Research article
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Six sigma metrics in biochemistry analytes in an accredited laboratory of a tertiary care hospital in India

Abstract

Background: Quality management in health care is of paramount importance. Six sigma in laboratory medicine is a tool for monitoring and improving performance of analytical process. The study was conducted to calculated sigma metrics and quality goal index (QGI) for 20 biochemistry analytes.

Material & methods- The retrospective observational study was conducted in laboratory of tertiary care National accreditation board of hospitals accredited hospital in western India from January to June 2026. EQA bias was calculated as mean of percentage deviation from peer group mean in last three surveys and IQC was calculated as (Laboratory control mean- manufacturer control mean / manufacturer control mean x 100). The analytes were classified as per their performance: Sigma <3- Poor, 3-4 as marginal, 4-5 as good, 5-6 excellent & >6 as world class.

Results: Chloride (L1) was the only analyte with sigma score less than 3., HDL Cholesterol (L1), Amylase (L2), Bilirubin (L2), Alkaline phosphatase (L1 & L2), LDH (L1 & L2), Aspartate aminotransferase (L2), Alanine aminotransferase (L1 & L2), Gamma GT (L1& L2),), Lipase (L1 & L2) & Triglyceride (L1 &L2), analytes had sigma score more than 6. The results of our study indicate excellent to good performance in comparison with other Indian studies.

Conclusion: Sigma matrix can be used as self-assessment tool regarding the performance of clinical laboratory analytes. Each and every laboratory can use sigma matrix as guideline and quality baseline for quality control studies.

Keywords: six sigma, quality control, laboratory

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Introduction

Quality management in health care is of paramount importance because majority of clinical decisions approximately 70% depend on laboratory reports.[1–3] Human intervention is involved at various steps despite automation making laboratory work prone to errors. Therefore, a reliable laboratory should establish and do quality control validation for clinical interpretation of tests.[4–6]

Quality control (QC) per se is not sufficient as it is prone to detect errors and reject false rejections. The main aim of Quality control measures in analytical process is getting accurate & precise results. QC consists of Internal quality control (IQC) and External quality control (EQAS) are major components of quality management system in laboratory.[7]

IQC is performed on daily basis to ascertain that the results are reliable. EQAS involves periodical analysis & reporting on control samples to external agency (third party). IQC is measure of precision whereas EQAS measures accuracy & bias. IQC & EQC as quality improvement tool are toothless unless the analytical process is scrutinized stringently, which can only be achieved by applying six sigma metrics in laboratory Quality management.

The history of quality control methods in process dates back to 1930 s when Shehwart and his colleagues used statistical analysis in the control process.[8] Six sigma system as quality tool was initially used by Motorola in 1980s to reduce product cost & eliminate defect and it was for the first time that a quantitative framework for evaluating process performance was available.[9]

One of the key aspects of quality management system is cost involved; therefore, it is prudent at laboratory level to identify tests that require stringent QC runs and prioritize tests at risk- six sigma which focuses on cost effective quality improvement. Six sigma in laboratory medicine is a tool for monitoring and improving performance of analytical process. The original framework of six sigma encompassed framework including- define, measure, analyze, improve & control. The various steps of six sigma principle in laboratory medicine[10,11] are depicted (Table 1 & Table 2).

Table 1 Six sigma phases and their corresponding quality management actions in laboratory medicine

Six sigma phases	Laboratory action
Define	Identification of gaps in specific process
Measure	Bias & CV
Analyze	Root cause analysis using statistical tools
Improve	Recalibration, reagent change, procedural correction
Control	Continual monitoring

Sigma matrix when applied in laboratory medicine is a scale to assess performance of laboratory to evaluate process by counting defects and converting them to defects per million opportunities rate.

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Table 2 Error per million reports corresponding to each sigma value[11]

Sigma	Error/million parts
1	690000
2	308000
3	66800
4	6210
5	230
6	3.4

The higher the sigma value the lower are the chances of errors or false reports. When performance falls below 3 sigma the process is considered unstable, unacceptable and should not be used for routine testing purpose.[12,13] Sigma metrics enables laboratory to move beyond subjective QC interpretation towards data driven performance benchmarking and therefore achieving six sigma is like feather in cap for any laboratory. The present study is aimed of evaluating six sigma metrics in accredited laboratory of a multispecialty tertiary care health care setting in India.

Material and methods

The retrospective observational study was conducted in laboratory of tertiary care National accreditation board of hospitals accredited hospital in western India from January to June 2026. The six-month data of IQC and proficiency testing (EQAS) were analyzed for 20 biochemistry parameters – Albumin, Alkaline phosphatase, Alkaline aminotransferase, Amylase, Aspartate aminotransferase, total bilirubin, Chloride, Total cholesterol, Creatinine, Gamma GT, Glucose, HDL, Iron, Lactate dehydrogenase, Lipase, Phosphorus, Total Protein, Triglyceride, Urea & Uric acid.

The study was aimed at assessment of six sigma metrics in clinical biochemistry which relied on measurement of Coefficient of Variance (CV), bias, total allowable error (TEa), IQC & EQAS.

According to our quality control schedule, we ran 2 levels of IQC samples (Bio-Rad, USA) every day and one level of EQA sample (Randox, UK) per month, either normal (N) – Level-1 or pathological (P)- Level-2 as defined by the external agency.

IQC data (Bio rad) of 20 biochemical parameters over six months period for Level 1 & 2 performance verifier of fully automated analyzer Vitros 5600 (Ortho clinic diagnostics, US) were analyzed. The IQC data was used to calculate mean, CV & SD whereas EQAS (Randox) data was used for deriving bias.

The bias was calculated from EQAS or proficiency testing that was derived by comparing laboratory measured result against an assigned consensus value or peer group mean.

% bias = (Laboratory result- comparator mean) / Comparator mean

TEa values of various parameters were taken from clinical laboratory improvement guidelines CLIA- 2024 [14] & RCPA [15]. TEa was taken from new CLIA guidelines which had narrower range of TEa in comparison to older CLIA guidelines.

The sigma value was calculated by equation- Sigma= (TEa-bias)/ CV%. The instruments were calibrated and maintained as per accreditation body guidelines. The analytes were classified as per their performance: Sigma <3- Poor, 3-4 as marginal, 4-5 as good, 5-6 excellent & >6 as world class. The CV, bias, sigma & quality goal index (QGI)were calculated by Microsoft excel and for other statistical calculations free online statistical software was used.

The root cause analysis for poor sigma score was done by calculating QGI to find out cause of poor performance.

QGI= Bias/ 1.5 CV

The QGI < 0.8 indicated imprecision, QGI more than 1.2 indicated in accuracy and QGI between 0.8-1.2 indicating both imprecision as well as inaccuracy.

Results

In the retrospective study aimed at calculating six sigma metrics for 20 biochemistry parameters- – Albumin, Alkaline phosphatase, Alkaline aminotransferase, Amylase, Aspartate aminotransferase, total bilirubin, Chloride, Total cholesterol, Creatinine, Gamma GT, Glucose, HDL, Iron, Lactate dehydrogenase, Lipase, Phosphorus, Total Protein, Triglyceride, Urea & Uric acid.

Table 3 shows mean CV % of L1 (Normal) &L2 (Pathological) performance verifiers was calculated from six-month data as shown in Table 3 & Table 4. Sigma score & QGI were calculated from Table 5, with individual sigma scores depicted in Figure 1 & Figure 2.

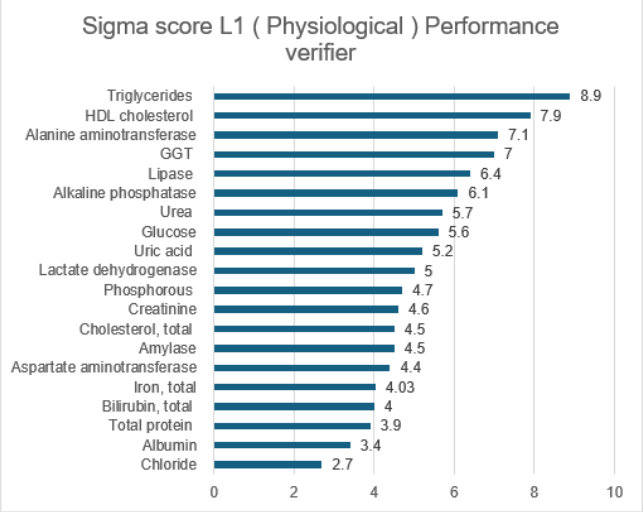

Figure 1 L1 Physiological – sigma score

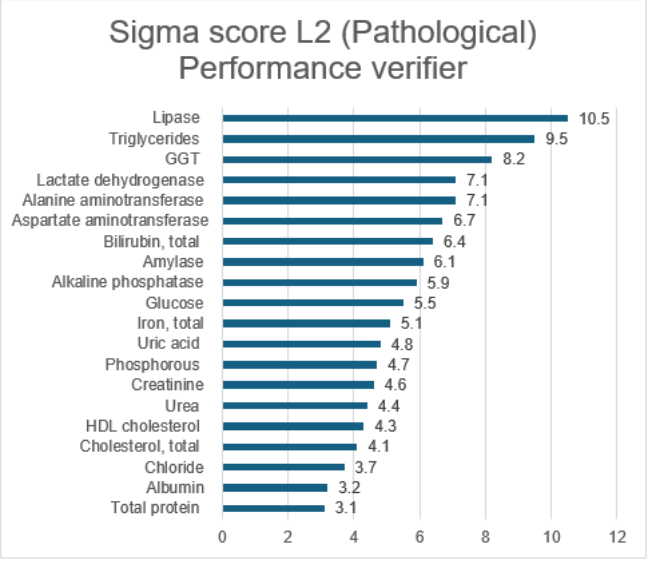

Figure 2 L2 Pathological– Sigma score

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Table 3 CV% of Level 1 performance verifier (Normal) for six-month period

	Parameter	Jan L1	Feb L1	Mar L1	Apr L1	May L1	Jun L1	Mean L1
Albumin	ALBUMIN	0.073	2.2	1.8	2.1	3.5	2.2	1.98
Alkaline phosphatase	ALKP	2.6	3.4	1.8	2.3	3	3.4	2.75
Alanine aminotransferase	ALT	2.1	1.4	2	2.5	2.1	1.8	1.98
Amylase	AMYLASE	3.7	3.3	4.5	3.8	3.7	3.4	3.73
Aspartate aminotransferase	AST	5.5	1.8	2.2	2	2.3	3.9	2.95
Bilirubin, total	TBIL	2.2	4.9	4.2	4.2	4.2	4.5	4.03
Chloride	CHLORIDE	1.3	1.3	1.7	1.7	1.5	1.7	1.53
Cholesterol, total	CHOL	2	2.1	1.5	1.8	2.1	1.9	1.9
Creatinine	CREATININE	2.4	1.8	2.6	1.8	1.8	1.7	2.02
GGT	GGT	1.6	2.9	2.3	1.3	2.6	1.6	2.05
Glucose	GLUCOSE	1.1	1.4	1.2	1.4	1.8	1.7	1.43
HDL cholesterol	DHDL	2.4	2.2	1.9	2.1	2.6	2.2	2.23
Iron, total	IRON	2.5	3.1	3	3.1	2.8	2.9	2.9
Lactate dehydrogenase	LDH	2.1	3.6	3.1	2.1	2.7	3.2	2.8
Lipase	LIPASE	2.7	2.8	1.9	2.3	3.7	3.9	2.88
Phosphorous	PHOS	1.4	2.9	2.3	1.4	1.8	1.4	1.87
Total protein	TP	1.7	1.4	1.7	3.2	1.3	1.6	1.82
Triglycerides	TRIG	1.2	1.6	1.2	1.7	1.4	2.4	1.58
Urea	UREA	1.4	3.1	1.8	1.7	2.1	1.7	1.97
Uric acid	URIC ACID	1.7	2.4	1.7	2	2	1.5	1.88

Table 4 CV% of Level 2 performance verifier (Pathological) for six-month period

	Parameter	Jan L2	Feb L2	Mar L2	Apr L2	May L2	Jun L2	Average L2
Albumin	ALBUMIN	0.129	3.9	1.8	1.7	3	2.1	2.1
Alkaline phosphatase	ALKP	2.2	3.8	2.2	2.2	3.8	3	2.87
Alanine aminotransferase	ALT	1.4	1.9	2	2.2	2.2	2.3	2
Amylase	AMYLASE	1.7	1.8	3.1	2.8	3.6	3.3	2.72
Aspartate aminotransferase	AST	1.7	1.8	2.4	1.7	2.2	2.1	1.98
Bilirubin, total	TBIL	4.5	2.3	2.8	4.1	2.1	2	2.97
Chloride	CHLORIDE	1.2	1.1	1.3	1.7	1.4	1.1	1.3
Cholesterol, total	CHOL	2.4	2.1	2.1	2.3	3	0.6	2.08
Creatinine	CREATININE	2.1	2	2	1.6	2.2	2	1.98
GGT	GGT	0.8	1.8	1.9	1	4	1.3	1.8
Glucose	GLUCOSE	1	1.5	1.5	1.1	1.7	1.8	1.43
HDL cholesterol	DHDL	3.3	2.9	2.7	2.7	5.7	7.3	4.1
Iron, total	IRON	1.5	2.5	2.5	1.9	1.8	3.5	2.28
Lactate dehydrogenase	LDH	1.7	1.9	2.2	2.6	1.6	1.9	1.98
Lipase	LIPASE	1.7	1.9	2.4	1.9	2.5	0.3	1.78
Phosphorous	PHOS	1.6	2.6	2.2	1.4	1.7	2	1.92
Total protein	TP	1.8	3.3	2.3	2.8	1.7	1.8	2.28
Triglycerides	TRIG	0.9	1.9	1.4	1.2	1.6	2	1.5
Urea	UREA	1.1	2	2	1.7	2.4	1.8	1.83
Uric acid	URIC ACID	1.7	1.4	1.8	2.5	3.5	1.4	2.05

Table 5 shows sigma score for all 20 biochemistry parameters along with bias (from EQAS) and TEa (from CLIA 2024, CLIA 2019 & RCPA). Table 6 shows six sigma scores of all parameters. Alkaline phosphatase, Alkaline aminotransferase, HDL, Gamma GT, Lipase & Triglyceride had sigma score more than 6 for L1 performance verifier.

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Table 5 Sigma metrics and QGI for parameters calculated using bias values derived from EQA data

S.no	Parameter	TEa Selection	TEa %	TEa %	Bias%	Mean CV% (L1)	Mean CV% (L2)	Sigma Score (L1)	Sigma Score (L2)	QGI (L1)	QGI (L2)
1	Albumin	CLIA 2024	8	8	1.3	1.98	2.1	3.4	3.2	0.44	0.4
2	Alkaline phosphatase	CLIA 2024	20	20	2.8	2.75	2.87	6.1	5.9	0.7	0.6
3	Alanine aminotransferase	CLIA 2024	15	15	0.9	1.98	2	7.1	7.1	0.3	0.3
4	Amylase	CLIA 2024	20	20	3.4	3.73	2.72	4.5	6.1	0.6	0.8
5	Aspartate aminotransferase	CLIA 2024	15	15	1.7	2.95	1.98	4.4	6.7	0.4	0.6
6	Bilirubin, total	CLIA 2024	20	20	1	4.03	2.97	4	6.4	0.1	0.2
7	Chloride	CLIA 2024	5	5	0.2	1.53	1.3	2.7	3.7	0.1	0.1
8	Cholesterol, total	CLIA 2024	10	10	1.4	1.9	2.08	4.5	4.1	0.5	0.4
9	Creatinine	CLIA 2024	10	10	0.8	2.02	1.98	4.6	4.6	0.3	0.3
10	GGT	CLIA 2024	15	15	0.2	2.05	1.8	7	8.2	0.1	0.1
11	Glucose	CLIA 2024	8	8	0.2	1.43	1.43	5.6	5.5	0.1	0.1
12	HDL cholesterol	CLIA 2024	20	20	2.5	2.23	4.1	7.9	4.3	0.8	0.4
13	Iron, total	CLIA 2024	15	15	3.3	2.9	2.28	4.03	5.1	0.7	0.5
14	Lactate dehydrogenase	CLIA 2024	15	15	1	2.8	1.98	5	7.1	0.2	0.3
15	Lipase	RCPA	20	20	1.3	2.88	1.78	6.4	10.5	0.3	0.5
16	Phosphorous	CLIA 2024	10	10	1	1.87	1.92	4.7	4.7	0.4	0.3
17	Total protein	CLIA 2024	8	8	1	1.82	2.28	3.9	3.1	0.4	0.3
18	Triglycerides	CLIA 2024	15	15	0.7	1.58	1.5	8.9	9.5	0.3	0.3
19	Urea	CLIA 2024	9	9	0.8	1.97	1.83	5.7	4.4	0.1	0.1
20	Uric acid	CLIA 2024	10	10	0.2	1.88	2.05	5.2	4.8	0.1	0.1

Table 6 Six sigma performance of biochemistry parameters

	Level 1 (Physiological)	Level 2 (Pathological)
Sigma >= 6 (World class)	Alkaline Phosphatase, Alanine aminotransferase, GGT, HDL, Lipase, Triglyceride	Amylase, Aspartate aminotransferase, Bilirubin, LDH, GGT, Lipase, Triglyceride, LDH
Sigma >=5 & < 6 (Excellent)	Glucose, LDH, Urea, Uric acid	Alkaline phosphatase, Glucose, Iron
Sigma >=4 & < 5 (Good)	Amylase, Aspartate aminotransferase, Bilirubin, Iron, Cholesterol, Creatinine, Phosphorous	Cholesterol, Creatinine, HDL, Phosphorous, Urea, Uric acid
Sigma >=3 & < 4 (Marginal)	Albumin, Total protein,	Albumin, Chloride, Total protein
Sigma <3 (Poor)	Chloride	

For L2 performance verifier, Alkaline phosphatase, Amylase, Aspartate aminotransferase, Total bilirubin, Gamma GT, Lactate dehydrogenase, Lipase & Triglyceride had more than 6 sigma score.

Discussion

Sigma quality management tool quantifies techniques to measure actual performance of process.[14–16] In the present study 20 biochemistry parameters were analyzed and their sigma value calculated using bias values from EQAS (Randox) and selected Westgard rules per case. The quality goal index for parameters with sigma value <3 was also calculated.[16–18] Similar studies have been done by Usha et al.,[9] Chakravarthy S et al.,[16] Justice Afrifa et al.,[18] & Sunil Nanda et al.,[17] with similar results as our study.

Such a case requires, root cause analysis and appropriate corrective. Revision in daily working protocols of run and frequency of run is needed. The difference in Sigma matrix between literature studies are attributed to variations in analysers, QC materials reagents, calibration frequency and reference sources for allowable error & bias.[14,15]

Our results show better sigma matrix on comparing with studies by Kumar B V et al.[19] evaluated 16 parameters and reported more than six sigma values for TGT, CK & amylase. In other studies, by Ram Tek et al.[20] (HDL, LDL, ALD, TG & CK) and Nanda et al.[7] had fewer parameters than our study with Sigma score more than six. It is pertinent to emphasise that the Sigma matrix depends on the type of system used for analysis. Vitros 5600 system was used in our study, a similar study on Vitros 5600 system showed that 86.4% of parameters had sigma score more than 5.[21] In the same study Abbot alinity system had 75.5% parameters above sigma score 5 and Siemens Atellica.[22] It is 6.4% that were 5 or 6 Sigma. Compared to Abbott alinity system that had 40 parameters,75.5 % and Seimens Alellica system having 67.6% of parameters falling above sigma score 5.[21,22]

The results of our study indicate excellent to good performance in comparison with other Indian studies. However, bear in mind that there is heterogeneity in Sigma performance across different studies. A perfect comparison between systems is difficult due to variations attributed to various factors – level of control fluid selected, testing days, multiple reagent lots, variables in shipping, vial to vial to handling by laboratory. The QGI for all analytes in normal (L1) & pathological (L2) controls for total protein, albumin & chloride (only L1) was below 0.8 indicating imprecision (Random error) Stringent Westgard rule application was implemented for the analyte falling below acceptable sigma score.

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Mao et al.[22] reported exceptional high Sigma for Amylase-19.93. Therefore, Sigma metrics cannot be generalised for laboratories, even for same analyte. This mandates that Sigma evaluation should be institution specific. Six Sigma, on other hand helps in QC planning as demonstrated by Zhou et al.[23] where they concluded that parameters with high sigma analytes require minimal QC event and those with low Sigma require more frequent quality control measurement. As earlier discuss Sigma scores are laboratory specific and cannot be generalised. Table 7 shows comparison of Sigma scores of our study with other contemporary Indian studies.

Table 7 Contemporary Indian studies on Six sigma for biochemistry parameters

S No	Study	Sigma >6	Sigma 3-6	Sigma <3
1	Panda et al [24]		Glucose, TP, Phosphorous, Potassium	Creatinine, HDL
2	Wadhwa et al [26]	GGT, TB	Anti TPO, CK-MB, PSA, TSH, Potassium	AFP
3	Ranteke et al [20]	TP, TG, Glucose, Urea, HDL, LDL	-	Creatinine, Sodium, Potassium, Chloride, Calcium, Phosphate (<4)
4	Nanda et al [7]	TB, Uric acid, SGOT, SGPT	Glucose, Creatinine, TG, Urea	TP, Albumin, CH, Chloride
5	Singh et al [10]	Creatinine, TG, SGOT, CPK, Amylase	-	Urea

TP- Total Protein, GGT-Gamma glutaraldehyde transferase, TB- Total Bilirubin, CK-Creatine kinase, PSA- Prostate specific antigen, TSH-Thyroid stimulating hormone, AFP- Alpha fetoprotein, CH- Cholesterol

During root cause analysis of sigma score less than 4 we calculated QGI for all three parameters, Albumin, total protein and chloride which was less than 0.8 in all three analytes which indicate imprecision. Table 8 To evaluate imprecision of these parameters we compared our CV % with the desirable specification of imprecision percentage as per Westgard QC rule.[24–25] It was concluded that the CV% in present study of all three parameters is significantly higher than the desirable specification. As corrective action to improve the quality of these parameters we included 8_X rule along with 1_{3S}, R_{4S}, $2_{2S,}$ 4_{1S}. We also made the control frequency more stringent by running six hourly two level control L1 & L2 daily for parameters with sigma value less than 4. (Table 9) It requires further analysis for the period of six months after application of Westgard sigma QC rules as mentioned.[24]

Table 8 Root cause analysis for analytes with low sigma score (<4)

	CV		Sigma		QGI		I %
Analyte	L1	L2	L1	L2	L1	L2	
Albumin	1.98	2.1	3.4	3.2	0.44	0.4	1.6
Total protein	1.82	2.28	3.9	3.1	0.4	0.3	1.38
Chloride	1.53	1.3	2.7	3.7	0.1	0.1	0.6

I %- Desirable specification for imprecision as per Westgard QC rules[24]

Table 9 Plan for QC rule application using Westgard Sigma rules[12]

Sigma score	Rule to apply	Control frequency
>6	1_{3S}	12 hourly 2 levels
5-6	1_{3S}, R_{4S}, 2_{2S}	12 hourly 2 levels
4-5	1_{3S}, R_{4S}, 2_{2S}, 4_{1S}	12 hourly 2 levels
3-4	1_{3S}, R_{4S}, 2_{2S}, 4_{1S}, 8_X	6 hourly 2 levels
<3	1_{3S}, R_{4S}, 2_{2S}, 4_{1S}, 8_X	6 hourly 2 levels

Our study has limitations with respect to being a single centre pilot study, small sample size and that VITROS 5600 which is a dry chemistry analyser might not be available or used in other laboratories that rely on only wet chemistry. There is scarcity of longitudinal data as this is a single point study, it requires further follow up after QC modification. The study however does not address the pre analytical process, sample collection and transport and post analytical phase reporting accuracy and clinical interpretation, which are its limitations.

In resource limited laboratories, adoption of six Sigma, nonetheless improves long-term efficiency, as it requires statistical expertise, good software support and adoption of computerised operations.[24] Therefore, interpretation of Sigma, as numeric target is not a prudent approach. Rather, it must be contextualised within clinical utility Sigma.

Conclusion

Our study depicts that six Sigma metrics a reliable quality tool for assessing analytical performance for biochemistry parameters. It helps in QC optimisation and identification of performance gaps, helping to build structured corrective action planning. With routine

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six sigma practice the 2 SD QC practices can be replaced with appropriate control limits and control measurements. It can be more efficient way to assess the quality by matching the QC rules to the analytical quality of each individual assay. A sustained laboratory improvement can only be achieved by integration of six Sigma matrix in quality assurance system of laboratory.

Conflicts of interest

None

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