ORIGINAL RESEARCH ARTICLE

Effect of Matrix and Source of Quality Specification Data on the Sigma Metrics of Common Chemistry Analytes in Clinical Laboratory

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Abstract

Introduction and aim: Internal and external quality control (IQC and EQC) is used to monitor and evaluate the analytical process. Six Sigma provides an objective assessment of performance. The Sigma metrics (σ) are calculated using the coefficient of variation (CV), bias, and total allowable error (TEa). One of the pitfalls of the Sigma metrics calculation is that it depends upon the source of the variables used in the formula and the measurand matrix. Hence, this study was conducted to calculate the Sigma metrics of urea, creatinine, Na, and K in serum and urine using Tea from biological variation (BV) (urine and serum) and Clinical Laboratory Improvement Amendments (CLIA) (serum) and subsequently comparing the Sigma metrics of all four analytes using TEa from BV between serum and urine control and using TEa from BV in the same matrix (serum).

Materials and methods: A cross-sectional study was conducted in the Department of Clinical Biochemistry, St. John's Medical College for 1 year (January–December 2018). Bio-Rad IQC (serum and urine) data have been used to calculate σ of urea, creatinine, Na, and K. The cumulative CV and bias were obtained using unity real-time software from Bio-Rad Laboratories. Total allowable error values were obtained from BV and CLIA guidelines.

Results: Urea, creatinine, Na, and K showed higher σ in the urine control than in serum controls indicating the better performance of these parameters in the urine matrix than in serum. In the same matrix (serum control), creatinine, Na, and K had higher σ using TEa from CLIA than TEa from BV. Na showed the highest difference in σ value between the two sources (p-value < 0.001). However, serum urea showed higher σ using TEa from BV compared to TEa from CLIA.

Conclusion: Our study showed that σ varies with the matrix; henceforth, one should be careful in extrapolating the performance characteristics in terms of Sigma of an analyte from one matrix to another. In the same matrix, σ also varies depending on the source of TEa used in the calculation. It is, thus, essential to mention the source of the variables used to calculate σ for a better interpretation.

Keywords: Biological variation, Clinical laboratory improvement amendments, Internal quality control, Matrix effect, The Sigma metric.

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Introduction

Today's health-care system relies heavily on laboratory investigations,[1] and hence accurate reports are the need of the hour to assist in the proper diagnosis and management of patients. Quality management, thus, is an absolute requirement in the analysis and release of patient reports. Six Sigma is one such quality management tool used in clinical laboratories for both the selection of analytical methods and the evaluation of analytical performance.[2–4]

Quality of the service provided is critical for user satisfaction.[5,6] The total quality management is broadly categorized into six processes: quality laboratory processes, quality control, quality assessment, quality improvement, quality planning, and quality goals.[7] The process is depicted in Figure 1.

Quality control is a statistical analysis of IQC and External Quality Assessment (EQA), which monitors and evaluates the analytical performance.[9]

Internal quality control both assayed and unassayed materials can be used as IQC. The performance of a parameter using IQC is evaluated on the levey–Jennings control charts using Westgard rules. This can be compared with the peer laboratories using the same method and instrument with the help of certain software available.[9]

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External Quality Assessment program: A program in which samples with unknown concentration of the analyte are periodically sent to the members of a group of laboratories participating for analysis. The results of each laboratory is compared against the method, mode, or the peer mean (depending on the number of laboratories participating for analysis) and reported to laboratories participating and others.[10]

Internal quality control and EQA collectively help in identifying the analytical errors. Data from these quality control programs can

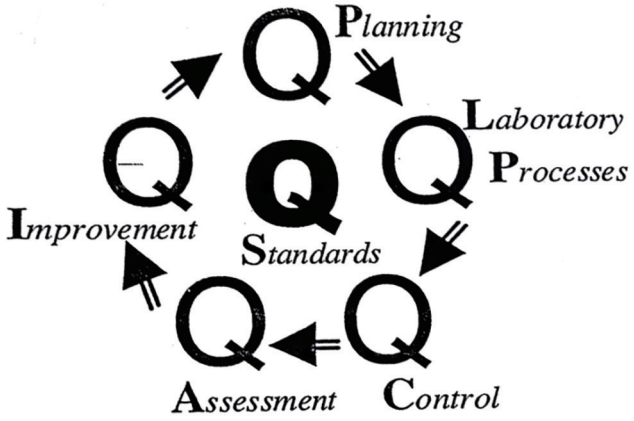

Fig. 1: Total quality management cycle[8]

be used to calculate the Sigma metrics. Six Sigma refers to a process quality measurement and improvement program by two engineers Bill smith and Mikel J Harry while working at Motorola in 1986. Jack Welch made it central to his business strategy at General Electric in 1999.[11] Sigma (σ) is the letter from Greek alphabets used by the statisticians, which measures the variability of a process.[12] Six Sigma was developed in order to reduce the cost, eliminate defects, and decrease variability in processing.[2] Quality is assessed on the Sigma (σ) scale with a criterion of 3σ as the minimum allowable Sigma for routine performance. Method having σ <3 is considered to be unreliable and should not be used for routine test purposes.[3] A Sigma of 6 is the goal for world-class quality.

The six Sigma methodology can be applied across the total testing process and can help in identifying the areas that need improvement to reach that goal. Improvements in quality lead to improvement in productivity and reductions in cost.[13]

The basic scientific model of this methodology is Define, Measure, Analyze, Improve, and Control (DMAIC).[2,14]

- Define the problem area in objective terms
- Measure the performance of products and processes
- Analyze the problems to identify root causes
- Improve the results by redesigning processes and reducing variation
- Control the processes to ensure that the improvements are permanent

Six Sigma strives to reduce variation, augment laboratory performance, reduce defects, reduce cost of poor quality, improve quality, improve equipment utilization, improve productivity, and improve supply utilization.[15] Even though Six Sigma concept has been introduced for many years now, many laboratories fail to implement it as a methodology to improve their quality control practices.

Aim

The aim of this study was to evaluate the effect of matrix and source of quality specifications data on the Sigma metrics of common chemistry analytes in clinical laboratory.

Objectives

The objective of this was:

- To calculate the Sigma metrics of urea, creatinine, sodium, and potassium in serum using TEa from BV.
- To calculate the Sigma metrics of urea, creatinine, sodium, and potassium in urine using TEa from BV.
- To compare the Sigma metrics of urea, creatinine, sodium, and potassium using TEa from BV between serum and urine control.
- To compare the Sigma metrics of urea, creatinine, sodium, and potassium using TEa from BV and CLIA in the same matrix (serum).

The evaluation of the performance of analytical methods on the Sigma scale helps to use it for root cause analysis to minimize the errors and improve process quality. The performances of an analyte are conventionally expressed in statistical terms such as CV and Bias.[4] The Sigma metrics can be calculated using CV, bias, and TEa.[2,3,6] The CV of an analyte can be obtained from IQC while bias can be obtained from EQC data such as EQA. Total allowable error for an analyte is obtained from published literature.

However, TEa specified for an analyte can vary based on the source of data used such as BV data or CLIA guidelines.[5] Thus, one of the pitfalls of calculating the Sigma metrics is that it depends on the source of variables used in the formula. This can either overestimate or underestimate the Sigma metrics and thus the performance. Hence, this study is undertaken to calculate and compare the differences in the Sigma metrics of common parameters in serum using TEa data from different sources.

Materials and Methods

Materials

The source of data: Data from consecutive runs of assay chemistry and urine IQC samples for urea, creatinine, sodium, and potassium were used for the study. The analysis was carried out in the clinical laboratory at St. John's Medical College and Hospital.

Data were collected over a duration of one year from January 2018 to December 2018.

The study was approved by the Institutional Ethics Committee.

Inclusion Criteria

The IQC data of creatinine, urea, sodium, and potassium from January 2018 to December 2018 were included in the study.

Exclusion Criteria

Any data points that have been rejected by the laboratory due to faulty runs are as follows:

- Errors in preparation (like pipetting errors)
- Errors during analysis (like equipment breakdown)

Methods

Type of Study

Cross-sectional study: Consecutive sampling of IQC data was used for the study.

Methodology

Internal quality controls were analyzed as a part of routine practice in the laboratory to monitor the performance of analytes. Creatinine, urea, sodium, and potassium in assay chemistry control (ACC) and urine control were analyzed on fully automated Siemens Dimension system as mentioned in Table 1. The control data were entered into the unity real time software (URT) software by Bio-Rad Laboratories, Inc. The laboratory mean, peer mean, and CV were extracted from the software, and the bias percentage was calculated. Total allowable error was obtained from two different sources, i.e., BV and CLIA.[23] These data were then used to calculate the Sigma metrics for the analytes.

Table 1: List of analytes, instruments, and method of analysis

Analyte	*Instrument*	*Method*
Urea	Siemens dimension EXL	Urease
Creatinine	Siemens dimension EXL	Alkaline Picrate kinetic
Sodium	Siemens dimension EXL	ISE Indirect
Potassium	Siemens dimension EXL	ISE Indirect

Statistical Analysis

- Mean, SD, CV, and bias were calculated for each analyte.
- Total allowable error values of various parameters were taken from the BV database by Dr Carmen Ricos and colleagues available at www.westgard.com[3,6,7] and CLIA'88 (February 4, 2019).[16]
- The Sigma metrics were then calculated for all analytes using the above variables as mentioned below under the section "Method of Calculation of the Sigma Metrics."
- Student's *t*-test was used to compare the Sigma metrics between two IQC matrices.
- *p*-value <0.001 was considered statistically significant.

Method of Calculation of the Sigma Metrics

- Calculation of the mean:

The sum of all values of control level divided by the number of value

$$\bar{x} = \frac{\Sigma X_i}{n}$$

Where:

Σ = sum, *Xi* = each value in data set, *n* = total number of values

- Calculation of standard deviation:

$$s = \sqrt{\frac{\Sigma (x_n - \bar{x})^2}{n-1}}$$

Where:

S = Standard deviation
$\bar{x}$ = Mean (average) of the values
$\Sigma(x_n - \bar{x})^2$ = The sum of the squares of difference between individual QC Values and the mean
n = The number of values in the data set

- Calculation of CV: It is the ratio of standard deviation to mean multiplied by 100.

$$CV = (SD/MEAN) \times 100$$

- Peer mean: The value is obtained from URT software.
- Calculation of bias: It is calculated by the following formula:

$$\text{Bias}\% = \frac{\text{Laboratory mean} - \text{Peer mean}}{\text{Peer mean}} \times 100$$

- TEa:

It is obtained from the BV database and CLIA'88 (updated on February 2019) guidelines by Dr Carmen Ricos and colleagues available at www.westgard.com.[23]

- Calculation of Sigma:

It is calculated by using the following formula:

$$\text{Sigma } (\sigma) = \frac{\text{TEa} - \text{Bias}}{\text{CV}}$$

Statistical Software

The data were entered in Microsoft Excel Version 2016 and analyzed on program for statistical analysis of sampled data (PSPP) software Version 1.2.0-g0fb4db.

Sample Size of Estimation

One-year data were used to calculate the Sigma metrics for the analyte. The two variables required for the calculation are CV and bias. The bias was obtained from the calculation. The corresponding CV percentage was obtained from IQC data. This corresponded to a sample size of 1000 (data points) per year.

Consecutive sampling of IQC data was used for the study.

Results

Urea, creatinine, sodium, and potassium were analyzed in two different matrices that are serum control (ACC from Bio-Rad lot no. 26430) and urine control (urine control from Bio-Rad lot no. 68500).

Table 2 illustrates the QC levels and the cumulative laboratory mean, SD, CV, peer mean, and bias for the analytes for the period of January–December 2018.

TEa from BV data and CLIA are depicted in Tables 3 and 4.

Table 5 shows the Sigma metrics of analytes in serum and urine control using TEa from BV (desirable).

Table 6 and Figure 2 illustrate the comparison of the Sigma metrics of analytes in level 1 of serum and urine controls using TEa from BV. The results show a statistically significant difference in the Sigma metrics of all parameters between the two matrices. The parameters show higher the Sigma metrics value in the urine control than in the serum control indicating better performance of these parameters in the urine matrix than in the serum matrix. Sodium shows the maximum difference followed by potassium, in the Sigma metrics value compared to others as shown in tables and graphs.

Table 7 and Figure 3 illustrate the comparison of the Sigma metrics of analytes in level 2 of serum and urine controls using TEa from BV. The results show a statistically significant difference in the Sigma metrics of all parameters between the two matrices. The parameters show higher the Sigma metrics value in the urine control than in serum controls indicating better performance of these parameters in the urine matrix than the serum matrix. Sodium shows the maximum difference followed by potassium and urea in the Sigma metrics value compared to others as shown in tables and graphs. Table 8 and Figure 4 illustrate the comparison of Sigma metrics of analytes using TEa from BV and CLIA in ACC (ACC, level 1). The results show a statistically significant difference in the Sigma metrics of all parameters between the two sources of TEa (*p*-value <0.001). The Sigma metrics of creatinine, sodium, and potassium show better performance using TEa from CLIA than TEa from BV in ACC, level 1 with sodium showing the maximum difference. However, the Sigma metrics of urea using TEa from BV show better performance than TEa from CLIA. This might be due to high TEa in BV than CLIA.

Table 9 and Figure 5 illustrate the comparison of the Sigma metrics of analytes using TEa from BV and CLIA in ACC, level 2. The Sigma metrics of creatinine, sodium, and potassium had

Table 2: Performance characteristics of parameters in assay chemistry control and urine chemistry control

Analyte (serum)	*Unit*	*Level*	*Lab mean*	*CV*	*Peer mean*	*Bias%*
Urea	mg/dL	1	32.41	4.03	32.37	0.12
		2	99.43	2.95	99.48	0.12
Creatinine	mg/dL	1	2.65	2.65	2.61	1.56
		2	6.18	1.83	6.17	–0.03
Sodium	meq/L	1	142.36	1.3	144.32	–1.35
		2	126.68	1.27	128.21	–0.81
Potassium	meq/L	1	3.87	1.21	3.91	–0.95
		2	6.19	0.99	6.21	–0.34
Analyte (urine)	*Unit*	*Level*	*Lab mean*	*CV*	*Peer mean*	*Bias%*
Urea	mg/dL	1	976.95	5.28	990.9	–1.41
		2	1702.5	1.83	1653	3.01
Creatinine	mg/dL	1	57.86	2.75	57.01	1.48
		2	134.43	2.3	134.61	–0.13
Sodium	meq/L	1	79.11	2.37	78.11	1.28
		2	166.27	2.09	164.39	1.13
Potassium	meq/L	1	30.85	1.83	30.62	0.79
		2	68.65	2.15	68.22	0.64

Table 3: BV data for the parameters in assay chemistry control and urine chemistry control[24]

	TEa from BV	
Parameter	*Serum*	*Urine*
Urea	15.55	22.1
Creatinine	8.87	42.1
Sodium	0.73	32
Potassium	5.61	28.4

Table 4: Modified CLIA testing criteria for the parameters in assay chemistry control[25]

Parameter	*Old criteria for AP*	*New criteria for AP (2019)*
Urea	TV ± 2 mg/dL or ± 9% (greater)	TV ± 2 mg/dL or ± 9% (greater)
Creatinine	TV ± 0.2 mg/dL or ± 15% (greater)	TV ± 0.2 mg/dL or ± 10% (greater)
Sodium	TV ± 4 mmol/L	TV ± 4 mmol/L
Potassium	TV ± 0.5 mmol/L	TV ± 0.3 mmol/L

Table 5: The Sigma metrics of serum and urine analytes using tea from BV

	Sigma metrics			
Serum level	*Urea*	*Creatinine*	*Sodium*	*Potassium*
1	3.86	2.75	1.70	5.41
2	5.60	4.85	1.46	6.66
Urine level	*Urea*	*Creatinine*	*Sodium*	*Potassium*
1	4.55	5.09	13.10	15.49
2	11.42	6.29	14.78	13.03

Table 6: Comparison of the Sigma metrics of analytes in level 1 of serum and urine controls using TEa from BV

	Level 1 quality control		
	Sigma metrics using TEa from BV		
Parameter	Serum	Urine	*p-value*
Urea	3.86	4.55	<0.001
Creatinine	2.75	5.09	<0.001
Sodium	1.7	13.1	<0.001
Potassium	5.41	15.49	<0.001

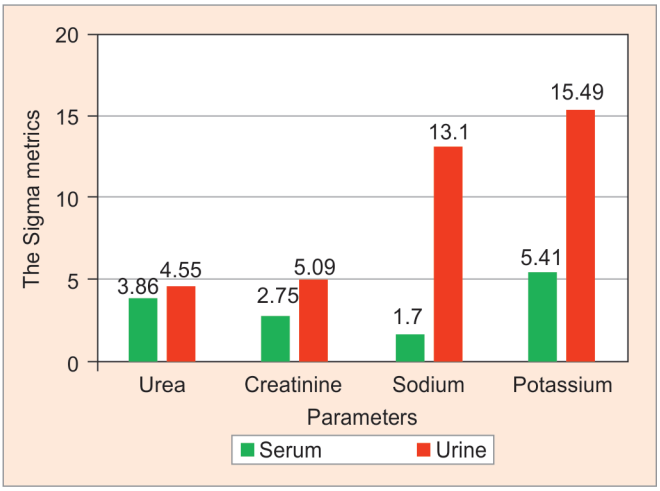

Fig. 2: Comparision of Sigma metrics of analytes in serum and urine (level 1)

better performance using TEa from CLIA than TEa from BV in ACC, level 2 with sodium showing the highest difference in the Sigma metrics value between the two sources using Student's *t*-test (*p*-value <0.001). However, the Sigma metrics of urea using TEa from BV shows better performance than TEa from CLIA. This might be due to high TEa in BV than CLIA.

Table 7: Comparison of the Sigma metrics of analytes in level 2 of serum and urine controls using TEa from BV

	Level 2 quality control		
	Sigma metrics using TEa from BV		
Parameter	*Serum*	*Urine*	*p-value*
Urea	5.26	11.42	<0.001
Creatinine	4.85	6.29	<0.001
Sodium	1.46	14.78	<0.001
Potassium	6.66	13.03	<0.001

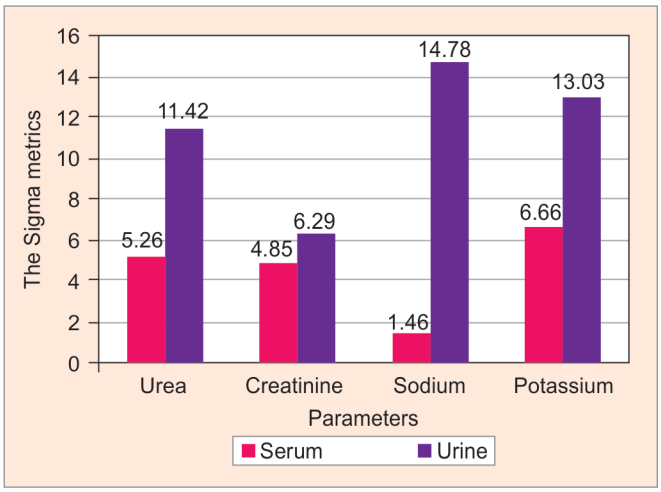

Fig. 3: Comparision of Sigma metrics of analytes in serum and urine (level 2)

Table 8: Comparison of the Sigma metrics of analytes using TEa from BV and CLIA in ACC level 1

		Level 1			
Analyte	*TEa from BV (Desirable)*	*TEa from CLIA*	*Sigma metrics from BV*	*Sigma metrics from CLIA*	*p-value*
Urea	15.55	9	3.86	2.22	<0.001
Creatinine	8.87	10	2.75	3.17	<0.001
Sodium	0.73	5	1.70	5.13	<0.001
Potassium	5.61	7	5.41	6.56	<0.001

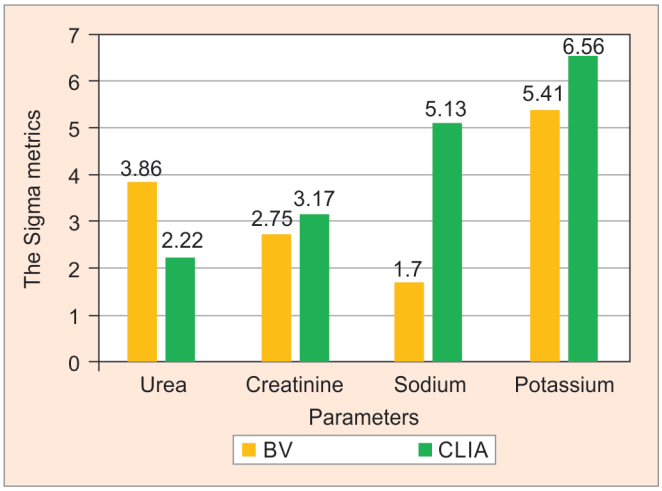

Fig. 4: Comparision of Sigma metrics of analytes in serum between BV and CLIA (level 1)

Table 9: Comparison of the Sigma metrics of analytes using TEa from Biological Variation and CLIA in ACC level 2

		Level 2			
Analyte	*TEa from BV (Desirable)*	*TEa from CLIA*	*Sigma metrics from BV*	*Sigma metrics from CLIA*	*p-value*
Urea	15.55	9	5.26	3.03	<0.001
Creatinine	8.87	10	4.85	5.47	<0.001
Sodium	0.73	5	1.46	5.11	<0.001
Potassium	5.61	7	6.66	7.69	<0.001

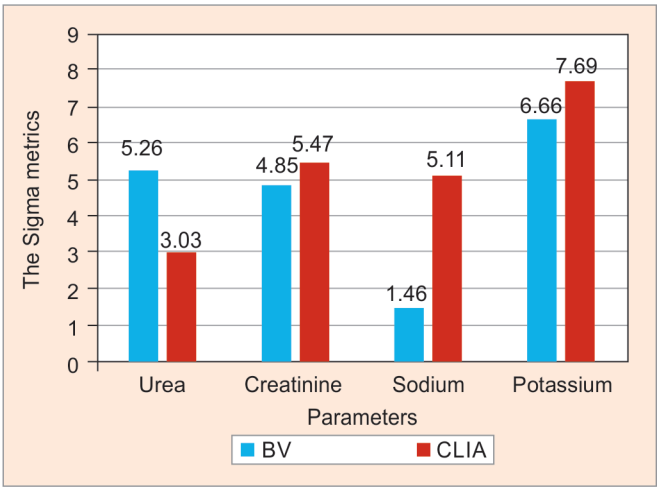

Fig. 5: Comparision of Sigma metrics of analytes in serum between BV and CLIA (level 2)

Discussion

Six Sigma is a management strategy that focuses on improving the quality of process outputs by the identification and removal of the causes of defects (errors) and decreasing the variations that occur in a process. It provides a quantitative definition of the desired specifications for the production processes and relates it to customer requirements.[16] Attainment of six Sigma is envisaged as the gold standard for defining world-class measure of quality in the clinical laboratory. When six Sigma performance is recognized as a fundamental goal for processes, quality can truly be measured and managed in a more quantitative way.[16,17] Using Sigma values, appropriate quality controls can be formulated based on inherent analytical quality of test. This ensures proper reporting of patients results as well minimizes false rejection of the results.[4]

The Sigma metrics of an analyte depends on the measurand and the source of variables used in the calculation. In the present study, the Sigma metrics of urea, creatinine, sodium, and potassium were calculated using different sources of variables TEa and in two matrices, i.e., serum and urine, using the respective IQC samples (assay chemistry and urine controls).

The variables used for calculation were CV, bias, and TEa. Coefficient of variation is used to describe the variation of the test. It also provides perception about general performance of the method. Lower CV denotes a better method performance whereas higher CV implies poorer performance.[7] The degree of precision is usually expressed on the basis of statistical measures of imprecision that is CV%.[3] In our study, the cumulative CV% of each parameter was obtained from IQC data.

Bias is more difficult to estimate realistically. It is ideal to calculate the bias by using reference method value as "true value." According to Friedecky et al., the peer group evaluation of EQA acceptance criteria is insufficient to determine the analytical quality. They recommend that EQA results can be compared to reference method targets, requiring metrological traceability and assessing absolute trueness rather than relative bias (i.e., peer group comparison).[18] In our study, the bias was calculated by comparing the cumulative laboratory mean of the controls for the said period with the corresponding cumulative peer group mean.

There are multiple sources for TEa targets and a laboratory should decide which TEa target is best suited for clinical decision. One must consider that a TEa goal is not available for every analyte and matrix. It is recognized that distinctly different Sigma metrics can be obtained depending on the source of TEa. There are many sources for Teas in the literature for chemistry.[19] The laboratory should be careful in the selection of TEa for calculating Sigma as the TEa varies with the source and has a major effect on the performance prediction of analytes if the Sigma metrics are used. The TEa for any analyte should be chosen based on the analytical performance required for optimum clinical decision-making. The most commonly used sources are the ones based on BV and CLIA guidelines. Total allowable error biological variability values are often proposed to be most stringent and perhaps too challenging for the analytical performance for some typical field assays.[4] When using biological variability as the basis of TEa, it must be noted that there are three possible TEa targets for analytes: minimal, desirable, and optimal. In this study, desirable BV specifications and CLIA'88 guidelines for TEa were used for the calculation of the Sigma metrics.

The recommended Sigma metric for parameters is minimum 3.[1,9] The root cause analysis should be done for tests or methods <3-Sigma and should be discussed with manufacturers as having room for improvement.

Our study showed statistically significant difference in the Sigma metrics of urea, creatinine, sodium, and potassium between serum and urine controls suggestive of a matrix effect. A matrix effect is defined as the influence of a property of the sample, independent of the presence of the analyte on the measurement and thereby on the value of the measurable quantity.[20]

The analysis of the Sigma metrics of sodium shows statistically significant difference between the two matrix as reflected in tables. It was also observed that the Sigma metrics obtained for sodium using TEa from CLIA were higher compared to TEa from BV. There was limited literature on the above stated results; however, Berth et al. reported similar findings in 2013. In this study, the analytical quality of clinical chemistry assays were assessed by using the Sigma metrics.[4]

The Sigma metrics of potassium show a statistical significant difference between the two matrix as indicated in tables. It was also observed that the Sigma metrics obtained for potassium using TEa from CLIA were higher compared to TEa from BV. An earlier study conducted by Huh et al. also observed similar results.[21]

The Sigma metrics of creatinine also show a statistical significant difference between the two matrix as indicated in tables. It was also observed that the Sigma metrics obtained for serum creatinine using TEa from CLIA were higher compared to TEa from BV. Berth et al. found similar results; their study showed the Sigma metrics for serum creatinine were higher in TEa from CLIA compared to TEa from BV. The Sigma metric values for serum control 1 while using CLIA targets were 3.17 and using BV were 2.75. Similarly, for serum control 2, the Sigma metric values using CLIA were 5.11 and using BV were 4.85.[4] lakshman et al. also showed the higher values of Sigma metrics for creatinine while using CLIA targets that are 6.4 for serum control 1 and 5.1 for serum control 2.[3] Similar findings were also reported by Kumar et al.[9]

The Sigma metrics of urea also show a statistical significant difference between the two matrix as indicated in tables. However, it has been observed that the Sigma metrics obtained for serum urea using TEa from BV were higher compared to CLIA. The study conducted by Xia et al. reported similar findings, which showed the values of Sigma metrics of serum urea were higher in TEa from BV compared to TEa from CLIA. The values of Sigma metrics for serum controls were 10.9 for TEa from BV and 5.81 for TEa from CLIA.[22]

The variations in the Sigma value between our study and others can be due to difference in methodology, traceability calibrators used, instruments used, quality control material used, and other preanalytical and analytical conditions.[4]

Most laboratories lack the understanding of how to define the tolerance limits or quality requirements for their process.[16] Choosing TEa is crucial and has a greater impact on the Sigma metrics. A laboratory must decide which TEa goal is most appropriate based on several other sources for TEa targets. One must consider that a TEa goal is not available for every analyte.

Although it seems logical to use TEa targets consistently from the same source, with experience a laboratory may find it desirable to choose TEa values from various sources, mixing, and matching as seems appropriate for individual assays. Some TEa targets are likely to be too liberal and give a falsely optimistic estimate of quality, while others, particularly those established using biological variability, are conversely too demanding and yield overly pessimistic estimates of quality.

Bias is more difficult to realistically estimate. It is ideal to calculate bias by using reference method value as "true value." Here, bias was assessed by comparing with peer group mean. A critical evaluation of EQA acceptance criteria by Friedecky et al. concluded that EQA peer group evaluation is not sufficient to determine the analytical quality. Rather than assessing relative bias, they recommended that EQA results should be compared to the reference method target values, requiring metrological traceability and assessment of absolute trueness instead of relative bias (i.e., peer group comparison).[18]

This study has a weakness in that it uses commercially available controls. It is unknown whether these controls are commutable. The metrological traceability of the controls is also uncertain. The Bio-Rad materials used are typical "precision" controls, as opposed to "trueness" controls, and are intended to assess assay performance based on precision, i.e., CV%, and not accuracy, i.e., bias or trueness.

Trueness controls, like calibrators, are manufactured following a strict traceability chain, anchored by established reference materials and/or reference method. The target values of trueness controls are established by direct linkage to "gold standard" reference materials/methods and accompanied by uncertainty estimates. This is not the case with precision controls as is readily apparent by examining the mean values listed in control package inserts, which typically vary for an analyte depending on the assay manufacturer. Realistic estimates of assay bias/trueness require proper metrological standardization of all field assays and analysis of trueness controls, of which there are few, which may not be prepared using appropriate reference materials, which often are not readily available, and which may be prohibitively expensive for typical clinical laboratories. In addition, the commutability of trueness controls and reference materials must be established, and commutability studies are challenging and rare.[23]

Our study shows that for any given parameter, the Sigma metrics vary with the matrix on the same automated platform and hence one should be careful in extrapolating the performance characteristics in terms of the Sigma of any analyte from one matrix to another matrix. Our study also showed that in the same matrix, the value of Sigma metrics of the parameters varies depending on the source of TEa used in the calculation. This is reflected in our evaluation of the Sigma metrics of the parameters in one of the matrices that is serum using the ACC. The Sigma values using TEa from BV were higher than CLIA for some parameters and vice versa for others. Our study showed that creatinine, sodium, and potassium had higher the Sigma metrics value using TEa from CLIA while urea showed the higher Sigma metrics when BV was used as the source of TEa in the calculation.

Conclusion

Our study shows that the performance of parameters varies depending on the matrix of the specimen used.

The Sigma metrics of urea, creatinine, sodium, and potassium were significantly lower (p <0.001) in serum controls compared to urine controls using same TEa. This could be due to higher TEa in urine controls from BV data for these parameters.

Our study also shows that in the same matrix, the Sigma metrics of creatinine, sodium, and potassium was found to vary with the source of TEa used. This could be due to higher TEa allowed under CLIA guidelines for these parameters than the BV database.

The lack of TEa targets for many analytes and sometimes inconsistent TEa targets from different independent sources are a major variable in the interpretation and application of the Sigma metrics.

Our study shows that for any given parameter, the Sigma metrics vary with the matrix on the same automated platform and hence one should be careful in extrapolating the performance characteristics in terms of Sigma of any analyte from one matrix to another matrix.

Our study also showed that in the same matrix, the Sigma metrics value of the parameters vary depending on the source of TEa used in the calculation.

The Sigma metrics thus can be misleading as they vary depending on the source of TEa used, and it hence is important to arrive at a consensus regards the source of variables used in the calculation of the Sigma metrics.

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