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The Application of Analytical Period Six Sigma in Tumor Markers in Clinical Biochemistry Laboratory

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ABSTRACT

Objective: Six Sigma Methodology is a quality management methodology that provides information on process performance, focuses on variables in the process, and is based on statistical calculations.

Methods: In the present study, analytical period sigma scores in tumor markers were calculated by using monthly and cumulative quarterly data. The present study is the first study in which sigma scores calculated with different Total Allowable Error (TEa (%)) and bias (%) values are compared by using statistical tests and the frequency of six sigma application is discussed.

Results: When it was examined whether there was a statistically significant difference between the sigma scores that were calculated according to the biases obtained from the Internal Quality Control (IQC) and External Quality Control (EQC) data, although there was a significant difference in the Alpha-Fetoprotein (AFP) and Cancer Antigen 15.3 (CA 15.3) tests, no significant difference was found in the other tests. When the sigma scores that were calculated according to the TEa (%) values determined by the reference institutions were analyzed statistically, it was found that different TEa (%) values caused significant differences in sigma scores. When the sigma scores obtained by months and cumulatively were examined, it was found that there were significant differences between the examined periods.

Conclusion: As a conclusion, it is important to determine the optimal TEa (%) value in sigma score examinations and to monitor the quality by analyzing the sigma scores on a monthly basis in terms of the sustainability of the result quality of the tests and for the early detection of problems.

Keywords: Six sigma, tumor markers, quality control

1. INTRODUCTION

Clinical laboratories have important functions in the diagnosis and treatment of patients. Laboratory tests are applied to approximately 85% of patients applying to healthcare institutions (1). Clinical laboratories affect 60% – 70% of the diagnosis and treatment decisions (2). For this reason, the performance of laboratories affects the quality of healthcare institutions significantly. In clinical laboratories, the Total Testing Process (TTP) is divided into five periods; pre-preanalytical, preanalytical, analytical, postanalytical, and post-postanalytical (3). The performance of a laboratory test is evaluated by dividing the test process into periods based on quality indicators, sigma scores, and statistical criteria such as accuracy and repeatability (4,5).

Six Sigma Methodology is a quality management methodology that provides information on process performance, focuses on variables in the process, and is based on statistical calculations (6). This methodology, which has proven its benefits in the industrial field, has started to gain importance in healthcare and clinical laboratories. The analytical period sigma scores can be calculated with the following formula (7):'(TEa (%) – Bias (%)) / CV (%)'

The Total Allowable Error (TEa %) represents the maximum permissible error for ensuring the clinical reliability of a test. Values for TEa (%) are established by reference institutions such as the Clinical Laboratory Improvement Amendments (CLIA 88) and Richtlinien der Bundesärztekammer (RiliBÄK) and can be employed to calculate sigma scores. The coefficient of variation (CV (%)) is the ratio of the standard deviation to the mean, reflecting the extent of variability relative to the population mean. This statistic is particularly useful for comparing the variability between different data sets, even when their means differ significantly. A higher CV

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indicates greater distribution. Bias refers to the discrepancy between the true value of an analyte and its measured value, serving as an indicator of accuracy. The bias is determined by comparing the analyte values obtained through a test method with those from a reference method. Additionally, bias can be calculated using results from External Quality and Internal Quality Control assessments.

In the present study, analytical period sigma scores in tumor markers were calculated by using monthly and cumulative quarterly data. The purposes of the study were;

- Examining the relations between monthly and cumulative sigma scores,

- Examining the relations between the sigma scores calculated according to the TEa (%) values determined by the reference institutions,

- Examining the relations between sigma scores calculated according to the bias (%) values obtained from IQC and EQC materials,

- With the data obtained, providing perspective on which data should be used to calculate analytical period sigma scores and how often six sigma should be evaluated.

- The present study is the first study in which sigma scores calculated with different TEa (%) and bias (%) values are compared by using statistical tests and the frequency of six sigma application is discussed.

2. METHODS

In the present study, the IQC and EQC data of the tumor markers AFP, CA 15.3, Cancer Antigen 19.9 (CA 19.9), Cancer Antigen 125 (CA 125), Carcinoembryonic Antigen (CEA), and Total Prostate Specific Antigen (TPSA) tests were used. The IQC and EQC samples were examined by using the Electrochemiluminescent Method on the Cobas 8000 e602 (Roche Diagnostics GmbH, Mannheim, Germany) autoanalyzer in the Biochemistry Laboratory. Elecsys PC TM 1 (Lot: 297057) and PC TM 2 (Lot: 297059) were used as the IQC samples. The two-level IQC results examined between April and June 2019 were obtained retrospectively from the recordings of the Cobas 8000 e 602 device in our laboratory. Internal quality results outside the acceptable range due to random errors were not included in our study. Random error causes may be the using of wrong quality control material by the staff, incorrect dilution of the quality control material, using of control material that is not suitable for storage conditions, etc. Single-level Quality Systems Immunoassay (Bio Group Medical System, Italy) EQC materials were used as the EQC samples. The EQC data of each month examined in April-May-June were obtained retrospectively from the Quality Systems Website.

TEa (%) Sources: The TEa (%) values determined by EQA standards of China, RCPA standards, Biological variation, RiliBÄK, and CLIA for each of the AFP, CA 15-3, CA 19-9, CA 125, CEA and TPSA tests, which were used in the study are shown in Table 1 (8,9).

Table 1. *Total Allowable Error (TEa (%)) values of references institutions*

	Total Allowable Error (TEa (%)) VALUES of REFERENCES INSTITUTIONS				
TESTS	**EQA Standards of China**	**RCPA standards**	**Biologicalvariation**	**RiliBÄK**	**CLIA**
AFP	25	20	21.8	24	24
CA 125	25	15	35.4	24	24
CA 15-3	25	20	20.8	24	24
CA 19-9	25	15	39	24	24
CEA	25	20	24.7	24	24
TPSA	25	20	33.6	25	24

EQA standards of China: External quality assessment standards of China; RCPA: The Royal Collage of Pathologists of Australasia; RiliBÄK: Guideline of the German Medical Association on Quality Assurance in Medical Laboratory Examinations; CLIA: Clinical Laboratory Improvement Amendments; AFP: Alpha-Fetoprotein; CA 125: Cancer Antigen 125; CA 15.3: Cancer Antigen 15.3; CA 19.9: Cancer Antigen 19.9; CEA: Carcinoembryonic Antigen; TPSA: Total Prostate Specific Antigen

CV (%) was calculated from the IQC data over the three-month period using the equality:

'(Standard deviation × 100)/ laboratory mean (IQC)'

Two different levels of IQC samples were analyzed. CV (%) was calculated using monthly IQC results and cumulative 3-month IQC results.

Bias was calculated from the EQC data using the equality:

'(mean of all laboratories – our mean)/ (mean of all laboratories) × 100'

The arithmetic mean of the calculated biases was used as the bias in the cumulative sigma calculation.

Bias was calculated from the IQC results using the equality:

'(Our mean – target mean)/ (target mean) × 100'

Our mean was calculated using monthly IQC results and cumulative 3-month IQC results.

The sigma scores was calculated separately according to the quality control material from which the bias value was obtained and according to each TEa (%) value that was employed. The process sigma levels were calculated monthly and cumulatively 3-month for both internal quality control levels. The following formula was used to calculate the sigma score:

'(TEa (%) – bias (%)) / CV (%)'

The sigma scores of each test were examined in 4 groups according to the periodically as April, May, June, and cumulative, and in 2 groups according to the quality control material from which the bias value was obtained. Sigma scores that were calculated according to TEa (%) values

determined by reference institutions were examined in 5 groups.

The comparison of sigma scores between periods, between the quality control material from which the bias value was obtained, and according to the different TEa (%) values determined by the reference institutions were evaluated with statistical tests. The relations between the sigma scores that were calculated according to the biases obtained from the IQC and EQC data were evaluated statistically with correlation tests. Microsoft Office Excel program was used to calculate the mean, standard deviation (SD), CV (%), bias (%), and sigma score. Statistical analyses were conducted using SPSS version 25.0 (SPSS, Chicago, IL, USA). The normality of the data distribution within groups was assessed using both visual and analytical methods. Data following a normal distribution were presented as mean ± standard deviation (SD), while non-normally distributed data were reported as median (minimum-maximum). For comparisons of more than two independent groups with non-normally distributed data, the Kruskal-Wallis test was utilized. The One-Way ANOVA test was employed for comparing normally distributed data across more than two independent groups. When comparing two independent groups, the Mann-Whitney U Test was used for non-normally distributed data, and the Independent-Sample T Test was applied for normally distributed data. Correlations for non-normally distributed data were assessed using the Spearman Correlation Coefficient, while correlations for normally distributed data were evaluated using the Pearson Correlation Coefficient. A P value of <0.05 was considered statistically significant.

3. RESULTS

April, May, June, cumulative, and 3-month sigma scores of AFP, CA 15-3, CA 19-9, CA 125, CEA, and total PSA tests are given in the table (Table 2).

Table 2. *Sigma scores of tumor markers*

CA 125 PROCESS SIGMA SCORES									
REFERENCES INSTITUTIONS	CONTROL MATERIAL	APRIL		MAY		JUNE		CUMULATIVE	
		LEVEL1	LEVEL2	LEVEL1	LEVEL2	LEVEL1	LEVEL2	LEVEL1	LEVEL2
EQA Standards of China	INTERNAL	10.65	15.36	9.14	11.52	9.39	9.55	8.60	10.88
	EXTERNAL	13.46	16.50	9.69	10.11	10.81	9.82	10.04	10.84
RCPA	INTERNAL	7.61	11.64	6.61	8.88	7.07	7.45	6.27	8.36
	EXTERNAL	10.42	12.77	7.15	7.46	8.49	7.71	7.71	8.32
Biological variation	INTERNAL	16.96	23.10	14.41	17.02	14.21	13.94	13.45	16.12
	EXTERNAL	19.77	24.24	14.96	15.61	15.64	14.21	14.89	16.07
RiliBÄK	INTERNAL	10.04	14.62	8.63	11.00	8.92	9.13	8.13	10.38
	EXTERNAL	12.85	15.75	9.18	9.58	10.35	9.40	9.57	10.33
CLIA	INTERNAL	10.04	14.62	8.63	11.00	8.92	9.13	8.13	10.38
	EXTERNAL	12.85	15.75	9.18	9.58	10.35	9.40	9.57	10.33
AFP PROCESS SIGMA SCORES									
EQA Standards of China	INTERNAL	9.36	12.78	8.17	7.55	9.99	11.42	9.12	8.30
	EXTERNAL	10.16	10.81	8.84	7.39	7.30	7.39	8.80	6.83
RCPA	INTERNAL	6.94	10.21	6.06	5.79	7.46	8.86	6.77	6.48
	EXTERNAL	7.75	8.24	6.73	5.62	4.77	4.83	6.46	5.01
Biological variation	INTERNAL	7.81	11.13	6.82	6.42	8.37	9.78	7.62	7.14
	EXTERNAL	8.62	9.17	7.49	6.26	5.68	5.75	7.31	5.67
RiliBÄK	INTERNAL	8.87	12.26	7.75	7.20	9.49	10.91	8.65	7.94
	EXTERNAL	9.68	10.30	8.41	7.03	6.80	6.88	8.34	6.46
CLIA	INTERNAL	8.87	12.26	7.75	7.20	9.49	10.91	8.65	7.94
	EXTERNAL	9.68	10.30	8.41	7.03	6.80	6.88	8.34	6.46
CA 15.3 PROCESS SIGMA SCORES									
EQA Standards of China	INTERNAL	9.75	8.22	7.27	7.11	5.48	6.34	6.89	7.13
	EXTERNAL	7.43	7.50	2.78	2.99	5.89	6.96	4.95	5.76
RCPA	INTERNAL	5.78	4.22	4.24	3.85	2.99	3.40	4.02	3.79
	EXTERNAL	3.47	3.50	-0.25	-0.27	3.40	4.02	2.07	2.41
Biological variation	INTERNAL	8.08	6.54	6.00	5.75	4.43	5.11	5.69	5.73
	EXTERNAL	5.77	5.82	1.51	1.62	4.84	5.73	3.74	4.35
RiliBÄK	INTERNAL	9.35	7.82	6.97	6.79	5.23	6.05	6.61	6.80
	EXTERNAL	7.04	7.10	2.48	2.66	5.64	6.67	4.66	5.42
CLIA	INTERNAL	9.35	7.82	6.97	6.79	5.23	6.05	6.61	6.80
	EXTERNAL	7.04	7.10	2.48	2.66	5.64	6.67	4.66	5.42

CA 19.9 PROCESS SIGMA SCORES									
EQA Standards of China	INTERNAL	11.88	8.71	9.16	13.85	6.75	5.18	8.51	7.69
	EXTERNAL	11.45	10.38	8.18	12.91	7.00	6.12	8.20	8.41
RCPA	INTERNAL	7.11	4.38	5.13	7.51	3.81	2.61	4.90	3.99
	EXTERNAL	6.67	6.04	4.16	6.56	4.06	3.55	4.59	4.70
Biological variation	INTERNAL	18.58	14.78	14.79	22.74	10.86	8.78	13.57	12.87
	EXTERNAL	18.14	16.44	13.82	21.79	11.11	9.72	13.25	13.59
RiliBÄK	INTERNAL	11.41	8.28	8.75	13.22	6.46	4.92	8.15	7.32
	EXTERNAL	10.97	9.94	7.78	12.27	6.70	5.86	7.84	8.04
CLIA	INTERNAL	11.41	8.28	8.75	13.22	6.46	4.92	8.15	7.32
	EXTERNAL	10.97	9.94	7.78	12.27	6.70	5.86	7.84	8.04
CEA PROCESS SIGMA SCORES									
EQA Standards of China	INTERNAL	5.83	5.97	13.44	17.19	10.44	11.79	7.55	8.76
	EXTERNAL	4.44	3.86	13.05	13.49	13.88	11.97	7.54	6.95
RCPA	INTERNAL	4.42	4.74	10.11	13.74	7.54	9.28	5.64	7.00
	EXTERNAL	3.03	2.63	9.71	10.04	10.98	9.47	5.63	5.19
Biological variation	INTERNAL	5.75	5.89	13.24	16.99	10.27	11.64	7.44	8.66
	EXTERNAL	4.36	3.79	12.85	13.29	13.70	11.82	7.43	6.84
RiliBÄK	INTERNAL	5.55	5.72	12.78	16.50	9.86	11.29	7.17	8.41
	EXTERNAL	4.16	3.62	12.38	12.80	13.30	11.47	7.16	6.60
CLIA	INTERNAL	5.55	5.72	12.78	16.50	9.86	11.29	7.17	8.41
	EXTERNAL	4.16	3.62	12.38	12.80	13.30	11.47	7.16	6.60
TOTAL PSA PROCESS SIGMA SCORES									
EQA Standards of China	INTERNAL	14.47	13.00	11.97	12.37	8.41	7.38	11.09	10.18
	EXTERNAL	12.87	11.71	13.33	13.81	8.38	7.31	11.10	10.23
RCPA	INTERNAL	11.21	10.03	9.21	9.51	6.55	5.76	8.58	7.87
	EXTERNAL	9.61	8.74	10.57	10.94	6.52	5.69	8.59	7.92
Biological variation	INTERNAL	20.09	18.11	16.73	17.30	11.60	10.17	15.40	14.15
	EXTERNAL	18.48	16.82	18.09	18.73	11.58	10.09	15.42	14.20
RiliBÄK	INTERNAL	14.47	13.00	11.97	12.37	8.41	7.38	11.09	10.18
	EXTERNAL	12.87	11.71	13.33	13.81	8.38	7.31	11.10	10.23
CLIA	INTERNAL	13.82	12.41	11.42	11.80	8.03	7.06	10.58	9.71
	EXTERNAL	12.22	11.12	12.78	13.23	8.01	6.98	10.60	9.76

EQA standards of China: External quality assessment standards of China; RCPA: The Royal Collage of Pathologists of Australasia; RiliBÄK: Guideline of the German Medical Association on Quality Assurance in Medical Laboratory Examinations; CLIA: Clinical Laboratory Improvement Amendments; AFP: Alpha-Fetoprotein; CA 125: Cancer Antigen 125; CA 15.3: Cancer Antigen 15.3; CA 19.9: Cancer Antigen 19.9; CEA: Carcinoembryonic Antigen; TPSA: Total Prostate Specific Antigen

Table 3. *Correlation and comparison of the sigma scores that were calculated according to the biases obtained from the Internal Quality Control (IQC) and External Quality Control (EQC) data*

	N	IQC (n=40)	EQC (n=40)	P value (Comparison)	Pearson Correlation	Spearman's rho	P value (Correlation)
CA 125**	40	10.04 (6.27-23.10)	10.34 (7.15-24.24)	0.223		0.862	<.001
AFP*	40	8.66±1.77	7.51±1.57	.003	0.543		<.001
CA 15 3*	40	6.22±1.61	4.48±2.08	<.001	0.557		<.001
CA 19.9**	40	8.28 (2.61-22.74)	8.13 (3.55-21.79)	0.977		0.955	<.001
CEA**	40	8.71 (4.42-17.19)	8.51 (2.63-13.88)	0.450		0.871	<.001
TPSA*	40	11.37±3.26	11.5±3.24	0.982	0.951		<.001

**Values were expressed as means±SD.*

***Values were expressed as median (min-max)*

IQC, internal quality control; EQC, external quality control; AFP: Alpha-Fetoprotein; CA 125: Cancer Antigen 125; CA 15.3: Cancer Antigen 15.3; CA 19.9: Cancer Antigen 19.9; CEA: Carcinoembryonic Antigen; TPSA: Total Prostate Specific Antigen

Table 4. *Comparison of the sigma scores that were calculated according to Total Allowable Error (TEa (%)) values determined by the reference institutions*

	EQA Standards of China	RCPA	Biological variation	RİLİBAK	CLIA	P value
CA 125**	10.38 (8.60-16.50)	7.71 (6.27-12.77)	15.62 (3.45-24.24)	9.81 (8.13-15.75)	9.81 (8.13-15.75)	<.001
AFP*	9.01±1.67	6.74±1.49	7.56±1.55	8.56±1.63	8.56±1.63	.001
CA 15 3**	6.92 (2.78-9.75)	3.48 (-0.27-5.78)	5.71 (1.51-8.08)	6.64 (2.48-9.35)	6.64 (2.48-9.35)	<.001
CA 19.9*	9.02±2.45	4.98±1.40	14.67±4.00	8.61±2.35	8.61±2.35	<.001
CEA*	9.75±3.92	7.44±3.15	9.62±3.88	9.29±3.77	9.29±3.77	.402
TPSA*	11.10±2.27	8.58±1.76	15.43±3.18	11.10±2.27	10.59±2.17	<.001

**Values were expressed as means±SD.*

***Values were expressed as median (min-max)*

EQA standards of China: External quality assessment standards of China; RCPA: The Royal Collage of Pathologists of Australasia; RiliBÄK: Guideline of the German Medical Association on Quality Assurance in Medical Laboratory Examinations; CLIA: Clinical Laboratory Improvement Amendments; AFP: Alpha-Fetoprotein; CA 125: Cancer Antigen 125; CA 15.3: Cancer Antigen 15.3; CA 19.9: Cancer Antigen 19.9; CEA: Carcinoembryonic Antigen; TPSA: Total Prostate Specific Antigen

The sigma scores of each test were examined in two groups according to the quality control material from which the bias value was obtained.The correlation of the sigma scores that were calculated according to the biases obtained from the IQC and EQC data in CA 125, CA 19.9, and CEA tests with the Spearman Test, and in AFP, CA 15.3, and TPSA tests with the Pearson Test was examined. In the CA 125, CA 19.9, and CEA tests a strong positive correlation, AFP and CA 15.3 tests a weak-moderate positive correlation, and TPSA test a strong positive correlation was found (r=0.862-0.955-0.871-0.543-0.557-0.951, respectively) (Table 3). The distribution of the point graphs of the sigma scores that were calculated according to the biases obtained from the IQC and EQC data of each test are given in figure 1.

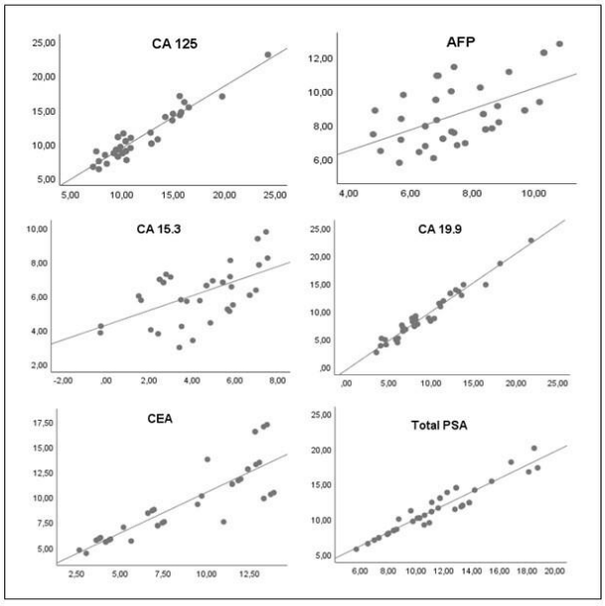

Figure 1. *Distribution of the point graphs of the sigma scores that were calculated according to the biases obtained from the Internal Quality Control (IQC) and External Quality Control (EQC) data (x-axis: sigma score determined according to the bias (%) value obtained from EQC data; y-axis: sigma score determined according to the bias (%) value obtained from IQC data)*

When it was evaluated whether there was a statistically significant difference between the sigma scores that were calculated according to the biases obtained from the IQC and EQC data, although there were significant differences in the AFP and CA 15.3 tests, no significant differences were detected in the other tests (Table 3).

Sigma scores that were calculated according to TEa (%) values determined by the reference institutions were examined in 5 groups. Only the CEA test sigma scores did not differ at significant levels according to different TEa (%) values determined by the reference institutions (Table 4).

The sigma scores of each test were examined in 4 groups according to the periodically as April, May, June, and cumulative. The each test, sigma scores were found to be significantly difference according to periodically (Table 5).

Table 5. *Comparison of sigma scores according to period*

	APRIL	MAY	JUNE	CUMULATIVE	P value
CA 125**	14.40 (7.61-24.24)	9.58 (6.61-17.02)	9.40 (7.07-15.64)	10.18 (6.27-16.12)	.001
AFP*	9.76±1.57	7.19±0.89	7.98±2.03	7.41±1.12	<.001
CA 15 3**	7.10 (3.47-9.75)	3.42 (-0.27-7.27)	5.56 (2.99-6.96)	5.42 (2.07-7.13)	<.001
CA 19.9**	10.67 (4.38-18.58)	10.71 (4.16-22.74)	6.29 (2.61-11.11)	8.04 (3.99-13.59)	<.001
CEA**	4.43 (2.63-5.97)	12.95 (9.71-17.19)	11.38 (7.54-13.88)	7.16 (5.19-8.76)	<.001
TPSA**	12.87 (8.74-20.09)	12.57 (9.21-18.73)	7.69 (5.69-11.60)	10.40 (7.87-15.42)	<.001

**Values were expressed as means±SD.*

***Values were expressed as median (min-max)*

AFP: Alpha-Fetoprotein; CA 125: Cancer Antigen 125; CA 15.3: Cancer Antigen 15.3; CA 19.9: Cancer Antigen 19.9; CEA: Carcinoembryonic Antigen; TPSA: Total Prostate Specific Antigen

4. DISCUSSION

Six Sigma shows the details necessary to improve the quality and efficiency of processes. The process begins with a clear understanding of what the required performance is. Then, with the help of Six Sigma, the root causes of problems are revealed, analyzed, and various statistical tools are applied to avoid them (10).

In the present study, two different sigma scores were calculated according to the bias values obtained from the IQC and EQC data. When it was examined whether there was a statistically significant difference between the sigma scores that were calculated according to the biases obtained from the IQC and EQC data, although there was a significant difference in the AFP and CA 15.3 tests, no significant difference was found in the other tests (Table 3). The significant difference detected in the two tests in our study shows that six sigma practitioners must consider the source of the bias data. The optimal method is to compare results obtained from fresh human specimens using the measurement procedure and a reference measurement procedure. In our literature review, it was found that the bias values obtained from the EQC data were generally used in sigma score calculations. In a study that was conducted by Aslan et al. (11), bias values that were obtained from IQC results were used in sigma score calculations. Some researchers recommend using the bias from EQC results (12). If bias calculation cannot be made with the optimal method, we recommend using the CV (%) value from the IQC data and the bias (%) value from the EQC data to ensure that the data of two quality control materials used in clinical biochemistry laboratories are included as a variable in the calculation of the sigma score.

When the sigma scores that were calculated according to the TEa (%) values determined by the reference institutions were analyzed statistically, it was found that different TEa (%) values caused significant differences in sigma scores (Table 4). Liu et al. calculated the sigma scores of tumor markers (AFP, CA 15-3, CA 19-9, CA 125, CEA, and TPSA) according to different TEa (%) sources, as was the case in the present study (8). There is no appropriate consensus to set a TEa (%) target for an assay. The choice of TEa (%) value can lead to significant differences in the evaluation of the sigma score and can also have a significant impact on laboratory operational routines. Choosing a high TEa (%) value leads to the possibility of missing errors while choosing a low TEa (%) value leads to false outliers. The optimal TEa (%) should be determined based on the requirements and conditions of the laboratory, and the suitability of the TEa (%) for clinical use should be evaluated.

The present study is the first in this field in which short and long-term sigma scores were compared. When the sigma scores obtained by months and cumulatively were examined, it was found that there were significant differences between the examined periods (Table 5). For this reason, we think that 3-month or longer-term sigma score calculations may be insufficient to reflect the problems occurring in the past. We suggest that laboratories must follow their sigma scores monthly and take corrective and preventive actions according to the data they obtain.

5. CONCLUSION

As a conclusion, it is important to determine the optimal TEa (%) value in sigma score examinations and to monitor the quality by analyzing the sigma scores on a monthly basis in terms of the sustainability of the result quality of the tests and for the early detection of problems.

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