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Research Article

EVALUATION OF SIGMA METRICS OF CLINICAL CHEMISTRY ASSAYS: IMPORTANCE OF THE ALLOWABLE TOTAL ERROR (TEA) TARGETS

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ABSTRACT

Introduction- Analytical quality is a prerequisite for the clinical laboratory, but it can be difficult to assess it. Sigma metrics is an objective way to measure and quantify quality. It combines total allowable error (TEa), bias and precision. TEa for an analyte is obtained from literature and can vary based on the source of data used such as Biological Variation data or Clinical Laboratory Improvement Amendments (CLIA) guidelines. Hence, we conducted this study to highlight the importance of TEa goals. The objective of our study was to calculate and compare sigma metrics of 16 clinical chemistry assays using TEa data from various sources. **Methodology-** Precision is expressed as coefficient of variation (%CV) and Bias was calculated from target mean provided by the manufacturer and lab mean. Sources of TEa used are Biological Variability (Desirable, Optimal & Minimum) and CLIA (Old Guidelines & New proposed guidelines 2019). Sigma metric was calculated by formula "Sigma metric= (TEa-Bias)/Precision"**. Results-** Triglyceride both the levels showed sigma>6, with TEa biological variability desirable and old CLIA guidelines while Amylase showed sigma >3 with Biological variability minimum and old CLIA guidelines whereas, it showed sigma <2 with the Biological variability optimal & New CLIA guidelines**. Conclusion-** Sigma metrics as a quality assurance tool should be periodically used to monitor changes in assay quality. Laboratories need to improve their performance to reach the desired quality goals. Inconsistent TEa targets from different independent sources can create a dilemma and should be chosen based on assay performance. We found Biological Variability TEa values to be too demanding for routine performance whereas; old CLIA guidelines can be considered lenient.

INTRODUCTION

One of the most important units of the healthcare sector is clinical laboratories. Hence, maintenance of quality is crucial for a clinical laboratory to constantly generate accurate test results.(1,2)

Quality control (QC) is a statistical process used to continuously monitor and evaluate the analytical methods that produce patient results. It helps ensure the reliability of laboratory test results.(3)

Six Sigma as a global management strategy was introduced in the 1980s and is currently being applied in several laboratories around the world. (4) Sigma metrics is used to measure quality in an objective and quantitative manner.(5) It is a process improvement scheme which focuses on removing defects using data gathering and its statistical analysis. It represents the assay ability to meet the desired quality requirement.(6)

Sigma metrics can be used to design control rules and can help laboratory maximize its efficiency by reducing control costs through less number of re-runs. (5) Sigma metric calculation combines three components: the allowable total error (TEa), bias and precision (CV).

Total allowable error (TEa) refers to the degree of change that needs to be detected in an analyte so as to make a clinically important decision.(7)

TEa for an analyte is obtained from literature and can vary based on the source of data used such as Biological Variation data or Clinical Laboratory Improvement Amendments (CLIA) guidelines. (5,8)

Hence, we conducted this study to highlight the importance of TEa goals in calculation of sigma metrics. The objective of this study was to calculate and compare sigma metrics of 16 clinical chemistry assays using TEa from various sources.

MATERIALS AND METHODS

This was a cross sectional analytical study.

The source of data was laboratory Internal Quality Control (IQC) records at Sri Aurobindo Medical College & PG Institute, Indore. The analyzer used was Vitros J & J 5,1 (Ortho Clinical Diagnostics). Internal Quality Control (IQC) data of both levels that was accepted for analytical run in the laboratory in the month of May in 2019 were included. Any data points that have been rejected by the laboratory due to faulty runs were excluded from the study.

16 chemistry parameters - Glucose, Urea, Creatinine, Total Bilirubin (T. Bil), Total Protein (T. Protein), Albumin, Calcium, Phosphorus, Uric Acid, Cholesterol, Triglyceride (TRIG), High Density Lipoprotein Cholesterol (HDL), Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP) and Amylase were included in the study.

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All the data was entered and analyzed on Microsoft Excel 2013. Following formulae were used:

Precision- Expressed as coefficient of variation and calculated by formula

CV%= Standard deviation/Mean X100
Bias- Calculated by formula

(Lab mean-Target mean)/Target mean X100
Sigma metric – calculated by standard formula

Sigma metric= (TEa - Bias)/Precision
(all values expressed as percentage)

The following Sources of TEa were considered (9):

- Biological Variability (BV): Desirable (BVD), Optimal (BVO) and Minimum (BVM).
- CLIA: Old Guidelines and New proposed guidelines 2019.

RESULTS

Sigma metrics for 16 assays for available TEa targets are shown in Table 1. Triglyceride Level 1 (L1) and Level 2 (L2) both showed sigma>6, with TEa biological variability desirable and old CLIA guidelines.

Amylase showed sigma >3 with BVM and old CLIA guidelines (as shown in figures 1 and 2 respectively) whereas, it showed sigma <2 with the BVO & New CLIA guidelines (as shown in figures 3 and 4 respectively). Similarly, HDL L1 and L2 both showed high variation in sigma with different TEa.

Table 1 Sigma metrics using three different sources for TEa target values (Biological variability, Old CLIA and New CLIA).

ANALYTE Level 1 & 2	SIGMA BVD	SIGMA BVO	SIGMA BVM	SIGMA OLD CLIA	SIGMA NEW CLIA (2019)
UREA L 1	3.07	1.34	-	-	-
UREA L 2	3.5	1.41	-	-	-
URIC ACID L 1	0.83	-0.1	-	1.63	0.52
URIC ACID L 2	1.26	0.5	-	1.91	1.01
T BIL L 1	3.08	0.72	-	1.89	1.86
T BIL L 2	4.78	1.72	-	3.2	3.2
HDL L 1	1.49	-	-	7.42	4.19
HDL L 2	0.8	-	-	4.2	2.35
ALT L 1	4.38	2.54	-	3.38	2.72
ALT L 2	4.94	1.95	-	3.32	2.23
AST L 1	2.32	-	-	3.38	-
AST L 2	2.91	-	-	3.68	-
ALP L 1	1.08	-	-	4.82	2.73
ALP L 2	0.25	-	-	2.97	1.46
CHOLESTEROL L1	1.08	0.14	-	1.28	1.28
CHOLESTEROL L2	1.91	0.81	-	2.15	2.15
GLUCOSE L 1	1.01	-	-	1.9	1.32
GLUCOSE L 2	1	-	-	1.55	1.19
CREATININE L 1	0.91	0.74	-	1.84	1.08
CREATININE L 2	0.2	0.05	-	0.99	0.35
T PROTEIN L 1	-1	-	-0.22	1.78	0.91
T PROTEIN L 2	0.34	-	0.71	1.64	1.24
ALBUMIN L 1	-0.4	-	0.23	1.38	0.79
ALBUMIN L 2	-0.9	-	-0.35	0.65	0.14
CALCIUM L 1	0.24	-	0.39	-	-
CALCIUM L 2	0.38	-	-0.58	-	-
PHOSPHORUS L 1	-1	-3.1	-	-	-1
PHOSPHORUS L 2	0.8	-0.5	-	-	0.77
TRIG L 1	8.65	-	-	8.29	4.72
TRIG L 2	6.32	-	-	6.08	3.64
AMYLASE L 1	2.33	0.87	3.79	5.41	1.41

Using BVD, Urea, T. Bil, ALT and TRIG showed sigma >3 whereas all other analytes showed a sigma of <3. With BVO, only Phosphorus L1 showed a sigma of >3. All assays except Amylase L1 showed poor performance with BVM TEa targets.

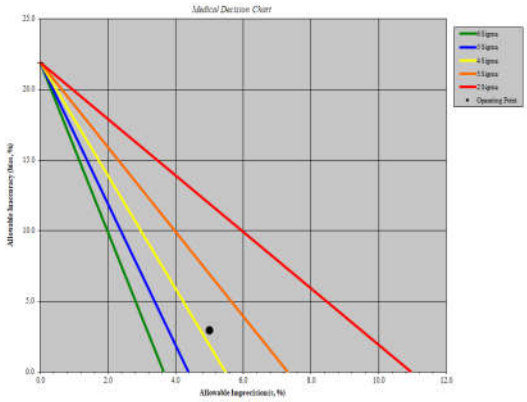

Figure 1 Method Decision Chart of Amylase Level 1 using BVM TEa target

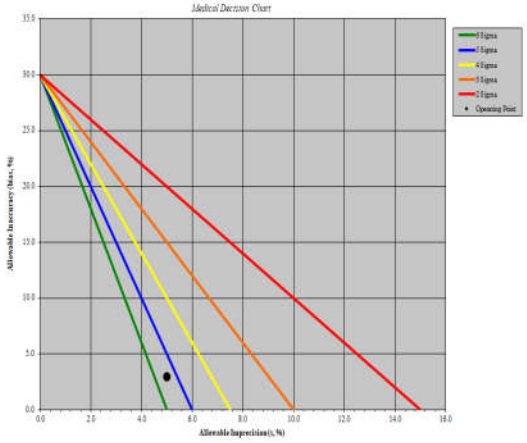

Figure 2 Method Decision Chart of Amylase Level 1 using Old CLIA TEa target

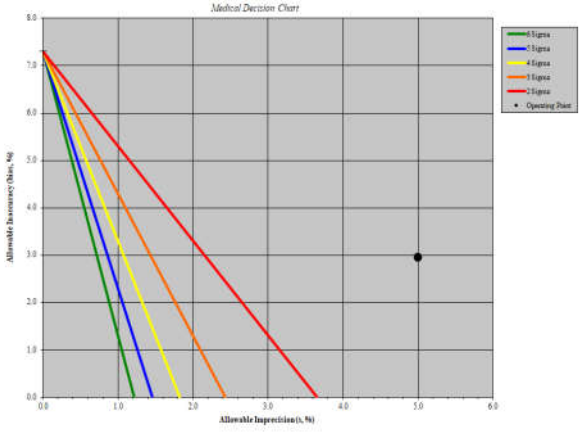

Figure 3 Method Decision Chart of Amylase Level 1 using BVO TEa target.

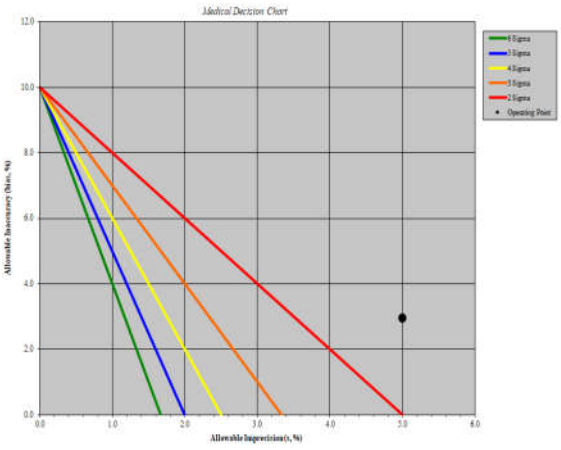

Figure 4 Method Decision Chart of Amylase Level 1 using New CLIA TEa target.

Using Old CLIA targets, T. Bil L2, HDL, ALT, AST, ALP L1, TRIG and Amylase L1 showed a sigma of >3. Whereas with new CLIA targets, only HDL L1 and TRIG L1 showed a sigma of >3.

DISCUSSION

The classical Westgard multirules need not always be used for every assay. Sigma metrics is a more efficient way to control quality by matching the QC rules to the analytical quality of individual assay. (10) It helps ensure that acceptable results are reported and false rejections are minimized.

By assessing sigma metrics, one can specify the number of control rules to be applied, the number of control materials to be used and even the frequency of running the controls. The best methods are reliable and require less effort to monitor and control. But the worse methods need more rules, more controls, and need to have QC run more frequently. It is suggested that for a 6-sigma process (or higher), to avoid false rejections, control limits should be relaxed up to 3.5 SD with N (number of controls to be run per day) =2 must be used; For a 5 sigma process, 3.0 SD control limits with N=2 have to be used; For a 4 sigma process, 2.5 SD control limits or a multirule procedure with N=4 have to be used; For a 3 sigma process, multirule procedure with N of 6 or 8 have to be used. For less than 3 sigma, method performance must be improved before the method can be used for routine diagnostic purposes.(11)

The Sigma metric QC design tools specify how much effort is required based on the performance of the method and the allowable total error (TEa). (12)

Choice of TEa has a major impact on sigma metric. One must consider that a TEa goal is not available for every analyte. In this study biological variability and CLIA guidelines for TEa were taken into consideration. There are several other sources of TEa.

Biological Variability TEa values are suggested to be too demanding for typical field assays whereas , old CLIA can be considered lenient. (5)

Inconsistent TEa targets from different sources are a major variable in the interpretation of sigma metrics. Laboratories may choose different TEa sources based on individual assay performance.

Similar study done by Westgard *et al*. for AST showed that by using either the 2014 “Ricos goal” or the 2017 revised “Ricos goal” provided a higher rate of success for laboratories to achieve acceptable performance on the Sigma scale. The RCPA goal, however, appeared difficult for a high percentage of laboratories to achieve good performance.(13)

In our study, precision was calculated from one-month QC data. We can get an even better estimate of precision from long-term QC data. Also, bias is based on the target value provided by the manufacturer as opposed to peer mean.

CONCLUSIONS

Sigma metrics is a quality assurance tool that is used to periodically monitor changes in the quality of an assay. Laboratories need to improve their performance to reach the desired quality goals.

With experience a laboratory may find it desirable to choose TEa values from various sources based on individual assay performance.

Conflict of interest: The authors declare no conflict of interest.

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