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Evaluation of Commercial Control Materials vs. Homemade Lyophilisates For Kidney Function Tests Using Sigma Metric

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ABSTRACT This study aims to determine the quality of commercial control materials and homemade lyophilisates using the sigma metric method for BUN and creatinine parameters in a primary clinical laboratory. This cross-sectional study conducted 20 examinations on both types of control materials. The results showed that for the BUN parameter, homemade lyophilisates had a sigma value of 1 (unacceptable), while the commercial control material had a sigma value of 2 (poor). For the creatinine parameter, both homemade lyophilisates and commercial control materials had a sigma value of 3 (marginal). There was a significant difference in quality between commercial control materials and homemade lyophilisates for the BUN parameter, so homemade lyophilisate cannot be used as an alternative to commercial control materials. However, for the creatinine parameter, there was no significant difference in quality between the two control materials, so homemade lyophilisates can be used as an alternative to commercial control materials. Thus, the study demonstrates that homemade lyophilisates are an effective and economical alternative for creatinine testing but not for BUN testing. This research can help primary clinical laboratories to develop more effective and efficient quality control strategies.

INDEX TERMS Sigma metric, Commercial control, Homemade lyophilisates, BUN, Creatinine.

I. INTRODUCTION

Laboratory quality improvement is an activity aimed at ensuring the accuracy and precision of laboratory test results at the right time, from the right specimen, and interpreted correctly based on the appropriate reference data [1]. One of the clinical chemistry laboratory tests is the blood urea nitrogen (BUN) and creatinine test. These parameters are commonly found in routine general check-up examinations [2]. To obtain good laboratory results, calibration of each instrument is necessary before conducting the testing process. Proper calibration and instrument testing require control materials. The control materials used for testing are commercial control materials. Commercial controls are control materials used to assess precision and accuracy in laboratory testing. One advantage of using commercial control materials in laboratory tests is their good stability and long shelf life, whereas a common disadvantage of commercial controls is their relatively high cost. The use of commercial control materials for quality control is economically less feasible for many countries due to unavailability and relatively high prices [3]. The increasing demand for laboratory services and the variety of tests can raise laboratory testing costs. However, increased laboratory costs do not always correlate with improved test quality as well as the lack of cost-effective alternatives for commercial control materials in primary clinical laboratories. Therefore, a managerial system is needed to effectively allocate funding with available resources to improve test quality [1]. Sigma metric is one of the methods used in process-based quality improvement and management programs developed by Bill Smith and Mikel Harry at Motorola in the 1980s and was first applied in the clinical laboratory field in the 21st century. The sigma metric method plays a role in assessing performance quality by dividing sigma levels, with a minimum sigma value of 3 and a maximum sigma value of 6, corresponding to a defect-free rate of 99.99966% [4]. The sigma metric method is used for monitoring internal quality control within a laboratory. Sigma values can serve as a guide to develop QC strategies. If the obtained results have a high sigma value, the laboratory can more easily formulate QC strategies [5]. According to research conducted by B. Vinodh Kumar and Thuthi Mohan on IQC (Incoming Quality Control) levels 1 and 2 for urea, the average performance showed a sigma level of less than 3 [6].

Clinical laboratory quality is assessed using different quality indicators across various phases of the entire testing process, including the pre-analytical, analytical, and post-analytical stages [7]. Control materials are substances used to monitor the accuracy of a laboratory test or to oversee the quality of daily test results. Besides commercial controls, there are control materials that can be prepared in-house, such as pooled sera and lyophilized materials. Pooled sera consist of a collection of leftover patient serum samples that can be processed into control materials [8]. Lyophilized material is a collection of leftover serum samples (pooled sera) that are processed into a freeze-dried form [9]. The lyophilized form is more stable and has a longer shelf life compared to the liquid form [10]. The serum used must meet certain criteria, namely it must not be icteric, hemolyzed, or lipemic [11]. The pooled serum must come from patient serum leftovers that are free from HIV and Hepatitis B, verified by screening tests for HIV and HBsAg, as these diseases are contagious and can affect test results[8].

Based on the above description of commercial control materials, homemade lyophilized controls, and the application of the sigma metric method, this study aims to determine whether homemade lyophilized control materials can be used as a cost-effective alternative to relatively expensive commercial control materials using the sigma metric method, especially for blood urea nitrogen (BUN) and creatinine tests.

II. METHOD

This study is a cross-sectional research observing the sigma metric values of commercial control materials and homemade lyophilized controls in the examination of blood urea nitrogen (BUN) and creatinine. The sample selection criteria for this study were students of Poltekkes Kemenkes Surabaya aged 19-25 years, who did not have kidney diseases such as kidney infection, kidney failure, kidney cancer, glomerulonephritis, and were free from infectious diseases such as HIV, hepatitis, and others. Additionally, the subjects were willing to participate as respondents and to complete the informed consent form. The test materials used in this study are commercial control materials and homemade lyophilized controls for the BUN and creatinine parameters.

The sample size replicated in this study consists of 20 tests for each of the 2 control materials (commercial control and homemade lyophilized control) on 2 parameters, namely BUN and creatinine. The data collection method in this study uses primary and secondary data from control material examinations at a primary clinical laboratory in the Bangkalan area, Madura. Primary data were obtained from the examination results of the homemade lyophilized control materials for the BUN and creatinine parameters. Meanwhile, secondary data were obtained from the laboratory's quality control results for the BUN and creatinine parameters.

To determine the true value, two accredited reference laboratories with the same equipment and methods were used to examine the homemade lyophilized samples in duplicate at one reference laboratory and eight times at the other reference laboratory for the BUN and creatinine parameters. After obtaining the results, the average was calculated to be used as the true value. The sigma metric value is calculated by subtracting the bias value from the TEa value obtained from the CLIA guidelines, then dividing by the coefficient of variation.

III. RESULTS

The results presented are from the examination of test materials consisting of commercial control materials and homemade lyophilisates for the BUN and creatinine parameters, obtained from two reference laboratories to determine the true value of the test materials used. The results of the reference laboratory examinations can be seen in the table below:

TABLE 1
Examination Results of Homemade Lyophilisates at the Reference Laboratory

Day	BUN (mg/dL)	CREATININE (mg/dL)
1.	7.7	0.82
2.	7.4	0.79
3.	7.6	0.78
4.	7.5	0.79
5.	7.4	0.79
6.	7.5	0.81
7.	7.6	0.79
8.	7.7	0.80
9.	7.6	0.78
10.	7.7	0.79
Mean / True Value	**7.6**	**0.79**
Standard Deviation(SD	**0.12**	**0.01**
Range (Mean ± 2 SD)	**7,36 -7,84**	**0,77 – 0,81**

In Table 1, the BUN parameter shows a mean or true value of 7.6, with a standard deviation (SD) of 0.12 and a range of 7.36 – 7.84. These results are still within the normal value range. For the creatinine parameter, the mean or true value is 0.79, with a standard deviation (SD) of 0.01 and a range of 0.77 – 0.81. These results are also within the normal value range.

TABLE 2
Target Values (True Value) of Commercial Controls at Pratama Clinical Laboratory

Commercial control brand: Normal level, MTD Diagnostics

No.	Parameter	Target Values (*True Value*)	Results Reference
1.	BUN	17,7	14,0 – 21,5
2.	Creatinine	1,15	0,92 – 1,38

In Table 2, the BUN parameter shows a target or true value of 17.7 with a reference result range of 14.0 – 21.5. For the creatinine parameter, the target or true value is 1.15 with a reference result range of 0.92 – 1.38.

TABLE 3
Examination Results of Homemade Lyophilisates at Pratama Clinical Laboratory

Day	BUN (mg/dL)	CREATININE(mg/dL)
1.	8.5	0.79
2.	8.2	0.80
3.	7.2	0.72
4.	7.3	0.74
5.	8.4	0.75
6.	8.4	0.79
7.	8.2	0.80
8.	8.6	0.75
9.	8.5	0.79
10.	8.3	0.78
11.	8.6	0.81
12.	7.2	0.82
13.	8.1	0.82
14.	7.2	0.76
15.	8.2	0.81
16.	8.0	0.79
17.	7.5	0.80
18.	7.2	0.79
19.	7.3	0.79
20.	8.1	0.80
Mean (x)	**7.95**	**0.79**
Standard Deviation (SD)	**0.54**	**0.03**
Range (Mean ± 2 SD)	**6.87 - 9.03**	**0.73 – 0.85**
Coefficient of Variation (CV%)	**6.77**	**3.47**
Bias (d%)	**5.02**	**- 1.13**
TEa	**9**	**10**
Sigma (σ)	**1**	**3**

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In Table 3, for the BUN parameter, the mean (x) is 7.95, the standard deviation (SD) is 0.54, the coefficient of variation (CV%) is 6.77, the bias (d%) is 5.02, the allowable total error (TEa) is 9, and the sigma (σ) value is 1. These results are still within the normal range based on the true value from the reference laboratory; however, the CV exceeds the maximum allowable limit for the BUN parameter. For the creatinine parameter, the mean (x) is 0.79, the standard deviation (SD) is 0.03, the coefficient of variation (CV%) is 3.47, the bias (d%) is -1.13, the TEa is 10, and the sigma (σ) value is 3. These results are still within the normal range based on the true value from the reference laboratory.

TABLE 4
Examination Results of Commercial Controls at Pratama Clinical Laboratory

Day	BUN (mg/dL)	CREATININE(mg/dL)
1.	16.8	1.12
2.	17.1	1.14
3.	16.9	1.09
Day	**BUN (mg/dL)**	**CREATININE(mg/dL)**
4.	17.7	1.12
5.	17.9	1.16
6.	18.2	1.18
7.	18.7	1.11
8.	17.5	1.08
9.	18.8	1.15
10.	18.9	1.17
11.	18.7	1.19
12.	19.0	1.14
13.	19.0	1.09
14.	18.0	1.13
15.	17.5	1.19
16.	18.1	1.14
17.	17.8	1.18
18.	19.0	1.19
19.	18.9	1.14
20.	17.5	1.14
Mean (x)	**18.1**	**1.14**
Standard Deviation (SD)	**0.74**	**0.03**
Range (Mean ± 2 SD)	**16.62 – 19.58**	**1.08 -1.2**
Coefficient of Variation (CV%)	**4.10**	**3.00**
Bias (d%)	**2.26**	**-0.65**
TEa	**9**	**10**
Sigma (σ)	**2**	**3**

In Table 4, for the BUN parameter, the mean (x) is 18.1, the standard deviation (SD) is 0.74, the coefficient of variation (CV%) is 4.10, the bias (d%) is 2.26, the allowable total error (TEa) is 9, and the sigma (σ) value is 2. These results are still within the normal range based on the target value of the commercial control at Pratama Clinical Laboratory. For the creatinine parameter, the mean (x) is 1.14, the standard deviation (SD) is 0.03, the coefficient of variation (CV%) is 3.00, the bias (d%) is –0.65, the TEa is 10, and the sigma (σ) value is 3. These results are also within the normal range based on the target value of the commercial control at Pratama Clinical Laboratory.

In Table 5, for the BUN parameter in homemade lyophilisates, the accuracy is considered poor because 12 data points exceed the BUN bias limit of 5.57%, while 8 other data points remain within the normal range. In contrast, for the commercial controls, the accuracy is good as only 8 data points exceed the BUN bias limit of 5.57%, and 12 data points remain within the normal range.

TABLE 5
Bias Values of the BUN Parameter in Homemade Lyophilisates and Commercial Control

Day	Bias Values (d%) BUN	
	Homemade Lyophilisates	**Commercial Control**
1.	11.84	5.08
2.	7.89	3.39
3.	5.26	4.52
4.	3.95	0
5.	10.53	1.13
Day	**Bias Values (d%) BUN**	
	Homemade Lyophilisates	**Commercial Control**
6.	10.53	2.82
7.	7.89	5.65
8.	13.16	1.13
9.	11.84	6.21
10.	9.21	6.78
11.	13.16	5.65
12.	5.26	7.34
13.	6.58	7.34
14.	5.26	1.69
15.	7.89	1.13
16.	5.26	2.26
17.	1.32	0.56
18.	5.26	7.34
19.	3.95	6.78
20.	6.58	1.13

TABLE 6
Bias Values of the Creatinine Parameter in Homemade Lyophilisates and Commercial Control

Day	Bias Values (d%) Creatinine	
	Homemade Lyophilisates	**Commercial Control**
1.	0	2.61
2.	1.27	0.87
3.	8.86	5.22
4.	6.33	2.61
5.	5.06	0.87
6.	0	2.61
7.	1.27	3.48
8.	5.06	6.09
9.	0	0
10.	1.27	1.74
11.	2.53	3.48
12.	3.8	0.87
13.	3.8	5.22
14.	3.8	1.73
15.	2.53	3.47
16.	0	0.87
17.	1.27	2.6
18.	0	3.47
19.	0	0.87
20.	1.27	0.87

In Table 6, for the creatinine parameter in homemade lyophilisates, good accuracy was obtained because only 3 data points exceeded the creatinine bias limit of 3.96%, while 17 other data points remained within the normal range. Similarly, for the commercial controls, good accuracy was also obtained as only 2 data points exceeded the creatinine bias limit of 3.96%, and 18 data points remained within the normal range.

In Table 8, showed a significant difference in the BUN parameter, while no significant difference was found for creatinine. The obtained sigma values indicate that homemade lyophilisate performs well and is suitable for use as a control material for creatinine testing. These findings support the research objective of finding an effective and affordable alternative control material for laboratories.

TABLE 7
Calculation Results of Sigma Metric Values for Homemade Lyophilisates and Commercial Controls on BUN and Creatinine Paarameters

Parameter	Control Type	TEa (%)	d (%)	CV(%)	*Sigma*
BUN	Homemade Lyophilisates	9	5,02	6,77	1
	Commercial Control	9	2,26	4,10	2
Creatinine	Homemade Lyophilisates	10	1,13	3,47	3
	Control Commercial	10	0,65	3,00	3

TABLE 8
Sigma Value Criteria for Commercial Controls and Homemade Lyophilisates on BUN and Creatinine Parameters

Parameter	Control Type	*Sigma*	Criteria
BUN	Homemade Lyophilisate	1	*Unacceptable*
	Control Commercial	2	*Poor*
Creatinine	Homemade Lyophilisate	3	*Marginal*
	Control Commercial	3	*Marginal*

TABLE 9
Normality Test Results of Bias Values for Commercial Control and Homemade Lyophilisates on BUN and Creatinine Parameters

Parameter	Control Type	Significance	Explanation
BUN	Homemade Lyophilisate	0,128	Normally distributed data
	Control Commercial		
Creatinine	Homemade Lyophilisate	0,004	Data is not normally distributed
	Control Commercial		

In Table 9, the decision rule for the normality test is that if the obtained significance value (p) > 0.05, the data are normally distributed, while if the significance value (p) < 0.05, the data are not normally distributed. The normality test results for the bias values of the BUN parameter in homemade lyophilisate and commercial control showed that the data were normally distributed with a significance value of 0.128, so parametric analysis was continued using the independent T-test. The normality test results for the bias values of the creatinine parameter in homemade lyophilisate and commercial control showed that the data were not normally distributed with a significance value of 0.004, so nonparametric analysis was continued using the Mann–Whitney test.

TABLE 10
Idependent T-Test Results of Bias Values for the BUN Paramter

Bias Value BUN	Significance	Sig. (2-tailed)	Explanation
	0,398	0,000	There is a significant difference

In Table 10, the independent T-test results of the bias values for the BUN parameter show homogeneous data and there is a significant difference between the commercial control material and homemade lyophilisates for the BUN parameter. In Table 11, the Mann-Whitney test results of the bias values for the creatinine parameter show that there is no significant difference between the commercial control material and homemade lyophilisates.

TABLE 11
Mann-Whitney Test Results of Bias Values for the Creatinine Parameter

Bias Value Creatinine	Asymp. Sig. (2–tailed)	Explanation
	0,605	There is no difference

IV. EXPLANATION

The obtained true value results showed good outcomes because the true values remained within the acceptable range and had a small standard deviation (SD). This statement aligns with [10], who explained that the smaller the coefficient of variation (CV, expressed as % SD), the more precise the system or method is, and vice versa[12]. A small SD indicates a narrow or close range of results, which means good precision. This is consistent with [13], who stated that good precision reflects a high level of accuracy because it can produce the same or similar results when tests are repeated[14]. Meanwhile, the target value (true value) of the commercial control material has been predetermined by the manufacturer.

The CV value, or imprecision, is used to measure how close repeated test results are on the same sample[15]. A low CV indicates good precision because it provides consistent measurements with minimal variation[16]. Precision is also used to indicate the presence of random errors [17]. This is in accordance with [10], who explained that precision values are used to measure the accuracy of a system or method and to indicate random errors; therefore, the smaller the precision value, the more accurate the system or testing method. The maximum allowable CV values are 5.7% for the BUN parameter and 8.9% for the creatinine parameter [10]. From the CV results obtained, only the CV of the homemade lyophilisates for the BUN parameter exceeded the maximum limit, indicating poor precision. The other results remained within the normal range, indicating good precision.

Bias or inaccuracy is a value used to measure how close test results are to the true value. Bias is used to assess the presence of systematic errors by measuring the inaccuracy of a method. The lower the bias value, or the closer the bias is to the true value, the higher the accuracy. This aligns with [13], who explained that the smaller the bias obtained, the higher the accuracy of the examination. Bias values can be positive or negative; a positive bias indicates a value higher than it should be, while a negative bias indicates a value lower than it should be [18]. Based on the bias results for both BUN and creatinine parameters, the bias values indicate good (acceptable) accuracy. Both the homemade lyophilisates and commercial control did not exceed the maximum allowable bias limits. According to CLIA, the maximum allowable bias is 5.57% for BUN and 3.96% for creatinine[19]. The variability of bias values exceeding the bias limit may be caused by several factors, such as the instability of homemade lyophilisate during storage or inconsistent rehydration processes. In addition, differences in technique or operator experience can also affect test results. The application of the sigma metric in internal quality control (IQC) can improve test quality by using sigma values as a reference to design effective internal quality improvement strategies [4]. The implementation of sigma in Internal Quality Control (IQC) explains the control rules using Westgard rules and the frequency of quality control execution based on the obtained sigma values[20]. For example, if the sigma value is ≤ 2, all Westgard rules (n=6) are applied, with quality control performed once every 10 patient samples. If the sigma value is 3, all Westgard rules are applied with quality control once every 45 patient samples [21]. A high sigma value indicates a low probability of error, and vice versa

[13]. If a parameter's sigma value is less than three, it can be concluded that the sigma method cannot be used as a routine method, indicating the need for evaluation due to process instability [22]. Variations in sigma values can be influenced by systematic and random errors. This aligns with [19], who explained that systematic errors affect all samples evenly and proportionally, causing shifts in control means either gradually or suddenly [23]. Causes of systematic errors include reagent or calibrator lot changes, improper reagent preparation, reagent or calibrator damage, incorrect calibrator values, inaccurate reagent or sample volumes due to pipette miscalibration, inappropriate room or incubation temperatures, cuvette or lamp damage or wear, and light source failure [24]. Random errors can be caused by bubbles in reagent or sample lines, poorly homogenized reagents or controls, power fluctuations, fluctuating room or incubation temperatures, clumps or small bubbles during pipetting, and operator variations in following procedural steps[25]. Parametric testing using an independent T-test on bias values for the BUN parameter showed a significant difference between commercial control material and homemade lyophilisates, with a significance value of 0.000. Non-parametric testing using the Mann-Whitney test on bias values for the creatinine parameter showed no significant difference between commercial control and homemade lyophilisates, with an Asymp. Sig. (2-tailed) of 0.605. Based on these results, it can be concluded that homemade lyophilized control materials cannot be used as an alternative to commercial control materials for the BUN parameter, whereas homemade lyophilized controls can be used as an alternative to commercial control materials for the creatinine parameter based on the sigma metric values. The use of homemade lyophilized controls can have a positive impact on laboratory testing, especially in areas with limited funding. With costs significantly lower than commercial controls, homemade lyophilized materials can maintain their quality as long as they are stored and used properly. Additionally, these homemade lyophilized controls are stable during storage, allowing them to be used for quality control over a relatively long period without compromising the accuracy of the results [2].The limitations of this study include a gap during the research process and the potential for pre-analytical errors.

V. CONCLUSION

This study shows that for the BUN parameter, both the homemade lyophilized material and the commercial control achieved good accuracy values because they did not exceed the maximum allowable BUN bias limit. However, the precision value for the homemade lyophilized material was poor as it exceeded the maximum allowable BUN CV limit, whereas the commercial control had good precision because it did not exceed the maximum allowable BUN CV limit. For the creatinine parameter, both the homemade lyophilized material and the commercial control achieved good accuracy values because they did not exceed the maximum allowable creatinine bias limit. The precision values for both the homemade lyophilized material and the commercial control were also good because they did not exceed the maximum allowable creatinine CV limit. Regarding the sigma metric results for the BUN parameter, both the homemade lyophilized material and the commercial control had sigma values less than 3, so the sigma method cannot be used as a routine method and requires evaluation. However, these results are still within the normal range based on the Levey-Jennings control chart method evaluated using Westgard rules. Therefore, quality control should be performed using all Westgard rules (n=6) with a quality control frequency of once per 10 patient samples. For the creatinine parameter, both the homemade lyophilized material and the commercial control had sigma values of 3, which is considered marginal. Thus, quality control should also be performed using all Westgard rules (n=6) with a quality control frequency of once per 45 patient samples. In conclusion, for the BUN parameter, there is a significant quality difference between the commercial control material and the homemade lyophilized material, so the homemade lyophilized material cannot be used as an alternative substitute in the implementation of internal quality control (IQC). Meanwhile, for the creatinine parameter, there is no significant quality difference between the commercial control material and the homemade lyophilized material, so the homemade lyophilized material can be used as an alternative substitute in the implementation of internal quality control (IQC). The benefits of using homemade lyophilized controls for laboratory testing include cost savings due to the high price of commercial control materials. Homemade lyophilized controls can also be tailored to the laboratory's needs, are easy to store, and remain stable for a long period if stored properly. This allows laboratories in resource-limited areas to maintain the quality of testing without compromising the accuracy of the results.

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REFERENCE

[1] H. Tewabe, S. K. Gc, L. Legesse, and F. Birhanu, "*Validation of the efficacy of pooled serum for serum glucose in-house quality control material in comparison with commercial internal quality control in clinical chemistry laboratory*," *Pract. Lab. Med.*, vol. 39, 2024, Art. no. e00339, doi: 10.1016/j.plabm.2024.e00339.

[2] R. Jamtsho, "*Stability of lyophilized human serum for use as quality control material in Bhutan*," *Indian J. Clin. Biochem.*, vol. 28, no. 4, pp. 418–421, Oct. 2013, doi: 10.1007/s12291-013-0328-x.

[3] S. Kulkarni, S. Alain, and P. Ramachandran, "*Efficacy of Pooled Serum Internal Quality Control in Comparison with Commercial Internal Quality Control in Clinical Biochemistry Laboratory*," 2020.

[4] R. McCafferty *et al.*, "*ICSH review of internal quality control policy for blood cell counters*," *Int. J. Lab. Hematol.*, vol. 46, no. 1, pp. 3–12, Jan. 2024, doi: 10.1111/ijlh.14220.

[5] H. Holt and T. Freedman, "*Internal quality control in point-of-care testing*," *Ann. Clin. Biochem.*, vol. 53, no. 4, pp. 406–419, 2016, doi: 10.1177/0004563215615148.

[6] B. V. Kumar and T. Mohan, "*Sigma metrics as a tool for evaluating the performance of internal quality control in a clinical chemistry laboratory*," *J. Lab. Physicians*, vol. 10, no. 02, pp. 194–199, 2018, doi: 10.4103/jlp.jlp_102_17.

[7] A. Devi and A. Negi, "*Pooled Sera as an Alternative to Commercial Internal Quality Control in Clinical Laboratories*," *J. Clin. Diagnostic Res.*, pp. 1–4, 2023, doi: 10.7860/jcdr/2023/64088.18567.

[8] R. D. Whitehead Jr *et al.*, "*Methods and analyzers for hemoglobin measurement in clinical laboratories and field settings*," *Ann. N. Y. Acad. Sci.*, vol. 1450, no. 1, pp. 147–171, 2019, doi: 10.1111/nyas.14124.

[9] P. J. Howanitz and D. J. Howanitz, "*Quality control for the clinical laboratory,*" *Clin. Lab. Med.*, vol. 3, no. 3, pp. 479–495, 1983.

[10] P. Hill (ed.), *Fundamentals for External Quality Assessment (EQA)*, IFCC, 2017.

[11] Y. Xia, L. Tang, Y. Ma, and Y. Liu, "*Sigma metrics application for validated and non-validated systems in clinical chemistry*," *Journal of Clinical Laboratory Analysis*, vol. 35, no. 5, e23676, 2021, doi: 10.1002/jcla.23676.

[12] R. Emekli, G. Turhan, B. T. Köken, and S. A. Aktaş, "*An evaluation of analytical performance for 19 analytes by Sigma metrics in a clinical chemistry laboratory*," *Turkish Journal of Biochemistry/Turk Biyokimya Dergisi*, vol. 44, no. 3, pp. 299–307, 2019, doi: 10.1515/tjb-2018-0171.

[13] K. Panda, S. Ahmed, and S. Mishra, "*The evaluation of the quality performance of biochemical analytes in clinical biochemistry laboratory using Six Sigma matrices*," *Cureus*, vol. 15, no. 12, e51884, 2023, doi: 10.7759/cureus.51884.

[14] J. Litten, "*Applying Sigma metrics to reduce outliers*," *Clinics in Laboratory Medicine*, vol. 37, no. 1, pp. 177–186, 2017, doi: 10.1016/j.cll.2016.09.014.

[15] Y. Xia, H. Xue, C. Yan, B. Li, S. Q. Zhang, and M. Li, "*Risk analysis and assessment based on Sigma metrics and intended use,*" *Biochemia Medica (Zagreb)*, vol. 28, no. 2, p. 020707, 2018, doi: 10.11613/BM.2018.020707.

[16] K. Moodley and R. Gounden, "*Assessment of Sigma metrics for routine clinical chemistry testing in 4 laboratories in KwaZulu-Natal, South Africa*," *Journal of Applied Laboratory Medicine*, vol. 7, no. 3, pp. 721–730, 2022, doi: 10.1093/jalm/jfab117.

[17] Z. Geto *et al.*, "*Sigma metric of chemistry department at Ethiopian Public Health Institute clinical chemistry laboratory*," *Indian Journal of Clinical Biochemistry*, vol. 37, no. 3, pp. 331–336, 2022, doi: 10.1007/s12291-021-00994-x.

[18] T. Jamtsho, S. Dorji, A. K. Sharma, and V. B. Gupta, "*Evaluation of stability of self-prepared lyophilized serum for biochemical quality control application,*" *Indian Journal of Clinical Biochemistry*, vol. 28, no. 4, pp. 384–389, 2013, doi: 10.1007/s12291-012-0290-2.

[19] S. Shah, R. Saini, S. Sb, O. Aggarwal, and G. Ak, "*Six Sigma Metrics and Quality Control in Clinical Laboratory*," vol. 2, no. 2, pp. 140–149, 2014.

[20] Mao, Xuehui et al. "*Evaluating analytical quality in clinical biochemistry laboratory using Six Sigma*." *Biochemia medica* vol. 28,2 (2018): 020904. doi:10.11613/BM.2018.020904.

[21] K. Aggarwal, S. Patra, V. Acharya, M. Agrawal, and S. K. Mahapatra, "*Application of six sigma metrics and method decision charts in improvising clinical Chemistry laboratory performance enhancement*," Int. *J. Adv. Med.*, vol. 6, no. 5, p. 1524, 2019, doi: 10.18203/2349-3933.ijam20194155.

[22] Geto, Zeleke 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 journal of clinical biochemistry : IJCB* vol. 37,3 (2022): 285-293. doi:10.1007/s12291-021-00994-x.

[23] Inal TC, Goruroglu Ozturk O, Kibar F, Cetiner S, Matyar S, Daglioglu G, et al. "*Lean six sigma methodologies improve clinical laboratory efficiency and reduce turnaround times. J Clin Lab Anal.*" 2018;32(1):1–5. doi: 10.1002/jcla.22180.

[24] Connell E. "*Tietz textbook of clinical chemistry and molecular diagnostics (5th edn)*" Ann Clin Biochem Int J Lab Med. 2012 doi: 10.1258/acb.2012.201217.

[25] Krouwer JS. "*Setting performance goals and evaluating total analytical error for diagnostic assays.*" Clin Chem. 2002;48(6):919–927. doi: 10.1093/clinchem/48.6.919.