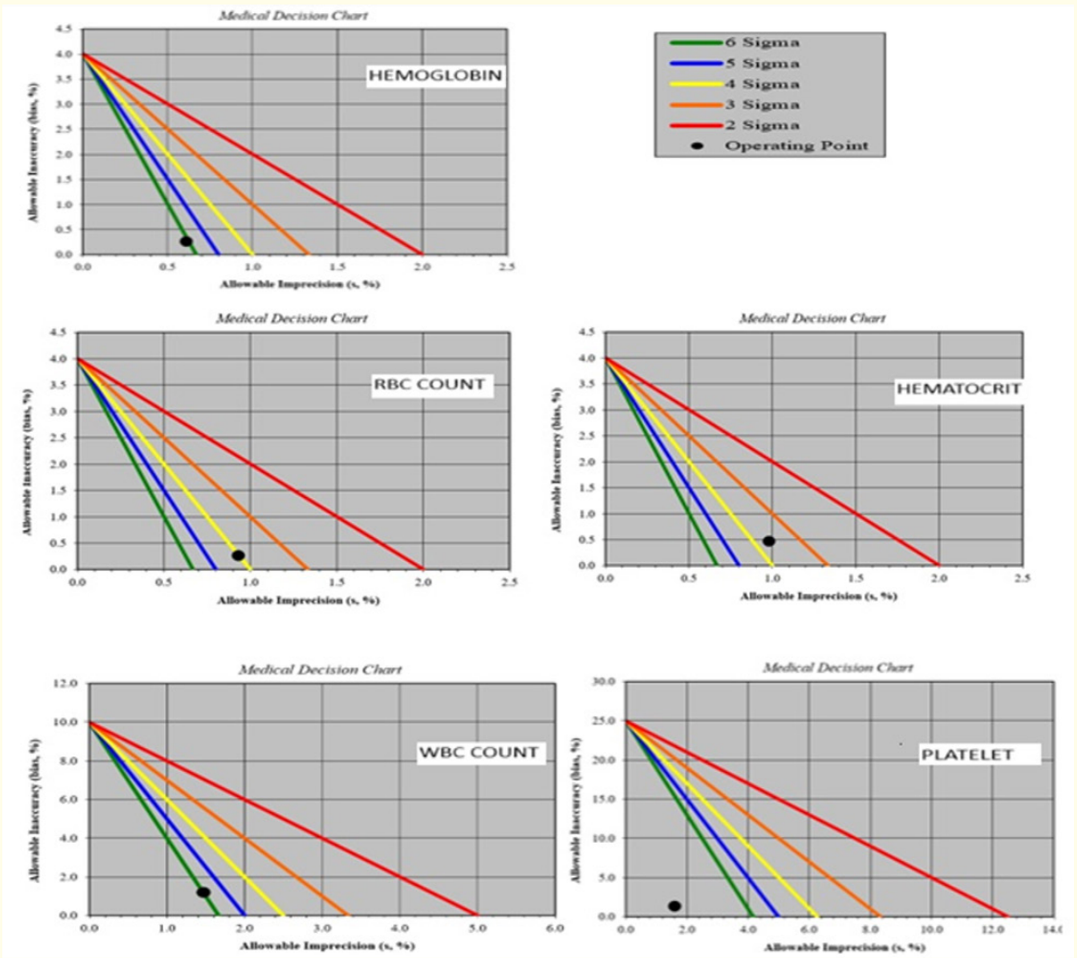

Figure 2: Medical Decision charts showing operating points for each parameter with respect to different sigma zones (obtained by plotting observed imprecision (CV%) on x-axis and inaccuracy (bias %) on y-axis, both expressed as percentages of Total allowable error goals).

Observations

Analysis and interpretation of parameter wise performance for the instrument:

- Hemoglobin
  - **Analysis:** The Hb parameter's overall sigma value of 6.12 is indicative of high-quality performance and correlates with World Class level on sigma scale (sigma ≥ 6). The relatively lower sigma noticed only for Level 1 suggests some room for quality control optimization.
  - **Recommendation:** Continuous monitoring and fine-tuning of testing procedures could help reduce variability and maintain consistency in results across all levels.
- RBC (Red Blood Cells) count
  - **Analysis:** With an average sigma of 3.97, RBC performance is above marginal and approaching nearly good levels. The slight variability between levels, particularly the lower sigma at Level 2, suggests that there may be issues related to equipment calibration or reagent quality. This could contribute to the observed lower consistency in measurements.
  - **Recommendation:** It is important to investigate the underlying causes of variability at Level 2 and ensure that all conditions (e.g., calibration, reagent quality, and equipment maintenance) are standardized to improve consistency.
- Hematocrit
  - **Analysis:** Hematocrit values show relatively stable but marginal performance, with an overall sigma of 3.60, indicating acceptable quality with an opportunity for improvement in quality .
  - **Recommendation**: Strengthening quality control protocols and improving the standardization of testing conditions will help reduce these inconsistencies. Implementing routine calibration and precision testing of equipment could contribute to better performance.
- WBC (White Blood Cells)
  - **Analysis:** WBC shows a strong performance with an average sigma of 5.97, categorizing it as Excellent. This indicates low variability and robust measurement consistency across all levels. However, while the performance is strong, there is still a slight gap to reach the World Class level (sigma ≥ 6), suggesting that slight improvements in testing protocols could further reduce defect rates.
  - **Recommendation:** While WBC performance is already excellent, further refinement of the processes, such as more stringent control over testing conditions, could further minimize defects and boost sigma values.
- Platelet:
  - **Analysis:** Platelet measurements show exceptional performance with a sigma value of 14.78, placing it firmly in the World Class category. This value indicates minimal defects, suggesting that the testing process for platelets is extremely well-controlled and consistently accurate.
  - **Recommendation:** Given its near-perfect performance, it may not require significant intervention. However, continuing to monitor and maintain basic quality control practices is essential to sustain this level of excellence.

Discussion

Sigma metric analysis is an efficient tool to assess the analytical methodologies and QC designs to enhance the performance of the laboratory. It can also be used as a guide to planning the frequency of QC accordingly.

Westgard Sigma Rules can be used as a guide to design QC rules based on observed sigma values [10].

Sigma rules to be applied for the three level of controls (routinely practices for hematology analyzers) are,

- 6-sigma quality requires only a 1-3s rule and 1 measurement on each of 3 levels of controls.
- 5-sigma quality requires adding the 2 of 3-2s and R-4s rules for use with 1 measurement on each of 3 levels of controls.
- 4-sigma quality requires adding a 3-1s rule for use with 1 measurement on each of 3 controls.
- < 4-sigma quality requires a multi-rule procedure that includes the 6x rule and a doubling of control measurements to a total of 6, which suggests that the 3 levels of controls be analyzed in duplicate in one run (N = 6, R = 1) or the day's work be divided into 2 runs with 3 control measurements per run (N = 3, R = 2). If a 9x rule were substituted for the 6x rule, then a day's work could be divided into 3 runs with 3 controls per run (N = 3, R = 3)

In the current study, six sigma methodologies allowed for performance evaluation of key hematology parameters. The tailored parameter wise QC rules recommended based of Westgard Sigma rules are given in the table below.

Table 8 summarizes the Sigma metric-based recommendations for QC rejection rules and control frequency, in order to optimize quality control for the DXH900 analyzer under study.

Table 8: Recommended QC design based on observed sigma values.

PARAMETER	SIGMA VALUE	QC DESIGN RECOMMENDATION
HEMOGLOBIN	6.12	13s rule and 1 measurement on each of 3 levels of controls
RED BLOOD CELL COUNT	3.97	Requires a multi-rule procedure that includes the 6x rule and a doubling of control measurements to a total of 6, which suggests that the 3 levels of controls be analyzed in duplicate in one run (N=6, R=1) or the day's work be divided into 2 runs with 3 control measurements per run (N=3, R=2). If a 9x rule were substituted for the 6x rule, then a day's work could be divided into 3 runs with 3 controls per run (N=3, R=3)
HEMATOCRIT	3.60	Requires a multi-rule procedure that includes the 6x rule and a doubling of control measurements to a total of 6, which suggests that the 3 levels of controls be analyzed in duplicate in one run (N=6, R=1) or the day's work be divided into 2 runs with 3 control measurements per run (N=3, R=2). If a 9x rule were substituted for the 6x rule, then a day's work could be divided into 3 runs with 3 controls per run (N=3, R=3)
WHITE BLOOD CELL COUNT	5.97	requires adding the 2 of 32s and R4s rules for use with 1 measurement on each of 3 levels of controls.
PLATELET COUNT	14.78	13s rule and 1 measurement on each of 3 levels of controls

The current analysis revealed that the DXH 900 hematology analyzer showed acceptable performance for all key parameters analyzed, with Platelets showing exceptional quality and consistency. While the overall performance is good, there is potential for further optimization, especially for parameters like RBC and Hematocrit, which show moderate performance. By fine-tuning testing protocols, ensuring consistency in equipment calibration, and focusing on areas of variability, the overall quality control could be significantly enhanced, particularly for those parameters that fall below the World Class benchmark.

Application of sigma metrics, as done in the current study, confirms that a poorly performing method requires additional QC rejection rules and control runs than what the laboratory traditionally practices. Given the tedious QC recommendations for such methods, the laboratory may not be able to practically monitor the performance adequately and hence opt for either the method to be improved, redesigned, or replaced. It also confirms that a world class method requires far fewer rules and control runs than what the laboratory may be currently implementing. Laboratories with high Sigma metrics performance have been able to reduce their use of controls, reduce the number of outliers, trouble-shooting requirements, recalibrations or even the consumption of reagent and materials. In addition to proven cost reductions through the implementation of Six Sigma techniques, there are important reductions in the labor effort of staff: fewer hours are spent chasing down false rejections, fewer hours are spent in unnecessary trouble-shooting and communicating with technical support [11].

Potential Sources of error in sigma metric calculations

Use of sigma metrics for performance evaluation of an analytical method can be influenced by some factors that might introduce errors. Some of these factors are:

- **Instrument related factors:** Issues like calibration drift or instrument malfunction can affect measurement accuracy and precision.
- **Reagent and specimen Handling:** Inconsistent quality, improper preparation, contamination, or deterioration of reagent/control material or specimens can result in unreliable results.
- **Operator Errors:** Variability in operator technique, lack of training, or failure to follow procedures can result in inconsistent data.
- **Lack of Standardization:** Differences in reference source used for allowable error and target mean will impact the calculations as Sigma values will depend on which source is used, leading to inconsistent or non-comparable performance evaluations across laboratories.
- **Environmental Factors:** Fluctuations in temperature and humidity can disrupt analyzer performance.
- **Statistical Considerations:** Small sample sizes or non-normal data distributions can distort sigma values, leading to inaccurate assessments.

To obtain reliable sigma values, it's crucial to control above variables through regular maintenance, proper training, and adherence to standardized protocols.

Limitations of applying Six Sigma methodology in hematology laboratories

While Six Sigma methodology is widely recognized for improving quality and efficiency across various industries including clinical chemistry laboratories, its application in a hematology laboratory does have some limitations [12,13].

- **Setting Appropriate Total Allowable Error:** Determining the correct allowable error limits for hematology parameters can be challenging. Multiple sources of allowable error are available for hematology parameters (including CLIA, as was used in current study) and establishing an accurate TEA for each parameter that reflects clinical relevance, rather than just statistical limits, can be difficult.
- **Test Complexity:** Hematology tests, including CBC, are highly complex due to the number of parameters involved and the intricacy of the methods used to analyze blood cells. Unlike chemical assays, which may measure a single analyte, CBC tests require multiple readings from different instrument components and use of multiple measuring techniques. The complexity of the testing method complicates the use of Six Sigma, which works best in environments with simpler, more consistent processes.
- **Inherent Biological Variation:** CBC parameters, such as hemoglobin (Hb), red blood cell (RBC) count, and platelet count, exhibit significant biological variability among individuals due to factors like age, gender, ethnicity, and underlying health conditions. This natural variation can complicate the application of Six Sigma, which assumes that processes are stable and predictable.

Despite the limitations, Six Sigma holds promise for hematology labs by providing a structured framework to identify, quantify, and reduce variability in testing processes. By focusing on continuous improvement and data-driven decision-making, it can enhance the overall quality assurance and efficiency in these laboratories, leading to more reliable patient results.

Conclusion

Sigma metrics in the clinical laboratory is a vital methodology to identify and correct any deviation of lab results from the prescribed standards. It can help us ascertain poor assay performance along with the assessment of the efficiency of the existing laboratory process Furthermore, sigma metrics can help in devising appropriate strategies for the judicious utilization of quality control process in a clinical laboratory.

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