Research Article

Maximizing Returns: Optimizing Biochemistry Lab Performance through Six Sigma application, a Yearlong Cost-Benefit Study in an Indian Laboratory

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Abstract

Introduction: One of the most essential components of a clinical laboratory's overall quality management system is quality control (QC) validation. We typically tend to use more reagents and resources than necessary in an attempt to preserve quality. Achieving higher results while using fewer resources is time imperative. We have attempted to address this issue by providing cost-benefit analysis by implementing effective QC procedures using six sigma methodology and their financial benefits.

Material and methods: Six sigma calculation of 23 routine chemistry parameters was performed over a period of one-year using bias% and cv%. New Westgard sigma rules were applied using Biorad Unity 2.0 software. A comparison was made before and after new sigma rules application including false rejection rate, probability of error detection rate, cost of all reruns, repeats, etc. Relative and absolute annual savings were computed and compared.

Results: Compared to the current rule, there was absolute savings of Indian Rupees (INR) 750105.27 when both internal failure and external failure costs were combined after the candidate rule was employed. The reduction in expenses varied with the quantity of samples examined and the quantity of QC operations carried out each day leading to an internal failure costs cut down by 50% (INR 501808.08) and external failure costs by 47% (INR 187102.8).

Conclusion: The study highlighted how quality control techniques in clinical laboratories need to be carefully planned in order to achieve significant cost reductions by lowering internal or external failure costs and effective prevention and appraisal cost planning activities prior.

Introduction

A clinical laboratory aims to produce reliable, reproducible, accurate, timely and correctly interpreted test results to aid in clinical decision-making. The analytical phase concentrates on errors ranging from 4 to 32% [1]. Often, quality is sacrificed in an attempt to save money and occasionally excessive expenditures arise from the overuse of labour, controls, reagents and calibrators [2]. Labs must prioritize cost-effectiveness while establishing and maintaining quality in all its procedures. Six Sigma is an analytical tool that can be used to find flaws in a million results. The Six Sigma scale normally ranges from 0 to 6 with a process's minimum acceptable performance being 3 sigma and values exceeding 6 being regarded as worldclass [3]. Although there are many models and techniques available globally, there isn't currently a structure in place that allows quality to be attained affordably [4].

The overall quality of a laboratory can be improved by converting sigma metrics into suitable and reliable quality control procedures. A process known as "QC validation" is used to ascertain the proper statistical QC protocols for a range of laboratory techniques [5].The idea behind it is that the best statistical quality control (QC) should have a low chance of false rejection (Pfr) and a high chance of error detection (Ped) [6]. The probability that a test run would be mistakenly designated as out of control by a quality control technique while, in reality, it is functioning correctly (i.e., there is no real error in the analytical process) is known as Pfr [7].When a genuine error arises in the analytical process Ped is the probability that a quality control procedure will accurately identify a test run as being out of control[8]. Thus Pfr is the percentage of test runs that will be refused when no errors are found and Ped is the likelihood of receiving an alert when an issue arises. Both internal and external failure costs could result from a poor application of QC methods [9]. Reprocessing control samples takes time and using more control and reagent materials as well as processing patient specimens more than once are additional costs associated with internal failure.

Incorrect diagnostic expenses and further tests performed by pathologists or physicians to confirm potentially erroneous laboratory results are examples of external failure costs [10]. Extra expenses for medical and surgical treatments are also taken into account when a patient receives an incorrect diagnosis [11]. Currently, laboratories are handling higher workloads with a wide variety of parameters with the same or fewer manpower. That being said, they still have to consistently provide high-quality results with quicker turnaround times (TATs) [12]. Choosing effective control rules for low sigma analytes and the importance of tailored QC procedures based on sigma performance are the challenges being faced by the laboratories presently [13]. In a study, sigma metrics for 21 biochemical parameters were assessed in a tertiary care hospital using external quality assurance programs and internal quality control (IQC) data. Parameters like cholesterol and glucose had high sigma levels (>6) and needed little QC work whereas stricter control guidelines were required for analytes like alkaline phosphatase with low sigma values (<3). Similar to this, CBC parameters were subjected to new westgard sigma rules at hematology labs where cut down on false rejection rates by selectively using the 13s and R4s rules improved turnaround time and financial savings. However, the challenge was striking a balance between the trade-off between sensitivity (error detection) and specificity (cutting false positives) [14]. Thus, proper planning of quality control procedures minimizes cost associated with internal failures by lowering erroneous rejections and lowers external failure costs by guaranteeing the detection of medically significant errors [15].

The purpose of this study was to ascertain combinations of QC rules and control materials which could result in more cost-effective quality control. We postulated that, while evaluating potential candidate QC rules found by QC validation, using financial analysis worksheets (six sigma cost worksheets) to calculate the costs associated with internal and external failures would be beneficial. To address this, we have attempted to apply lean six sigma and analyse the performance of 23 routine biochemistry parameters with sigma scores. Using, Biorad 2.0 unity software, the implementation of new Westgard sigma QC rules would be employed depicting number and frequency of control runs to strengthen the underperforming analytes along with a flexible quality control procedure for the outstanding and good parameteINR Following this, Internal and external failure costs would be calculated before and after implementation of Westgard QC rules and cost difference estimated in relative and absolute values with regard to reruns, repeat, control and reagent use, rework and labour use.

Material and Methods

This is a retrospective study analysis conducted on Autoanalyzer Beckman coulter AU680 based on spectrophotometry for 23 routine biochemistry parameters from September 2021 to October 2022 for a duration of one year. Third party Biorad assayed lyphocheck clinical chemistry control lot 26490(Exp11/23) was run with standard protocols as per manufacturer's instructions .It included constituting and aliquoting both low and high level of controls. The parameters that were analysed were Glucose, urea, creatinine ,total bilirubin, AST, ALT, total Protein, albumin, cholesterol, sodium, potassium, amylase and iron. Sigma metric analysis was done using MS Excel sheets. Three quality indicators Bias%, CV%, and Tea (Total allowable error) were used to calculate sigma metrics.

Bias% (inaccuracy) is the difference between the lab result and the target value [16].The target value could be the mean set by the manufacture, peer or the result of a competence exam or EQAS (External Quality Assessment Scheme). In our study, the manufacturer mean yielded the bias percentage using the formula Bias %=(Observed Value−Target Value)/Target value×100% [17].

CV% (imprecision) is the test method's analytical coefficient of variation derived from the daily IQC data. It is calculated as CV % = Standard deviation/ Laboratory mean ×100 [18]. Tea (Total allowable error) is the amount of error that can be accepted without negating the medical utility of an analytical result. TEa can be obtained from various regulatory bodies like Clinical Laboratories Improvement Act (CLIA),Biological Variation database (minimum, optimum or desirable), RCPA (Royal College of Pathologists of Australasia), Westgard site, etc. CLIA criteria for TEa has been applied here followed by BV(Biological Variation) for those [12] who did not have TEa in CLIA [19].

Sigma metric calculation

Sigma metrics were calculated from CV% (daily IQC), Bias% (manufacture mean) and TEa using formula: Sigma (σ) = (TEa%− bias%) / CV% [20]. After calculating sigma for both the levels for all the parameters,L1,L2 with different sigma scores were averaged to get a single sigma value [21].

Using Biorad Unity 2.0 software, the existing QC (Westgard Control Rule,1 2 s, 2 2 s, 1 3 s, and R4 s with n = 2) was characterized and candidate QC selections were identified and characterized [22]. A number of QC choices were determined as substitutes for the current QC, taking into account the availability of a high sigma value (> 4), low Pfr (< or = 5%) and high Ped (> or = 90%).The costs related to the current QC (1-2s,22s, R4s rule with n=2) and the candidate QC procedures were computed using the six sigma costs worksheets, specifically internal failure cost and external failure cost sheets which includes waste and rework and Quality Cost Worksheet.

Internal failure costs were broken down into three categories: the false rejection test cost (total cost of re-analyzing all patients in a test group upon finding an out-of-control QC result), the false rejection control cost (total cost of re-analyzing only control materials) and the rework labour cost [23]. In order to complete the worksheet, the information that was needed: the number of working days in a year, number of runs of the control materials per day, type of control being used, the likelihood of a false rejection, number of controls, cost of a single control material, the number of tests in each test group, estimated cost of each test, average hourly rate of employees who perform the rework and the average amount of time spent when a test needs to be repeated.

The external failure costs are the costs incurred by a laboratory to reanalyse all patients with incorrect results that were missed by quality control procedures and extra patient care cost which is the additional patient cost that arises from an incorrect test result [24]. The worksheet was completed by calculating the number of runs annually, the number of samples each run, the frequency of errors, the likelihood that an error will be detected, the estimated cost of repeating the test and the estimated cost of further patient care. Based on the frequency of the real errors recorded during the examination of the twelve months' worth of internal QC data, error frequency was determined.

For the Beckman AU auto analyzer connected to the existing QC and the candidate QC processes, two sets of costs for each single variable and each control level were computed and added up to determine the possible yearly internal, external, and total failure costs. At the end, these expenses were compared and the savings amount was determined as an absolute number (Indian rupees (INR)) and a relative savings (%).

Results

We aimed to calculate sigma scores of 23 analytes from sept' 2021 to Oct' 2022 for a period of one year run with third party Biorad controls. Results have been divided into different categories. Table 1 (1A,1B and 1C) presents the month-by-month summary of each parameter's performance characteristics together with the thorough sigma calculation

Table 1A: Sigma performance characteristics for each parameter for 12 months (Oct'2021 to Jan' 2022).

Analyte	TEa %	Level	CLIA Oct. 2021				CLIA Nov. 2021				CLIA Dec. 2021				CLIA Jan. 2022			
			CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ
Albumin	10	L1	1.08	0.84	8.481481	9.113081	3.18	2.08	2.490566	3.659917	1.95	0.3	4.974359	5.6991	2.37	2.54	3.147679	3.25402
		L2	0.94		9.744681		1.64		4.829268		1.51		6.423841		2.22		3.36036	
Alkaline Phosphatase	30	L1	3.21	6.81	7.224299	7.62426	2.59	3.2	10.34749	9.596187	2.91	8.82	7.278351	7.665791	3.23	17.9	3.74613	3.981079
		L2	2.89		8.024221		3.03		8.844884		2.63		8.053232		2.87		4.216028	
ALT	20	L1	3.09	0.82	6.20712	10.26028	4.32	1.78	4.217593	6.87843	3.52	1.03	5.389205	10.66519	3.11	1.05	6.093248	6.791683
		L2	1.34		14.31343		1.91		9.539267		1.19		15.94118		2.53		7.490119	
Amylase	30	L1	1.51	0.25	19.70199	23.25189	2.2	3.16	12.2	13.85723	1.38	-0.6	22.17391	27.90014	2.05	7.04	11.2	9.851852
		L2	1.11		26.8018		1.73		15.51445		0.91		33.62637		2.7		8.503704	
AST	20	L1	3.25	6.4	4.184615	7.363626	2.41	3.38	6.896266	7.915875	1.98	-8.17	14.22727	20.40137	3.21	2.74	5.376947	7.025157
		L2	1.29		10.54264		1.86		8.935484		1.06		26.57547		1.99		8.673367	
Bilirubin, Direct	44.5	L1	3.89	2.88	10.69923	18.60439	3.18	4.97	12.43082	18.26724	5.1	-1.79	9.076471	11.98036	4.32	0.27	10.23843	18.85524
		L2	1.57		26.50955		1.64		24.10366		3.11		14.88424		1.61		27.47205	
Bilirubin, Total	20	L1	2.4	1.71	7.620833	11.30632	2.28	1.7	8.026316	9.99355	2.57	-0.33	7.910506	11.65601	2.8	1.54	6.592857	8.128889
		L2	1.22		14.9918		1.53		11.96078		1.32		15.40152		1.91		9.664921	
Calcium	8.2	L1	1.9	1.2	3.684211	4.002599	1.64	0.55	4.664634	4.481193	0.89	-1.17	10.52809	11.19442	2.21	2.5	2.579186	2.528723
		L2	1.62		4.320988		1.78		4.297753		0.79		11.86076		2.3		2.478261	
Chloride	5	L1	1.19	0.14	4.084034	4.573267	1.39	1.28	2.676259	2.594886	1.03	0.14	4.718447	4.917118	1.63	0.15	2.97546	2.897614
		L2	0.96		5.0625		1.48		2.513514		0.95		5.115789		1.72		2.819767	
Cholesterol, HDL	30	L1	5.92	9.79	3.413851	3.328916	2.97	10.73	6.488215	5.727355	2.22	4.05	11.68919	12.08258	3.34	1.38	8.568862	8.22658
		L2	6.23		3.243981		3.88		4.966495		2.08		12.47596		3.63		7.884298	
Creatine Kinase	30	L1	1.87	2.41	14.75401	17.30147	2.17	3.28	12.31336	14.25365	2.17	1.27	13.23963	16.80776	3.3	7.08	6.945455	8.588799
		L2	1.39		19.84892		1.65		16.19394		1.41		20.37589		2.24		10.23214	
Creatinine	15.84	L1	1.39	7.72	5.841727	5.366646	1.93	0.67	7.860104	8.365724	1.86	0.41	8.295699	9.190333	2.23	8.82	3.147982	3.740658
		L2	1.66		4.891566		1.71		8.871345		1.53		10.08497		1.62		4.333333	
GGT	15	L1	1.52	2.92	7.947368	9.366541	1.27	2.07	10.1811	10.06363	1.08	-0.32	14.18519	15.79714	1.86	4.15	5.833333	5.756981
		L2	1.12		10.78571		1.3		9.946154		0.88		17.40909		1.91		5.680628	

	TEa %	Level	CLIA Oct. 2021				CLIA Nov. 2021				CLIA Dec. 2021				CLIA Jan. 2022			
			CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ
Glucose	10	L1	2.04	2.78	3.539216	3.59284	1.43	2.5	5.244755	4.753059	1.78	0.28	5.460674	6.252076	2.57	0.37	3.747082	3.985383
		L2	1.98		3.646465		1.76		4.261364		1.38		7.043478		2.28		4.223684	
Iron	20	L1	2.4	8.19	4.920833	3.805519	1.4	0.11	14.20714	10.42966	1.96	-2.58	11.52041	9.071055	2.92	6.47	4.633562	3.595609
		L2	4.39		2.690205		2.99		6.652174		3.41		6.621701		5.29		2.557656	
LDH	20	L1	7.62	0.01	2.62336	3.4751	12.13	1.4	1.533388	2.038924	9.77	1.03	1.941658	2.5283	12.1	0.49	1.612397	2.133409
		L2	4.62		4.32684		7.31		2.54446		6.09		3.114943		7.35		2.654422	
Lipase	14.2	L1	11.1	1.07	1.182883	1.529299	3.88	0.16	3.618557	4.734278	7.27	2.6	1.595598	1.90891	5.35	5.63	1.601869	2.046574
		L2	7		1.875714		2.4		5.85		5.22		2.222222		3.44		2.491279	
Phosphorus	10	L1	2.31	7.22	1.203463	1.396017	2.27	0.13	4.348018	4.679085	1.36	-0.84	7.970588	8.698338	1.64	4.31	3.469512	3.696825
		L2	1.75		1.588571		1.97		5.010152		1.15		9.426087		1.45		3.924138	
Potassium	10.98	L1	1.08	2.32	8.018519	7.445767	1.37	0.17	7.890511	7.672842	0.98	-1.14	12.36735	12.84301	1.58	4.7	3.974684	4.053131
		L2	1.26		6.873016		1.45		7.455172		0.91		13.31868		1.52		4.131579	
Protein, Total	10	L1	1.38	0.69	6.746377	6.899704	2.01	0.9	4.527363	4.216471	0.77	-0.64	13.81818	12.28283	1.58	1.25	5.537975	5.573475
		L2	1.32		7.05303		2.33		3.905579		0.99		10.74747		1.56		5.608974	
Sodium	2.73	L1	1.18	1.05	1.423729	1.605481	1.22	0.35	1.95082	1.784934	1.03	-1.42	4.029126	4.346024	1.44	1.55	0.819444	0.776182
		L2	0.94		1.787234		1.47		1.619048		0.89		4.662921		1.61		0.732919	
Urea	17.74	L1	2.19	5.18	5.73516	6.172843	2.62	0.94	6.412214	7.041723	1.82	1.47	8.93956	9.400083	2.91	4.56	4.52921	4.859093
		L2	1.9		6.610526		2.19		7.671233		1.65		9.860606		2.54		5.188976	
Uric Acid	17	L1	1.97	0.09	8.583756	9.015342	1.82	0.4	9.120879	9.120879	1.24	-2.03	15.34677	19.13724	3.17	0.07	5.340694	5.427676
		L2	1.79		9.446927		1.82		9.120879		0.83		22.92771		3.07		5.514658	

Table 1B: Sigma performance characteristics for each parameter for 12 months (Feb'2022 to May' 2022).

Analyte	TEa %	Level	CLIA Feb. 2022				CLIA March 2022				CLIA April 2022				CLIA May 2022			
			CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ
Albumin	10	L1	1.89	0.65	4.94709	4.973545	2.72	1.62	3.080882	3.293579	1.72	1.71	4.819767	4.674911	2.73	1.08	3.267399	3.115427
		L2	1.87		5		2.39		3.506276		1.83		4.530055		3.01		2.963455	
Alkaline Phosphatase	30	L1	2.82	8.77	7.528369	7.959837	2.97	8.37	7.282828	7.307516	3.67	13.58	4.474114	4.894015	2.14	17.4	5.88785	5.624776
		L2	2.53		8.391304		2.95		7.332203		3.09		5.313916		2.35		5.361702	
ALT	20	L1	3.53	1.28	5.303116	10.13956	3.25	0.23	6.083077	8.658016	3.71	3.21	4.525606	6.377999	2.44	5.12	6.098361	6.385503
		L2	1.25		14.976		1.76		11.23295		2.04		8.230392		2.23		6.672646	
Amylase	30	L1	1.42	3.88	18.39437	19.72944	1.44	2.2	19.30556	17.92659	1.19	1.59	23.87395	21.80156	1.81	3.61		16.09146
		L2	1.24		21.06452		1.68		16.54762		1.44		19.72917		1.64		16.09146	
AST	20	L1	1.96	3.32	8.510204	12.67934	2.57	3.5	6.420233	8.939283	1.87	6.17	7.395722	8.247203	1.96	6.84	6.714286	6.952771
		L2	0.99		16.84848		1.44		11.45833		1.52		9.098684		1.83		7.191257	
Bilirubin, Direct	44.5	L1	3.32	2.12	12.76506	21.30507	5.16	3.12	8.01938	11.2949	4.31	4.09	9.37587	14.94428	4.6	12.88	6.873913	10.22236
		L2	1.42		29.84507		2.84		14.57042		1.97		20.51269		2.33		13.57082	
Bilirubin, Total	20	L1	1.78	2.71	9.713483	11.66383	2.92	1.47	6.34589	7.692457	1.85	1.4	10.05405	10.28126	8.01	14.05	0.742821	1.363077
		L2	1.27		13.61417		2.05		9.039024		1.77		10.50847		3		1.983333	
Calcium	8.2	L1	1.4	0.18	5.728571	7.085338	1.82	2.76	2.989011	2.783605	1.77	4.23	2.242938	2.310092	1.75	3.16	2.88	2.669268
		L2	0.95		8.442105		2.11		2.578199		1.67		2.377246		2.05		2.458537	
Chloride	5	L1	1.41	1.2	2.695035	2.527642	1.33	2.88	1.593985	1.463659	1.41	0.22	3.390071	3.887696	1.19	0.03	4.176471	4.598336
		L2	1.61		2.360248		1.59		1.333333		1.09		4.385321		0.99		5.020202	
Cholesterol, HDL	30	L1	4.55	7.6	4.923077	4.217024	5.39	2.43	5.115028	5.411551	2.31	0.7	12.68398	9.741063	2.16	18.23	5.449074	3.749798
		L2	6.38		3.510972		4.83		5.708075		4.31		6.798144		5.74		2.050523	
Creatine Kinase	30	L1	2.73	6.02	8.783883	11.16595	2.58	6.62	9.062016	10.43505	3.77	9.05	5.557029	7.650608	3.29	9.97	6.088146	7.131828
		L2	1.77		13.54802		1.98		11.80808		2.15		9.744186		2.45		8.17551	
Creatinine	15.84	L1	4.87	0.88	3.071869	3.590879	3.66	1.59	3.893443	5.372202	2.48	3.75	4.875	5.088816	3.46	10.55	1.528902	1.69908
		L2	3.64		4.10989		2.08		6.850962		2.28		5.302632		2.83		1.869258	
GGT	15	L1	1.4	4.96	7.171429	8.869925	1.24	4.75	8.266129	8.403898	1.37	6.21	6.416058	6.964439	1.78	8.16	3.842697	4.201348
		L2	0.95		10.56842		1.2		8.541667		1.17		7.512821		1.5		4.56	

	TEa %	Level	CLIA March 2022				CLIA Nov. 2021				CLIA April 2022				CLIA Jan. 2022			
			CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ
Glucose	10	L1	2.93	1.25	2.986348	3.92373	2.91	0.4	3.298969	3.657853	2.39	2.06	3.322176	3.417725	2.81	1.53	3.014235	2.977604
		L2	1.8		4.861111		2.39		4.016736		2.26		3.513274		2.88		2.940972	
Iron	20	L1	2.14	3.04	7.925234	7.870451	2.22	0.69	8.698198	6.768899	1.64	2.35	10.7622	7.477297	3.49	12.21	2.232092	1.707991
		L2	2.17		7.815668		3.99		4.839599		4.21		4.192399		6.58		1.183891	
LDH	20	L1	9.55	0.83	2.00733	2.656251	9.05	4.56	1.706077	1.878271	9.7	10.1	1.020619	1.181951	10.49	1.58	1.755958	2.528517
		L2	5.8		3.305172		7.53		2.050465		7.37		1.343284		5.58		3.301075	
Lipase	14.2	L1	5.48	5.22	1.638686	2.132209	5.84	11.4	0.479452	0.405407	12.67	3.65	0.832676	1.322695	10.24	15.03	0.081055	0.083488
		L2	3.42		2.625731		8.45		0.331361		5.82		1.812715		9.66		0.085921	
Phosphorus	10	L1	1.06	0.44	9.018868	9.941252	1.95	0.74	4.748718	5.753921	1.29	0.83	7.108527	6.652237	1.92	0.48	4.958333	5.761925
		L2	0.88		10.86364		1.37		6.759124		1.48		6.195946		1.45		6.565517	
Potassium	10.98	L1	1.4	1.28	6.928571	7.609585	1.2	1.13	8.208333	8.541104	1.33	0.18	8.120301	9.627161	1.01	2.48	8.415842	8.681605
		L2	1.17		8.290598		1.11		8.873874		0.97		11.13402		0.95		8.947368	
Protein, Total	10	L1	1.63	1.17	5.417178	5.147815	1.42	1.95	5.669014	5.070618	1.16	0.16	8.482759	8.51964	1.55	1.57	5.43871	6.091355
		L2	1.81		4.878453		1.8		4.472222		1.15		8.556522		1.25		6.744	
Sodium	2.73	L1	1.24	1.5	0.991935	0.887687	1.29	1.4	1.031008	1.031008	1.35	0.52	1.637037	1.891334	0.98	0.33	2.44898	2.367347
		L2	1.57		0.783439		1.29		1.031008		1.03		2.145631		1.05		2.285714	
Urea	17.74	L1	2.7	2.87	5.507407	6.345491	2.52	1.14	6.587302	6.934002	2.89	4.96	4.422145	4.252606	4.18	4.06	3.272727	3.110502
		L2	2.07		7.183575		2.28		7.280702		3.13		4.083067		4.64		2.948276	
Uric Acid	17	L1	1.64	1.86	9.231707	9.43751	1.62	1.52	9.555556	9.803752	1.64	0.91	9.810976	8.664834	2.43	**2.16**	6.106996	5.603326
		L2	1.57		9.643312		1.54		10.05195		2.14		7.518692		2.91		5.099656	

Table 1C: Sigma performance characteristics for each parameter for 12 months (Jun'2022 to Sep' 2022).

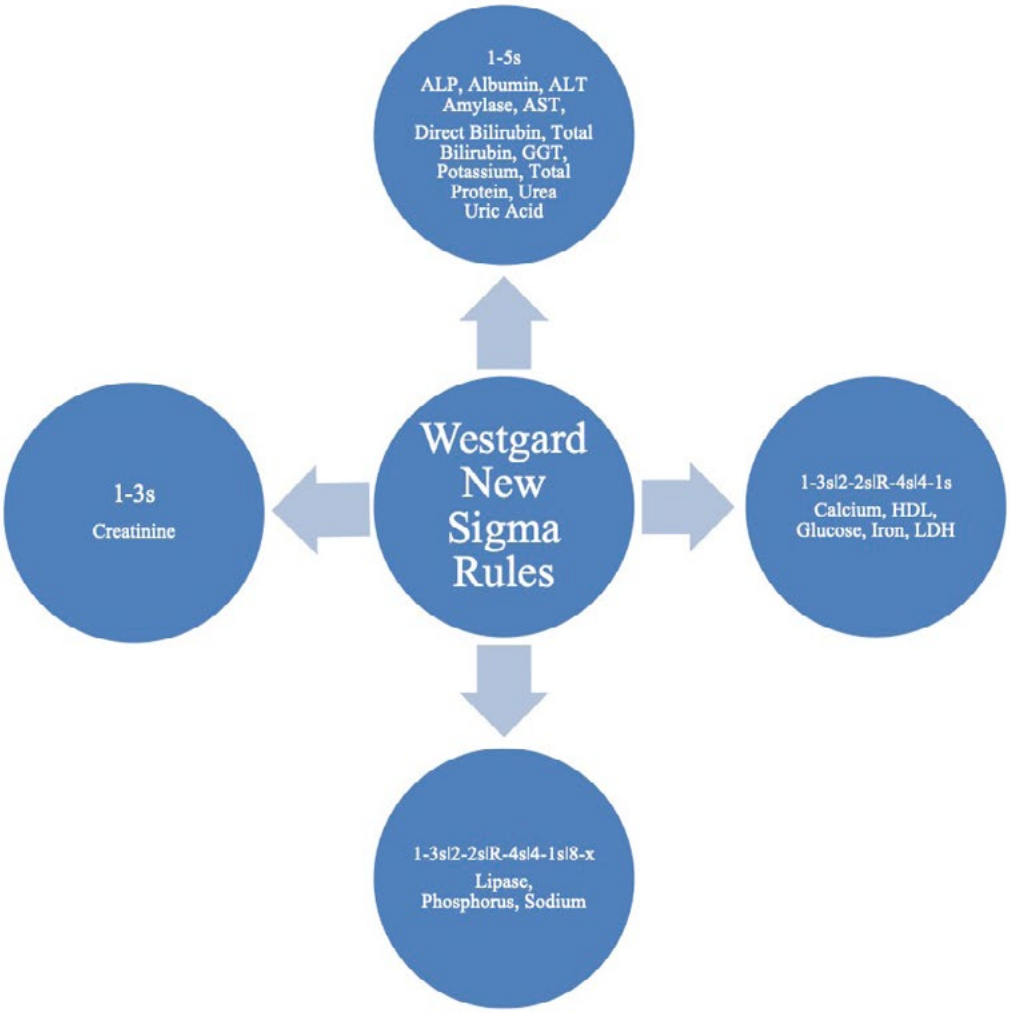
Analyte	TEa %	Level	CLIA Feb. 2022				CLIA March 2022				CLIA April 2022				CLIA May 2022			
			CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ
Albumin	10	L1	2.67	0.52	3.550562	4.09881	2.6	2.02	3.069231	2.860197	0.94	2.59	7.882979	7.003473	1.25	1.59	6.728	6.130447
		L2	2.04		4.647059		3.01		2.651163		1.21		6.123967		1.52		5.532895	
Alkaline Phosphatase	30	L1	1.76	**8.37**	12.28977	12.62093	2.8	10.39	7.003571	7.674126	1.74	9.02	12.05747	10.62961	2.13	4.29	12.07042	13.13742
		L2	1.67		12.9521		2.35		8.344681		2.28		9.201754		1.81		14.20442	
ALT	20	L1	2.25	5.84	6.293333	7.656221	2.41	3.5	6.846473	7.122788	4.34	3.08	3.898618	4.380343	3.1	0.04	6.43871	7.558485
		L2	1.57		9.019108		2.23		7.399103		3.48		4.862069		2.3		8.678261	
Amylase	30	L1	1.92	**1.1**	15.05208	17.15938	1.9	2.95	14.23684	16.13509	1.65	1.7	17.15152	18.13657	1.6	0.79	18.25625	24.34167
		L2	1.5		19.26667		1.5		18.03333		1.48		19.12162		0.96		30.42708	
AST	20	L1	3.05	10.52	3.108197	4.516598	1.71	0.43	11.44444	11.83785	2.88	3.5	5.729167	7.117161	2.76	1.46	6.717391	10.32862
		L2	1.6		5.925		1.6		12.23125		1.94		8.505155		1.33		13.93985	
Bilirubin, Direct	44.5	L1	5.61	**3.22**	7.358289	10.14936	4.5	3.55	9.1	9.8	3.64	0.22	12.16484	16.98882	3.55	1.45	12.12676	22.3702
		L2	3.19		12.94044		3.9		10.5		2.03		21.81281		1.32		32.61364	
Bilirubin, Total	20	L1	3.66	1.67	5.008197	7.992122	8.01	0.62	2.419476	4.439738	2.42	0.39	8.103306	9.439016	2.37	0.24	8.337553	9.879759
		L2	1.67		10.97605		3		6.46		1.82		10.77473		1.73		11.42197	
Calcium	8.2	L1	2.6	**5.42**	1.069231	1.199687	1.75	0.38	4.468571	4.141603	1.03	2.87	5.174757	5.054971	1.51	1.15	4.668874	5.066995
		L2	2.09		1.330144		2.05		3.814634		1.08		4.935185		1.29		5.465116	
Chloride	5	L1	1.65	1.21	2.29697	2.606177	1.19	2.3	2.268908	2.49809	1.21	0.43	3.77686	4.2441	1.2	0.01	4.158333	5.237395
		L2	1.3		2.915385		0.99		2.727273		0.97		4.71134		0.79		6.316456	
Cholesterol, HDL	30	L1	3.25	4.77	7.763077	7.624862	2.16	8.73	9.847222	6.776399	1.69	2.5	16.27219	14.35781	1.77	2.76	15.38983	15.17843
		L2	3.37		7.486647		5.74		3.705575		2.21		12.44344		1.82		14.96703	
Creatine Kinase	30	L1	2.45	9.21	8.485714	10.18286	3.29	3.84	7.951368	9.314459	3.05	5.46	8.045902	7.955643	3.17	2.04	8.820189	18.82247
		L2	1.75		11.88		2.45		10.67755		3.12		7.865385		0.97		28.82474	
Creatinine	15.84	L1	3.28	0.09	4.801829	5.154411	3.46	2.31	3.910405	4.345662	2.48	0.22	6.298387	6.211939	2.27	3.04	5.638767	5.663828
		L2	2.86		5.506993		2.83		4.780919		2.55		6.12549		2.25		5.688889	
GGT	15	L1	1.81	**11.05**	2.18232	**2.482005**	1.78	**0.51**	8.140449	**8.900225**	1.24	**2.63**	9.975806	**10.01636**	1.57	**3.01**	7.636943	**9.527995**
		L2	1.42		2.78169		1.5		9.66		1.23		10.05691		1.05		11.41905	

	TEa %	Level	CLIA March 2022				CLIA Nov. 2021				CLIA April 2022				CLIA Jan. 2022			
			CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ	CV %	Bias %	Sigma	σ
Glucose	10	L1	2.72	0.28	3.573529	4.750179	2.81	4.87	1.825623	1.803436	2.19	3.61	2.917808	3.295111	2.46	4.48	2.243902	3.521951
		L2	1.64		5.926829		2.88		1.78125		1.74		3.672414		1.15		4.8	
Iron	20	L1	3.92	3.47	4.216837	3.713273	3.49	**3.78**	4.647564	**3.556305**	1.18	**0.2**	16.77966	**12.11164**	2.52	**1.2**	7.460317	**6.091968**
		L2	5.15		3.209709		6.58		2.465046		2.66		7.443609		3.98		4.723618	
LDH	20	L1	9.27	0.32	2.122977	2.690628	10.49	1.5	1.763584	2.539498	8.02	7.75	1.527431	2.14322	12.9	2.62	1.347287	1.796382
		L2	6.04		3.258278		5.58		3.315412		4.44		2.759009		7.74		2.245478	
Lipase	14.2	L1	4.7	1.31	2.742553	2.97451	10.24	**3.05**	1.088867	**1.121556**	5.99	**2.69**	1.921536	**2.00334**	14.1	**2.28**	0.84539	**1.498507**
		L2	4.02		3.206468		9.66		1.154244		5.52		2.085145		5.54		2.151625	
Phosphorus	10	L1	1.8	0.16	5.466667	6.76612	1.92	0.53	4.932292	5.731663	1.84	4.73	2.86413	2.841156	2.01	0.19	4.880597	7.890299
		L2	1.22		8.065574		1.45		6.531034		1.87		2.818182		0.9		10.9	
Potassium	10.98	L1	1.09	1.51	8.688073	10.92043	1.01	**1.12**	9.762376	**10.07066**	0.89	**0.73**	11.51685	**12.16468**	1.04	**0.39**	10.18269	**12.65563**
		L2	0.72		13.15278		0.95		10.37895		0.8		12.8125		0.7		15.12857	
Protein, Total	10	L1	2.2	0.12	4.490909	5.134343	1.55	0.31	6.251613	7.001806	1.35	1.9	6	6.681818	1.4	**1.95**	5.75	6.501126
		L2	1.71		5.777778		1.25		7.752		1.1		7.363636		1.11		7.252252	
Sodium	2.73	L1	1.12	1.59	1.017857	1.067752	0.98	1.33	1.428571	1.380952	0.97	0.23	2.57732	2.725441	1.02	0.06	2.617647	3.243606
		L2	1.02		1.117647		1.05		1.333333		0.87		2.873563		0.69		3.869565	
Urea	17.74	L1	5.1	1.23	3.237255	3.499037	4.18	2.85	3.562201	3.385626	3.11	1.63	5.180064	5.239703	4.12	1.86	3.854369	3.917159
		L2	4.39		3.76082		4.64		3.209052		3.04		5.299342		3.99		3.97995	
Uric Acid	17	L1	3.17	1.33	4.943218	5.722646	2.43	1.2	6.502058	5.965805	2.95	1.27	5.332203	5.123914	3.17	0.36	5.249211	11.20193
		L2	2.41		6.502075		2.91		5.429553		3.2		4.915625		0.97		17.15464	

The comprehensive sigma calculation and month-by-month summary of each parameter's performance characteristics is shown in table 1A, 1B and 1C where majority of parameters were above six sigma zones such as ALT, Amylase, Direct Bilirubin and Creatine Kinase. Potassium, lipase and LDH had been performing poorly for few months (potassium in April, January 2022, lipase in October, December 2021 and January, February, March 2022, LDH in November, December 2021, January, February 2022), with less than two sigma score.

Table 2 (2A and 2B),the internal failure cost worksheet summarizes the performance characteristics for each single variable and control and contains the chosen candidate QC methods using Biorad Unity 2.0 software taking into account the availability of a high sigma value (> 4), low Pfr (< or = 5%) and high Ped (> or = 90%). The "number of tests for each group" matched the daily sample count of 300 for glucose,200 for ALT and AST and so on. Internal quality control was conducted once in the morning and evening and operations were deemed stable during that period. A cost of INR9.19 was determined for each run of the control material. After dividing the cost of a full test kit by the number of tests in a kit, the cost per measurand was projected to be different for different analytes. One test retesting took an estimated 1.0 minute and the average hourly pay of employees was calculated to be INR 150 per hour. Table 2 represents the performance characteristics of each analyte's selected candidate QC methods with the internal failure cost worksheet. New Westgard sigma rules based on sigma performance are shown in Figure 1.

Figure 1: Summarizes New Westgard Sigma Rules according to sigma performance.



With a few exceptions, such as lipase, phosphorus and calcium which call for a strict quality management strategy, the majority of the parameters in Figure 1 fall within the outstanding sigma zone with a rule of 1 5s and 1 3s.

Table 2A: Internal Failure Cost sheet.

Analyte	Sigma	New Westgard Sigma Rule	No. of control run	False Rejection (Pfr)	Ped	Estimated cost per control(in Rs)	Number of tests in each group test	Cost per test (INR)	False rejection cost test (INR)	False rejection control cost test (INR)	Patients test +control
Albumin	9.11	1-5s	2	0.03	0.95	9.19	300	4	22320.00	341.79	22661.79
Alkaline Phosphatase	7.62	1-5s	2	0.03	0.95	9.19	300	5	27900.00	341.79	28241.79
ALT	10.26	1-5s	2	0.03	0.95	9.19	300	4	22320.00	341.79	22661.79
Amylase	23.25	1-5s	2	0.03	0.95	9.19	50	15	13950.00	341.79	14291.79
AST	7.36	1-5s	2	0.03	0.95	9.19	300	5	27900.00	341.79	28241.79
Bilirubin, Direct	18.60	1-5s	2	0.03	0.95	9.19	100	6	11160.00	341.79	11501.79
Bilirubin, Total	11.31	1-5s	2	0.03	0.95	9.19	100	5	9300.00	341.79	9641.79
Calcium	4.00	1-3s|2-2s| R-4s|4-1s	4	0.02	0.95	9.19	50	5	3100.00	455.72	3555.72
Chloride	4.57	1-2.5s	2	0.03	0.9	9.19	250	5	23250.00	341.79	23591.79
Cholesterol, HDL	3.33	1-3s|2-2s| R-4s|4-1s	4	0.02	0.95	9.19	100	45	55800.00	455.72	56255.72
Creatine Kinase	17.30	1-5s	2	0.03	0.95	9.19	150	18.09	50468.31	341.79	50810.10
Creatinine	5.37	1-3s	2	0.01	0.92	9.19	300	3.5	6510.00	113.93	6623.93
GGT	9.37	1-5s	2	0.03	0.95	9.19	50	9	8370.00	341.79	8711.79
Glucose	3.59	1-3s|2-2s| R-4s|4-1s	4	0.02	0.95	9.19	400	3	14880.00	455.72	15335.72
Iron	3.81	1-3s|2-2s| R-4s|4-1s	4	0.02	0.95	9.19	50	19	11780.00	455.72	12235.72
LDH	3.48	1-3s|2-2s| R-4s|4-1s	4	0.02	0.95	9.19	50	15	9300.00	455.72	9755.72
Lipase	1.53	1-3s|2-2s| R-4s|4-1s|8-x	4	0.02	0.98	9.19	50	57.60	35712.00	455.72	36167.72
Phosphorus	1.40	1-3s|2-2s| R-4s|4-1s|8-x	4	0.02	0.98	9.19	50	6	3720.00	455.72	4175.72
Potassium	7.45	1-5s	2	0.03	0.95	9.19	250	5	23250.00	341.79	23591.79
Protein, Total	6.90	1-5s	2	0.03	0.95	9.19	200	4	14880.00	341.79	15221.79
Sodium	1.61	1-3s|2-2s| R-4s|4-1s|8-x	4	0.02	0.98	9.19	250	5	15500.00	455.72	15955.72
Urea	6.17	1-5s	2	0.03	0.95	9.19	300	4	22320.00	341.79	22661.79
Uric Acid	9.02	1-5s	2	0.03	0.95	9.19	50	8	7440.00	341.79	7781.79
Total									441130.31	8544.84	449675.15

Table 2B: Reanalyzing Cost sheet.

Analyte	Rework labour cost (INR)	Reanalyzing only control	Reanalyzing tests+Control	Total cost of waste and rework (INR)	Relative Savings (%)	Absolute Savings
Albumin	2790	3131.79	25451.79	25451.79	40%	15107.87
Alkaline Phosphatase	2790	3131.79	31031.79	31031.79	40%	18827.87
ALT	2790	3131.79	25451.79	25451.79	40%	15107.87
Amylase	2790	3131.79	17081.79	17081.79	40%	9527.87
AST	2790	3131.79	31031.79	31031.79	40%	18827.87
Bilirubin, Direct	2790	3131.79	14291.79	14291.79	40%	7667.87
Bilirubin, Total	2790	3131.79	12431.79	12431.79	40%	6427.87
Calcium	1860	2315.72	5415.72	5415.72	60%	5333.59
Chloride	2790	3131.79	26381.79	26381.79	40%	15727.87
Cholesterol, HDL	1860	2315.72	58115.72	58115.72	60%	84383.59
Creatine Kinase	2790	3131.79	53600.10	53600.10	40%	33873.41
Creatinine	930	1043.93	7553.93	7553.93	80%	26495.73
GGT	2790	3131.79	11501.79	11501.79	40%	5807.87
Glucose	1860	2315.72	17195.72	17195.72	60%	23003.59
Iron	1860	2315.72	14095.72	14095.72	60%	18353.59
LDH	1860	2315.72	11615.72	11615.72	60%	14633.59
Lipase	1860	2315.72	38027.72	38027.72	60%	54251.59
Phosphorus	1860	2315.72	6035.72	6035.72	60%	6263.59
Potassium	2790	3131.79	26381.79	26381.79	40%	15727.87
Protein, Total	2790	3131.79	18011.79	18011.79	40%	10147.87
Sodium	1860	2315.72	17815.72	17815.72	60%	23933.59
Urea	2790	3131.79	25451.79	25451.79	40%	15107.87
Uric Acid	2790	3131.79	10571.79	10571.79	40%	5187.87
Total		63414.84	504545.15	504545.15		449728.08

(Day: 310.00, R:2, Avg hourly rate of employee who perform repeat/rerun (in Rs): 150.00 and Avg amount of time consumed when one run of this test must be redone (in minutes): 1.00)

The Biorad unity software provided the probability of error detection and false rejection which changed based on the variables taken into consideration and the internal QC rule chosen. A total of 310 working days were computed annually with annual statistics showing that the laboratory completed a median of 50-300 tests every day. The internal failure costs for the parameters were determined to be INR 63414.84 for re-analyzing only the control materials (false rejection control cost + rework labour cost) and INR 504545.15 for re-analyzing the controls and all patients (false rejection test cost + false rejection control cost + rework labour cost).Total false rejection cost test amounted to be INR 441130.31. It also presented the total cost reductions both in absolute savings of INR 501808.04 and a relative of 50% for each variable that was achieved by implementing the candidate QC controls that biorad unity software recommended. The internal failure cost sheet with previous rule (1 2s,2 2s,R4s) amounted to a total expenditure of INR 1006353.19.

Using the 1 5s, 1 3s, and 2.5 s rule instead of the existing 1-2 s/2 2s/R4s rule resulted in a 50% reduction in internal failure costs to summarize. However, the low-performing parameters necessitated higher QC run and frequency which came out to be 2-2s, R4s, 8x resulting in an additional costing. Thus table 2 calculates the costs related to the current QC (1-2s,2 2s,R4s rule with n = 2) and candidate QC procedures using the six sigma costs worksheets containing all the parameters with regard to the cost of each analyte according to their batch size, Ped ,Pfr, reruns ,number of reruns.

Table 3,represented the second worksheet, Quality cost worksheet to ascertain the external failure using Westgard sigma rules which offered the external QC rule selection and the variable that determined the chance of error detection and error frequency. The anticipated expenses for rerunning the test matched the cost of a patient's test. The additional patient care costs based on an incorrect test result to be INR 0 (zero) as it was not possible to calculate other extra expenses like misdiagnosis which entails the expense of both not receiving necessary therapy and cost of receiving it erroneously. Table 3 described the Westgard sigma rules to illustrate the external failure worksheet.

Table 3: Westgard sigma rules to illustrate the external failure worksheet.

Analyte	New Westgard Sigma Rule	Runs /year	Patients / run	Error frequency	Probability of error detection	Cost per test (INR)	Estimated cost (time, labour) to repeat the test	Estimated cost of extra patient care
Albumin	1-5s	310	300	0.03	0.95	4	10602	0
Alkaline Phosphatase	1-5s	310	300	0.03	0.95	5	13252.5	0
ALT	1-5s	310	300	0.03	0.95	4	10602	0
Amylase	1-5s	310	50	0.03	0.95	15	6626.25	0
AST	1-5s	310	300	0.03	0.95	5	13252.5	0
Bilirubin, Direct	1-5s	310	100	0.03	0.95	6	5301	0
Bilirubin, Total	1-5s	310	100	0.03	0.95	5	4417.5	0
Calcium	1-3s|2-2s| R-4s|4-1s	310	50	0.02	0.95	5	1472.5	0
Chloride	1-2.5s	310	250	0.03	0.9	5	10462.5	0
Cholesterol, HDL	1-3s|2-2s| R-4s|4-1s	310	100	0.02	0.95	45	26505	0
Creatine Kinase	1-5s	310	150	0.03	0.95	18.09	23972.44725	0
Creatinine	1-3s	310	300	0.01	0.92	3.5	2994.6	0
GGT	1-5s	310	50	0.03	0.95	9	3975.75	0
Glucose	1-3s|2-2s| R-4s|4-1s	310	400	0.02	0.95	3	7068	0
Iron	1-3s|2-2s| R-4s|4-1s	310	50	0.02	0.95	19	5595.5	0
LDH	1-3s|2-2s| R-4s|4-1s	310	50	0.02	0.95	15	4417.5	0
Lipase	1-3s|2-2s| R-4s|4-1s|8-x	310	50	0.02	0.98	57.60	17498.88	0
Phosphorus	1-3s|2-2s| R-4s|4-1s|8-x	310	50	0.02	0.98	6	1822.8	0
Potassium	1-5s	310	250	0.03	0.95	5	11043.75	0
Protein, Total	**1-5s**	**310**	**200**	**0.03**	**0.95**	**4**	**7068**	**0**
Sodium	**1-3s|2-2s| R-4s|4-1s|8-x**	**310**	**250**	**0.02**	**0.98**	**5**	**7595**	**0**
Urea	**1-5s**	**310**	**300**	**0.03**	**0.95**	**4**	**10602**	**0**
Uric Acid	**1-5s**	**310**	**50**	**0.03**	**0.95**	**8**	**3534**	**0**
Total							**209681.9773**	

Considering that the probability of error detection was 0.95 and 0.98 in majority of parameters and that the error frequency varied based on the rule (0.02,0.03), number of runs and run size, the total external failure cost with candidate rule was determined to be INR 209681.97. When the 1-2.5s, 1 3s, and 1 5s rules were used (with n = 2), the external failure costs which were INR396784.73 with the previous rule (1-2s,2 2s, R4s, n = 2), only slightly rose due to the marginally decreased chance of error detection (90%) and high chance of false rejection (5%) leading to INR 209681.97.Absolute savings amounted to INR 187102.8 while we encountered a relative savings of 47%.

In a laboratory that processes a higher number of samples per day and where control materials were routinely analyzed twice a day, like ours, Table 4 simulates the potential annual savings on one variable when the 1-2.5s, n = 2,1 3s,1 5s rule was used instead of the current 1-2s,2 2s,R4s n = 2. Table 4 represents cost savings of each parameter with current and candidate rule.

Table 4: Cost Savings=(External failure costs + internal failure costs) for current rule-(External failure costs + internal failure costs) of candidate rule.

Analyte	Total External+Internal Cost with Previous rule	Total Internal+External Failure Cost with Candidate rule	Difference between candidate Rule cost and the Previous Rule cost
Albumin	53021.66	36053.79	16967.86
Alkaline Phosphatase	64972.16	44284.29	20687.86
ALT	53021.66	36053.79	16967.86
Amylase	35095.91	23708.04	11387.86
AST	64972.16	44284.29	20687.86
Bilirubin, Direct	29120.66	19592.79	9527.86
Bilirubin, Total	25137.16	16849.29	8287.86
Calcium	15011.81	6888.22	8123.59
Chloride	54432.16	36844.29	17587.86
Cholesterol, HDL	171794.31	84620.72	87173.59
Creatine Kinase	113305.95	77572.55	35733.40
Creatinine	40764.26	10548.53	30215.72
GGT	23145.41	15477.54	7667.86
Glucose	50057.31	24263.72	25793.59
Iron	40834.81	19691.22	21143.59
LDH	33456.81	16033.22	17423.59
Lipase	112568.19	55526.60	57041.59
Phosphorus	16912.11	7858.52	9053.59
Potassium	55013.41	37425.54	17587.86
Protein, Total	37087.66	25079.79	12007.86
Sodium	52134.31	25410.72	26723.59
Urea	53021.66	36053.79	16967.86
Uric Acid	21153.66	14105.79	7047.86
Total	INR 1216035.16	INR 714227.13	INR 501808.04

In contrast to the previous (1-2s/2 2s/R4s, n = 2), the application of the candidate (1-2.5s/13s/1 5s, n = 2) rule resulted in a considerable saving, according to the final calculations (total of both internal and external failure cost for all variables with candidate QC procedure and previous QC procedure at 2 levels of control material).The previous internal + external cost difference from the present internal +external cost lead to a difference of (1216035.16-714227.13) INR 501808.08 and a relative savings of 41%. Table 5 demonstrates the annual savings with rerunning both patient samples and controls and only controls.

Table 5: Annual savings (INR) by rerunning both Patients and control and only controls.

Analyte	Rerunning only Control	Rerunning Patients+Control
Albumin	3131.79	25451.79
Alkaline Phosphatase	3131.79	31031.79
ALT	3131.79	25451.79
Amylase	3131.79	17081.79
AST	3131.79	31031.79
Bilirubin, Direct	3131.79	14291.79
Bilirubin, Total	3131.79	12431.79
Calcium	2315.72	5415.72
Chloride	3131.79	26381.79
Cholesterol, HDL	2315.72	58115.72
Creatine Kinase	3131.79	53600.10
Creatinine	1043.93	7553.93
GGT	3131.79	11501.79
Glucose	2315.72	17195.72
Iron	2315.72	14095.72
LDH	2315.72	11615.72
Lipase	2315.72	38027.72
Phosphorus	2315.72	6035.72
Potassium	3131.79	26381.79
Protein, Total	3131.79	18011.79
Sodium	2315.72	17815.72
Urea	3131.79	25451.79
Uric Acid	3131.79	10571.79
Total	63414.84	504545.15

According to the calculations, if the QC rule is changed from 1-2s/22s /R4s with n = 2 to 1-2.5s,1-5s,1 3s (with n = 2), there can be an annual savings of 50% (INR 504545.15) if all patient samples and controls are reanalyzed, and INR 63414.84 (49%) if just the controls are reanalysed (Table 5).

If the laboratory's policy is to seek for a potential issue, solve it and reanalyse only the control materials and not all patient samples when a QC material goes out of control, then the latter is thought to be the true lab savings.

Table 6 focuses on actual overall savings potential annual internal failure costs, external failure costs, total costs and combined data calculated for all the parameters using 1-2s/2 2s/R4s and 1-2.5s/1 3s/1 5s rules with 2 levels of quality control material. Table 6 demonstrates internal and external failure costs, total costs, and integrated data computed for all parameters using the preceding and candidate rule .

Table 6: Internal and external failure costs, total costs, and integrated data computed for all parameters using the preceding and candidate rule.

	Internal Failure Cost (INR)		**External Failure Cost (INR)**	**Total internal+External (INR)**
	Rerun(control)	Rerun (Patients+control)		
Cost with New Rule	63414.84	504545.15	209681.97	777641.96
Previous cost	124609.34	1006353.19	396784.7	1527747.23
Relative and total Savings with candidate QC compared to old QC ,12s,22s,1 3s,R4s				
				750105.27
Cost savings=(external failurecosts+internal failurecosts) for current rule -(external failure costs+internal failure costs) for candidate rule.				
Relative Cost Savings (% of total cost savings)				49%

In a high-volume laboratory like ours and a laboratory where the QC procedures were carried out twice a day, the potential annual savings were demonstrated to be proportionately higher (INR 750105.27).When rerun of controls and controls along with patient tests in internal failure were added along with extra care cost of external failure, a total of INR 777641.96 was found to be with the new rule while a total of INR 1527747.23 was observed with the previous rule reflecting an absolute saving of INR 750105.27 and a relative savings of 49.09 %. **On applying Mann Whitney U test, the value of U is 145. The Z-score is 2.61433 and the P value is 0.00453. The result is significant at P <0.05. The result is found to be statically significant.**

Discussion and Conclusion

Using the proposed 1-2.5s,1 3s,1, 5s n = 2 rule instead of the present 1-2s,2 2s,R4S, n = 2 rule for quality control, resulted in absolute cost savings of INR 501808 and relative savings of 50%. These savings have significantly impacted laboratory budgets, especially in ours which is a high-volume settings. Re-evaluating all patient samples and controls resulted in a 50% annual savings (INR 504545.15) whereas re-analyzing only control materials resulted in a 49% annual savings (INR 63414.84). Reanalyzing controls and patient samples resulted in higher internal failure costs due to the high false rejection rate. On the other hand, the probability of a false rejection dropped to 3% when the candidate 1-2.5s,1 3s,1 5s rule was used. The internal failure costs consequently dropped significantly to INR 504545.15. Comparing the candidate rule to the present 1-2s rule/2-2s, there was a significant (50%) reduction in internal failure costs due to the lower erroneous rejection rate. In order to illustrate the possible cost savings advantages of applying this QC technique in the laboratory context, this comparison showed how effective the candidate 1-2.5s/1 3s/1 5s rule is at lowering internal failure costs by eliminating false rejections. However, there was a minor rise in external failure costs, which might be attributed to a decrease in the likelihood of error detection when the 1-2.5/2-2s s rule was applied with the same quantity of QC materials. The importance of selecting appropriate QC procedures lies in its utility to enhance cost-effectiveness without compromising quality. Furthermore, fewer technician hours were needed to repeat and reanalyze out-of-control runs, freeing up time for additional laboratory activities. Nevertheless it cannot be overlooked that the poor performing parameters like LDH, lipase and sodium that had called for rigorous control measurements and runs by application of 1-3s|2-2s|R-4s|4-1s which raised concerns over the quality and quality control material use, reagent consumption, retests, reruns, rework etc. **It's possible reasons for subpar performance were investigated and addressed in terms of electrode replacement, enhanced cleaning, reagent storage, meticulous instrument maintenance and more personnel training.** Proper validation of QC rules thus is essential for minimizing both internal and external failure costs, thereby improving the overall quality of laboratory results. Additionally, the importance of selecting appropriate QC procedures to enhance cost-effectiveness is the need of time as there is a the necessity of integrating new QC procedures into existing laboratory workflows.

To enhance QC, a study on POCT glucose monitoring devices applied Westgard Sigma Rules and sigma metrics. Devices with sigma >6 required fewer quality control inspections, maximizing resource use, while low-performing devices (sigma <3) were identified for prompt calibration and maintenance. The difficulties were that low-performing analyzers required regular recalibration and device replacement, which momentarily raised expenses [25]. Similarly, using the revised Westgard sigma rules, laboratories from various nations assessed thyroid function tests (TFTs) in a multi-center evaluation of QC performance adopting tailored QC strategies according to sigma levels which enhanced Ped (Probability of Error Detection) and

decreased erroneous rejections. It was difficult to reach an agreement on acceptable sigma levels across several sites, though. However, inter-lab standardization and overall test accuracy were enhanced by cooperative efforts [26].

In addition to controls, reagents, repeats and rework, the price of calibration also has an impact on laboratory expenses. Vaneeta et al. investigated the use of excess quality control material where the laboratory saved almost 13,051 Canadian dollars (CAD) (43%) as a result of the annual cost of calibrators being lowered from CAD 30,568.42 (2019–20) to CAD 17,517 (2020–21) [27]. Another by Francesco Cian showed that by applying the candidate 1-2.5s, n = 3 rule in place of the already used 1-2s, n = 3 rule resulted in savings of 75% annually (GBP 8232.5) on reassessing every patient sample along with the controls, whereas reanalyzing just the control materials resulted in savings of 72% annually (GBP 822.4) [28]. Our laboratory was already using 12s/2 2s/R4s before switching to candidate sigma rules therefore the relative cost savings were up to 50%. Teams using six sigma methodology need to always remember that quality has a price. The costs related to upholding high standards across an organization or process are included in the cost of quality (CoQ) [29].Before results are delivered, internal failure costs such as problems with samples, recollection, invalid instrument runs, expired reagents and delays in turnaround time like reruns, retestings, repairs, or equipment downtime have to be identified and fixed inside the laboratory. We can boost the profit margin if we can eliminate the cost of failure. Laboratories would become more error-free and lean if we eliminate both internal and external failures. A process operating at 4 sigma would use 15-20% of revenue and produce 6000 errors [30]. Less than 1% of revenue is lost in fixing extremely rare errors that occur when the lab process goes from 4 to 6 sigma [31]. Users who get inaccurate reports, recalls, customer complaints resulting from incorrect results, misdiagnosis, etc. are the ones who identify external failure costs outside of the laboratory. For handling failure, the majority of labs dedicate most of their budgets and resources. Sadly, this is the region that needs the most attention. It is best to minimize incurring internal and external failure costs as much as possible and to focus more on preventive and appraisal costs. When a lab has poor quality, it loses 25% of its revenue fixing the problems [32]. Repeat tests, revise results, replace samples and redo are examples of low-quality actions that incur significant costs. An attempt should be made to avoid wasteful practices like overprocessing, overproduction, supply management, patient waiting for test results and improper use of scales through effective preventative and assessment activities. This study is just one which underscores the need of choosing a suitable quality control method and evaluating the financial effects of various quality control regulations. **Labs seeking to implement similar methodologies may include specific actionable recommendations such as adopting process improvements like standardization, automation and lean practices along with identifying root causes using tools like Pareto analysis and Fishbone diagrams. It is possible to monitor and decrease variability by improving quality control through the use of statistical process control, stronger standards and more QC tests. Method validation, appropriate equipment maintenance, calibration and frequent personnel training and competency evaluations are essential for accuracy and dependability. Continual benchmarking against laboratory standards, risk management techniques like FMEA and error-proofing techniques all help to sustain continual quality improvement.**

Future perspectives and limitations

Understandably, there are limitations as well of this model as we have used the manufacturer mean to calculate the bias percentage. More research can be done utilizing the bias% from the EQAS (External Quality Assessment Scheme), peer or lab mean. **It can be challenging to create a statistical quality control strategy that fits the unique requirements of the laboratory .More resources such as training and quality control materials could be needed to implement a scientifically based quality control system.** This study can be applied not only in clinical biochemistry laboratory but also for assessing QC procedures in other areas of immunoassay, molecular or genetic laboratories. Further long-term effects of improved QC procedures on patient outcomes and laboratory efficiency can be explored.

Competing interests

The authors declare that they have no competing interests to disclose.

Declaration of conflict of interest

The authors affirm that this study is free from any conflicts of interest.

Ethical Approval

This investigation was carried out in compliance with the institutional research committee's ethical guidelines.

Abbreviations

CLIA-Clinical Laboratory Improvement Act, EQAS-External Quality Assessment Scheme, IQC-Internal Quality Control, QC-Quality Control

References

1. Zemlin AE. Errors in the Extra-Analytical Phases of Clinical Chemistry Laboratory Testing. Indian J Clin Biochem. 2018;33:154–162.
2. Hawkins R. Managing the Pre- and Post-analytical Phases of the Total Testing Process. Ann Lab Med. 2012;32:5–16.
3. Vincent A, Pocius D, Huang Y. Six Sigma performance of quality indicators in total testing process of point-of-care glucose measurement: A two-year review. Pract Lab Med. 2021;25:e00215.
4. Caetano BDL. Laboratory Quality Management System (LQMS) [Internet]. SimplerQMS. 2023 [cited 2024 Oct 8]. Available from: https://simplerqms.com/laboratory-quality-management-system/

5. QC - The Planning Process - Westgard [Internet]. [cited 2024 Oct 8]. Available from: https://westgard.com/lessons/quality-management/lesson3.html
6. Westgard JO, Groth T, Aronsson T, Falk H, de Verdier CH. Performance characteristics of rules for internal quality control: probabilities for false rejection and error detection. Clin Chem. 1977;23:1857–1867.
7. Plebani M. The detection and prevention of errors in laboratory medicine. Ann Clin Biochem. 2010;47:101–110.
8. (PDF) Performance Characteristics of Rules for Internal Quality Control: Probabilities for False Rejection and Error Detection [Internet]. [cited 2025 Jan 17]. Available from: https://www.researchgate.net/publication/22253366_Performance_Characteristics_of_Rules_for_Internal_Quality_Control_Probabilities_for_False_Rejection_and_Error_Detection
9. (PDF) Performance evaluation of internal quality control rules, EWMA, CUSUM, and the novel machine learning model [Internet]. [cited 2024 Oct 8]. Available from: https://www.researchgate.net/publication/357225950_Performance_evaluation_of_internal_quality_control_rules_EWMA_CUSUM_and_the_novel_machine_learning_model
10. Balogh EP, Miller BT, Ball JR, Care C on DE in H, Services B on HC, Medicine I of, et al. Overview of Diagnostic Error in Health Care. Improv Diagn Health Care [Internet]. National Academies Press (US); 2015 [cited 2024 Oct 8]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK338594/
11. Epner PL, Gans JE, Graber ML. When diagnostic testing leads to harm: a new outcomes-based approach for laboratory medicine. BMJ Qual Saf. 2013;22:ii6–ii10.
12. Hawkins RC. Laboratory Turnaround Time. Clin Biochem Rev. 2007;28:179–194.
13. Kumar BV, Mohan T. Sigma metrics as a tool for evaluating the performance of internal quality control in a clinical chemistry laboratory. J Lab Physicians. 2018;10:194–199.
14. Geto Z, Getahun T, Lejisa T, Tolcha Y, Bikila D, Bashea C, et al. Evaluation of Sigma Metrics and Westgard Rule Selection and Implementation of Internal Quality Control in Clinical Chemistry Reference Laboratory, Ethiopian Public Health Institute. Indian J Clin Biochem. 2022;37:285–293.
15. Lhajjam, Azzouzi, Sefiani N, Elmrabet, Ihendyane, Professor P. The importance of Internal Quality Controls in medical laboratories to ensure high quality results. J Bras Patol E Med Lab. 2023;59:7–17.
16. Coskun A. Bias in Laboratory Medicine: The Dark Side of the Moon. Ann Lab Med. 2024;44:6–20.
17. Ercan Ş. Comparison of Sigma metrics computed by three bias estimation approaches for 33 chemistry and 26 immunoassay analytes. Adv Lab Med. 4:236–245.
18. Wang W, Zhang Z, Zhang C, Zhao H, Yuan S, Liu J, et al. Evaluation of Coefficients of Variation for Clinical Chemistry Tests Based on Internal Quality Control Data Across 5,425 Laboratories in China From 2013 to 2022. Ann Lab Med. 2024;44:245–252.
19. Yadav D, Rathore M, Banerjee M, Tomo S, Sharma P. Beyond the basics: Sigma scores in laboratory medicine with variable total allowable errors (TEa). Clin Chim Acta. 2025;565:119971.
20. Luo Y, Yan X, Xiao Q, Long Y, Pu J, Li Q, et al. Application of Sigma metrics in the quality control strategies of immunology and protein analytes. J Clin Lab Anal. 2021;35:e24041.
21. Kumar BV, Mohan T. Sigma metrics as a tool for evaluating the performance of internal quality control in a clinical chemistry laboratory. J Lab Physicians. 2018;10:194–199.
22. Yadav D, Rathore M, Banerjee M, Tomo S, Sharma P. Beyond the basics: Sigma scores in laboratory medicine with variable total allowable errors (TEa). Clin Chim Acta. 2025;565:119971.
23. Mrazek C, Lippi G, Keppel MH, Felder TK, Oberkofler H, Haschke-Becher E, et al. Errors within the total laboratory testing process, from test selection to medical decision-making – A review of causes, consequences, surveillance and solutions. Biochem Medica. 2020;30:020502.
24. Saarela U, Kivinen T, Sarkkinen H. External failures as descriptor of quality in clinical microbiology laboratory services. Clin Chem Lab Med. 2005;43:54–63.
25. Martin CL. Quality Control Issues in Point of Care Testing. Clin Biochem Rev. 2008;29:S79–S82.
26. Geto Z, Getahun T, Lejisa T, Tolcha Y, Bikila D, Bashea C, et al. Evaluation of Sigma Metrics and Westgard Rule Selection and Implementation of Internal Quality Control in Clinical Chemistry Reference Laboratory, Ethiopian Public Health Institute. Indian J Clin Biochem. 2022;37:285–293.
27. Thakur V, Anthony Akerele O, Brake N, Wiscombe M, Broderick S, Campbell E, et al. Use of a Lean Six Sigma approach to investigate excessive quality control (QC) material use and resulting costs. Clin Biochem. 2023;112:53–60.
28. Cian F, Villiers E, Archer J, Pitorri F, Freeman K. Use of Six Sigma Worksheets for assessment of internal and external failure costs associated with candidate quality control rules for an ADVIA 120 hematology analyzer. Vet Clin Pathol. 2014;43:164–171.
29. Castillo-Villar KK, Smith NR, Simonton JL. A model for supply chain design considering the cost of quality. Appl Math Model. 2012;36:5920–5935.
30. Group KI. Understanding the Cost of Quality in Laboratory [Internet]. Kewaunee Int. Group. 2021 [cited 2024 Oct 8]. Available from: https://www.kewaunee.in/blog/understanding-the-cost-of-quality-in-laboratory/
31. Levtzow CB, Willis MS. Reducing Laboratory Billing Defects Using Six Sigma Principles. Lab Med. 2013;44:358–371.

32. PV TH Ramana. Cost of Poor Quality (COPQ) [Internet]. Six Sigma Study Guide. 2014 [cited 2024 Oct 8]. Available from: https://sixsigmastudyguide.com/cost-of-poor-quality/