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Evaluation of Blood Gas Instruments with 6 Sigma Methodology

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ABSTRACT

Purpose: 6 sigma is one of the most effective quality tools for demonstrating laboratory analytical performance. 6 sigma tells us what level we are at and what rules to follow in case of poor performance. Blood gas analysis plays an important role in the assessment of critical illness, determining the aetiology and severity of disease. In our study, we aimed to evaluate the test performance of blood gas instruments in our hospital with 6 sigma methodology.

Methods: The study included pH, p0₂, pCO₂, glucose, lactate, ionised Ca, Na, K and Cl parameters analysed on Siemens RAPIDpoint 500e blood gas instruments in the emergency laboratory. In the sigma metric calculation TEa (total permissible error) rates, the values determined by RiliBAK (German Guidelines for Quality) were used. The causes of errors of poorly performing tests were evaluated with the quality goal index (QGI).

Results: At the results, PCO_2 (Level 2) in Instrument I, Lactate (Level 1-2) in Instrument II and pCO_2 (Level 1-2) in Instrument III are the tests with sigma values below 4. When we look at the low performance problems, precision in Instrument I pCO_2 (Level 2), accuracy in Instrument II lactate (Level 1-2) and accuracy in Instrument III pCO_2 (Level 1-2) were detected.

Conclusion: This study has allowed us to monitor laboratory blood gas testing performance very closely. With the 6 sigma methodology we have captured underperforming tests and investigated the reasons behind them

Keywords: Quality goal index, 6 Sigma, Total allowable error, Westgard rule, Bias

ÖZET

Amaç: 6 sigma, laboratuvar analitik performansını göstermek için en etkili kalite araçlarından biridir. 6 sigma bize hangi seviyede olduğumuzu ve kötü performans durumunda hangi kuralları izlememiz gerektiğini söyler. Kan gazı analizi, kritik hastalıkların değerlendirilmesinde, hastalığın etiyolojisinin ve ciddiyetinin belirlenmesinde önemli bir rol oynar. Çalışmamızda, hastanemizdeki kan gazı cihazlarının test performansını 6 sigma metodolojisi ile değerlendirmeyi amaçladık.

Yöntem: Çalışmaya acil laboratuvarında Siemens RAPIDpoint 500e kan gazı cihazlarında analiz edilen pH, pO₂, pCO₂, glukoz, laktat, iyonize Ca, Na, K ve CI parametreleri dahil edildi. Sigma metrik hesaplamasında TEa (toplam izin verilebilir hata) oranlarında RiliBAK (Alman Kalite Rehberi) tarafından belirlenen değerler kullanılmıştır. Kötü performans gösteren testlerin hata nedenleri kalite hedef indeksi (QGI) ile değerlendirildi.

Bulgular: Sonuçlara bakıldığında Cihaz I'de PCO₂ (Seviye 2), Cihaz II'de Laktat (Seviye 1-2) ve Cihaz III'de pCO₂ (Seviye 1-2) sigma değerleri 4'ün altında olan testlerdir. Düşük performans sorunlarına baktığımızda ise Alet I pCO₂'de hassasiyet (Seviye 2), Alet II laktatta doğruluk (Seviye 1-2) ve Alet III pCO₂'de doğruluk (Seviye 1-2) tespit edilmiştir.

Sonuç: Bu çalışma, laboratuvar kan gazı test performansını çok yakından izlememizi sağladı. 6 sigma metodolojisi ile düşük performans gösteren testleri yakaladık ve bunların arkasındaki nedenleri araştırdık.

Anahtar Kelimeler: Kalite hedef indeksi, 6 Sigma, İzin verilen toplam hata, Westgard kuralı, Yanlılık

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aboratory specialists are required to monitor point of care (POCT) devices that perform medical measurements at the patient's bedside, in addition to their own medical devices, in terms of quality requirements. The most important of these is blood gas devices.Blood gas analysis has an important role in the evaluation of critical illnesses and in determining the etiology and severity of diseases. It is widely used to assess the patient's metabolic status, causes of impaired gas exchange, oxygenation and all metabolic functions.In addition to the importance of arterial blood gas in making a diagnosis, especially in emergency situations, blood gas evaluation is extremely important in monitoring the effectiveness of invasive and noninvasive mechanical ventilation applied in patients with respiratory failure, monitoring long-term oxygen therapy users, and evaluating early targeted treatment in patients with sepsis and septic shock (1-3).

Apart from the oxygenation-ventilation (pO₂, SaO2, pH, pCO₂ and HCO3) parameters examined in the blood gas, tests (Glucose, Lactate, iCa, Na, K, Cl,...etc.) are nowadays being added in such a way that they almost look like biochemistry analysers and blood counting devices (4-6). These parameters can be analysed in a very small blood sample and in a very short period of time, saving the clinician a great deal of time and enabling early diagnosis and treatment.Nowadays, due to the high number of patients admitted to the emergency department, clinicians use blood gas test requests until the routine laboratory tests of the patients are concluded, making the operation of the emergency department faster. In this case, laboratory specialists should follow the device follow-up and responsibility even more seriously considering the increasing blood gas test requests.

Each laboratory maintain its own quality monitoring and performancemonitoring at the most basic level with internal quality control and external quality control programmes. In addition to these, measurement uncertainty, precision, bias and total analytical error measurements are other quality indicators of analytical performance (7). It is not possible to capture and demonstrate laboratory errors only with internal quality control (IQC) and eksternal quality assessment programs (EQAS). This leads us to the 6 Sigma methodology, which is one of the different quality strategies.6 Sigma is a data-driven quality management system for identifying and reducing errors and variations in clinical laboratory processes. 6 Sigma is the ultimate measure of all processes that can fit within 6 Standard Deviations (SD) (\pm 3SD) on either side of the mean (8,9). It is a uniform way of defining quality in terms of defects per million opportunities.6 Sigma performances represent 3.4 defects per million operations. It shows how close the 6 Sigma value is to the world standard quality value or deviates from perfection (10).

A high sigma level means that analytical errors are low and test results are acceptable, whereas a low sigma level is considered an error and reduces the reliability of the process. When the sigma value is low, the quality target index (QGI) should be calculated to determine the underlying causes and test-specific performance deficiencies (11).

In our study, we aimed to evaluate the test performance of blood gas devices in our hospital with 6 sigma methodology.

Materials and Methods

The study included three Siemens RAPIDpoint 500e gas analysers in Ümraniye Training and Research Hospital's emergency laboratory. The pH, pO₂, pCO₂, glucose, lactate, ionised Ca, Na, K and Cl parameters in blood gases were used.

From the IQC data, %CV values for each level were calculated according to the formula below.

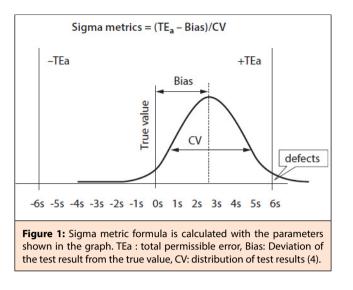
 $CV\% = SD/mean \times 100$

External control membership of the instruments belong to the Qualicont programme. Bias data were taken from one month external quality control report. Bias data were calculated according to the formula below.

Bias %= (mean of laboratories using the same instrument and method) - (laboratory result)/ mean of laboratories using the same instrument and method x 100

Total allowable error percentages (TEa%) are taken from the RILIBAK 2014 guidelines (12).

The sigma metric values for each parameters were calculated according to the following formula and are shown graphically in Figure 1 in the appendix (11).



Sigma $\Sigma(\sigma) = (TEa \% - Bias\%) / CV\%$

Defects defined in Sigma metrics are measured in percentage defects or defects per million (DPM: defects per million). 1 Sigma represents 690,000 defects/million reports. 2 Sigma represents 308,000 defects/million reports. 3 Sigma represents 66,800 defects/million reports. 4 Sigma represents 6,210 defects/million reports. 5 Sigma represents 230 defects/million reports. 6 Sigma represents 3.4 defects/million reports. Therefore, any process greater than 6 Sigma indicates a very low variability and error rate. Depending on the sigma obtained, the process is divided into the following categories (8-10).

- >6: World class performance
- 5-6 : Excellent
- 4-5 : Good
- 3-4 : Acceptable
- 2-3 : Poor
- <2 : Unacceptable

For analytes with sigma metric values of 4 and below, the QGI (quality goal index) value was calculated according to the formula below. QGI is calculated to identify the reasons for analytes deviating from accuracy and precision. QGI<0.8 indicates deviation from accuracy, QGI =0.8-1.2 indicates deviation from accuracy and deviation from precision, QGI>1.2 indicates deviation from accuracy (10).

 $QGI = Bias / (1.5 \times CV)$

Results

The 1-month internal quality control two-level CVs of 3 different blood gas instruments in our emergency laboratory, bias values obtained from the external quality control report and 6 Sigma metric values calculated for each control level are given in Table 1(A-B) below. TEa percentages obtained from the RILIBAK 2014 guideline are also shown in the Table 1A.

Ta	ible 1A: Intern	al quality cont	rol CVs fror	n 3 different b	lood gas devi	ces and RIL	IBAK 2014 gui	deline TEa per	centages.	
Α	I	nstrument l		h	nstrument II		Ir			
	Level 1 CV	Level 2 CV	% bias	Level 1 CV	Level 2 CV	% bias	Level 1 CV	Level 2 CV	% bias	TEA %
рН	0,10	0,09	0,171	0,07	0,10	0,144	0,08	0,09	0,367	0,8
pO2	1,72	1,75	3,225	1,74	1,97	3,16	2,12	2,18	0,322	12
pCO2	2,51	2,72	1,364	2,29	2,13	0,455	2,25	2,47	10,908	12
Glucose	0,82	0,70	1,882	0,72	0,73	4,441	0,91	0,64	2,861	15
Lactate	3,25	3,45	2,793	3,20	3,15	8,382	3,20	3,12	2,058	18
iCa	1,10	1,48	2,173	1,13	0,94	6,521	1,05	0,71	2,173	15
Na	0,52	0,67	1,528	0,76	0,64	0,063	0,59	0,64	1,591	5
к	0,34	0,35	1,432	0,37	0,33	0,158	0,55	0,70	1,433	8
CI	0,38	0,61	1,638	0,38	0,80	1,638	0,39	0,49	0,82	8

Table 1B: 6 Sigma metric calculations and performance results											
В	Instru	ment l	Instru	ment II	Instrun	nent III					
	Level 1 CV	Level 2 CV	Level 1 CV	Level 2 CV	Level 1 CV	level 2 CV					
рН	6,51	6,87	10,08	6,79	5,45	4,70					
pO2	5,10	5,01	5,08	4,49	5,51	5,36		6 Sigma Metric			
pCO2	4,24	3,91	5,04	5,42	0,49	0,44		values			
Glucose	15,96	18,65	14,58	14,53	13,36	18,83		>6			
Lactate	4,68	4,41	3,01	3,05	4,98	5,11		5 - 6			
iCa	11,67	8,66	7,48	9,05	12,20	18,08		4 - 5			
Na	6,65	5,15	6,50	7,76	5,78	5,33		3 - 4			
к	19,28	18,62	21,25	23,89	11,86	9,34		2-3			
сі	16,83	10,49	16,83	7,98	18,55	14,68		<2			

When we look at the 6 Sigma metric values of the parameters from the Instrument I blood gas anaylser in our emergency laboratory, the parameters that resulted as >6 are pH (Level 1-2), Glucose (Level 1-2), iCa (Level 1-2), Na (Level 1-2), K (Level 1-2) and Cl (Level 1-2), respectively. Parameters with a 6 Sigma metric value between 5-6 are pO₂ (Level 1-2) and Na (Level2), respectively. Parameters with a 6 Sigma metric value between 4-5 are pCO₂ (Level 1) and Lactate (Level 1-2), respectively. Parameters with a 6 Sigma metric value between 3-4 are pCO₂ (Level 2). There are no parameters with a 6 Sigma metric value of 2-3 and <2. (Table 1.B).

When we look at the 6 Sigma metric values of the parameters from the instrument II blood gas analyser, the parameters that resulted as >6 were pH (Level 1-2), Glucose (Level 1-2), iCa (Level 1-2), Na (Level 1-2), K (Level 1-2) and Cl (Level 1-2), respectively.Parameters with a 6 Sigma metric value between 5-6 are pO₂ (Level 1) and pCO₂ (Level 1-2), respectively. Parameters with a 6 Sigma metric value between 4-5 are pO₂ (Level 2). Parameters with a 6 Sigma metric value between 3-4 are Lactate

(Level 1-2). There are no parameters with a 6 Sigma metric value of 2-3 and <2 (Table 1.B).

When we look at the 6 Sigma metric values of the parameters from the instrument III blood gas analyser, the parameters that resulted as >6 were Glucose (Level 1-2), iCa (Level 1-2), K (Level 1-2) and Cl (Level 1-2), respectively. Parameters with 6 Sigma metric values between 5-6 are pH (Level 1), pO₂ (Level 1-2), Lactate (Level 2) and Na (Level 1-2). Parameters with 6 Sigma metric values between 4-5 are pH (Level 2) and Lactate (Level 1). There are no parameters with a 6 Sigma metric value of 3-4 and 2-3. Parameters with a 6 Sigma metric value <2 are pCO₂ (Level 1-2) (Table 1.B).

The 6 Sigma Method decision graphs of the parameters whose metric values were calculated are shown in Figure 2 (A-B-C-D-E-F) below. In Instrument I, 94% of the tests resulted in sigma metric values above 4. In Intrument II, 88.8% of the tests resulted in sigma metric values above 4 and in Intrument III, 88.8% of the tests resulted in sigma metric values above 4 (Table 3).

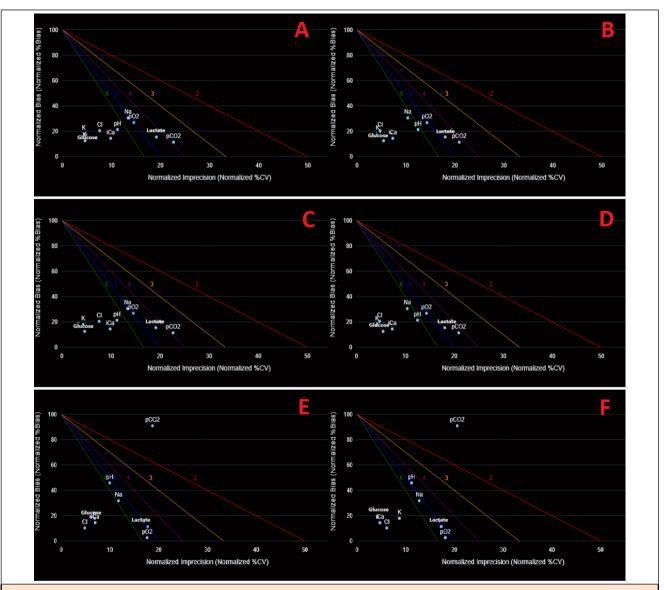


Figure 2. 6 Sigma Method Decision Graph.

A: Instrument I Level 1 Sigma calculations, B: Instrument I Level 2 Sigma calculations, C: Instrument II Level 1 Sigma calculations, D Instrument II Level 2 Sigma calculations, E: Instrument III Level 1 Sigma calculations, F: Instrument III Level 2 Sigma calculations

Table 2: QGI values for analytes with Sigma metric values of 4 and below for all 3 instruments and reasons for poor performance and recommended Westgard rules.													
	Sigma Value						QGI						
Test		I		1	I			I II III		п			
	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	L1	L2	
pCO2		3,91			0,49	0,44		0,33			3,23	2,95	
Lactate			3,01	3,05					1,75	1,77			
		a	n		n			n	n				

Recommended Westgard Rules

	poor performance result								
Test	I	П	Ш						
pCO2	Level 2 precision		Level 1 ve 2 accuracy						
Lactate		Level 1 ve 2 accuracy							

Table 3 : Blood gas instruments performance chart, Number of defects (%)										
	none precision accuracy both									
Instrument I	17 (94.4%)	1 (5.5%)	0	0						
Instrument II	16 (88.8%)	0	2 (11.1%)	0						
Instrument III	16 (88.8%)	0	2 (11.1%)	0						

For tests with sigma metric values below 4, QGI values were calculated and the reason for the poor performance was shown. PCO_2 (Level 2) in Instrument I, Lactate (Level 1-2) in Instrument II and pCO_2 (Level 1-2) in Instrument III are the ones with sigma values below 4. Instrument I pCO_2 (Level 2) deviates from precision, Device II lactate (Level 1-2) deviates from accuracy and Device III pCO_2 (Level 1-2) deviates from accuracy (Table 2).

However, the recommended Westgard Sigma rules are also specified (Table 2).

Discussion

Sigma metrics is an improvement method that focuses on reducing variability in laboratory results. Unlike the traditional total quality management model, the six sigma model advocates five steps. These five steps are define, measure, analyze, improve and control (DMAIC: define, measure, analyze, improve and control). 6 Sigma is an excellent tool for estimating and comparing measurement and instrument quality and is a pointer for tests that require minimum quality control rules to monitor the performance of the method. Based on the sigma values obtained, quality control can be adapted as follows (9,13,14):

1.> 6σ (Excellent performance): IQC (internal quality control) can be run once a day and one level (alternating levels) and is followed by the 13.5s rule.

2. 4σ-6σ (fit for purpose): IQC can be run once a day and two levels at a time. The single IQC rule is followed.

3. 3σ - 4σ (Poor performers): IQC can be run twice a day and two levels at a time and is followed using multiple rules.

4.<3σ (Problematic): IQC must be run three times a day with three levels. The test can be run repeatedly and should use the maximum IQC rule.

As this classification suggests, analytes with >6 sigma require very few quality control rules to monitor method performance. If the sigma is <3 or shows a wide variation between the two levels, it is imperative to closely monitor and even modify the method using multiple quality control rules (15).

In our Emergency Laboratory, the levels of pCO2 (Level 2) in Instrument I, Lactate (Level 1-2) in Instrument II and pCO₂ (Level 1-2) in Instrument III, which resulted in a sigma value <4 in blood gases, have started to be monitored more closely and have been put under monitoring. For the test where we scored low sigma value in Instrument III pCO₂ (Level 1-2), corrective preventive action was initiated to investigate the factor affecting the test performance and to find the root cause. calibration frequencies were increased to reduce bias or in-service training of employees was renewed to reduce CV. For instrument-related errors, issues such as review of temperature, humidity and optical parts, proper preparation of kit/control material, kit expiry date monitoring were taken into consideration. The number of daily control runs was ensured to be more in line with quality control procedures.

In diseases requiring intensive care, intensive monitoring such as arterial blood gas is needed to detect acute and life-threatening changes in condition, to initiate treatment interventions and to evaluate the response to treatment. In daily practice, blood gas measurement is widely used to assess the patient's metabolic status, causes of impaired gas exchange, severity, oxygenation and all metabolic functions. Blood gas analysis provides direct measurement of pH, partial pressure of oxygen (pO_2) and partial pressure of carbon dioxide (pCO_2) in arterial blood. In addition to these; other calculated parameters such as total hemoglobin concentration, oxyhemoglobin, carboxyhemoglobin and methemoglobin saturation, anion gap, base deficiency, base excess and bicarbonate can be used clinically (4,5,6).

Blood gas instruments are bedside testing instruments that require close laboratory attention. They are urgent laboratory equipment that usually require urgent results and whose results are of high importance for the patient and help the clinician to initiate preliminary diagnosis and treatment until the patient's routine tests are completed. Laboratory specialists need to personally monitor both the preanalytical and analytical phases. The responsibility for the performance and efficiency of the instruments also rests with the laboratory specialist.

In the literature, 6 sigma metric studies have been carried out mainly in biochemistry tests. V.Thomas et al and JS Koshy et al studies can be shown (10,15). Y.Ustundag et al. also performed sigma metric calculations in electrolyte tests which are common in blood gas and biochemistry instruments. They found the scores of Na and K tests in the blood gas instrument between 5-6 and the score of Cl test between 4-5. Y.Ustundag et all use the target values from the SEKK (EQA programme of the Czech Republic) guidelines, whose TEa % used in the sigma score is wider than that of RILIBAK (16). In our study, we used the RILIBAK guideline which contains a narrower target value. In our study, we calculated K and Cl test scores above 6 in all 3 instruments. Na test scores were level 1 in device I and both level scores were above 6 in instrument II. Instrument I Level 2 and instrument III scored between 5-6 at both levels. Xia Y. et al. also calculated scores from some parameters (pH, PO2 and PCO2) in blood gas in their study. pH test scored between 5-6, pCO2 between 3-4 and PO2 below 2 (17). In our study, we scored below 2 in PCO2 test only in instrument III like Xia Y. et al. In other instruments, it was generally scored between 5-6.

There is no blood gas 6 sigma scoring study in which the number of tests is more comprehensive and the emergency laboratory is examined in more than one device as in our study.

The limitation of this study is that the sigma metric calculation of the instruments within a period of 1 month. The reason for this is that the internal control samples of the instruments are selected in periods when there are few lot changes and the external quality control results are selected in periods when there are no deviations or warnings. In future studies, laboratories are recommended to perform new calculations by increasing the study period.

Conclusion

Blood gas instruments are easier to use and give faster results than other laboratory devices. The laboratory specialist's approach to these devices should not be like the devices used in other laboratories. When we look at the tests that we stay within the limits of internal quality control and external quality control, which we normally think everything is going well, with 6 Sigma Methodology, we see our device performance more clearly. With 6 Sigma, we have been able to further improve test performance by implementing corrective and preventive actions such as changes in quality control rules, maintenance or changes in the technical equipment of the device, and control of preanalytical factors. This study has allowed us to monitor laboratory blood gas testing performance very closely.

Declarations

Funding

This study had no external funding.

Conflicts Of Interest

The authors declare that they have no conflicts of interest.

Ethics Approval

This study was approved by the Ethical Committee for Istanbul Health Sciences University Umraniye Training and Research Hospital, with the assigned decision no: 363 and date: 17.10.2024.

Availability Of Data And Material

Data are available from medical records.

References

- Bloom BM, Grundlingh J, Bestwick JP, Harris T. The role of venous blood gas in the emergency department: a systematic review and meta-analysis. Eur J Emerg Med. 2014 Apr;21(2):81-8. https://doi. org/10.1097/mej.0b013e32836437cf
- Ochs M, O'Brodovich. The structural and physiologic basis of respiratory diseases. In: Kendig and Chernick's Disorders of the respiratory tract in children 8th edit. WB Saunders Company, Philadelphia, 2012;35-74.
- Ziegenfuß T, Zander R. Understanding blood gas analysis. Intensive Care Med. 2019 Nov;45(11):1684-1685. https://doi.org/10.1007/ s00134-019-05688-w
- Davis MD, Walsh BK, Sittig SE, Restrepo RD. AARC clinical practice guideline: blood gas analysis and hemoximetry: 2013. Respir Care 2013;58:1694-703. https://doi.org/10.4187/respcare.02786
- 5. Barthwal MS. Analysis of arterial blood gases a comprehensive approach. JAPI 2004;52:573-6. 3.
- Culver BH. Acid-base balance and control of ventilation. Eds. Albert RK, Spiro SG, Jett JR. İn Clinical respiratory Medicine, Philadelphia 2004.pp.99-106
- Fraser CG. The 1999 Stockholm Consensus Conference on quality specifications in laboratory medicine. Clin Chem Lab Med. 2015 May;53(6):837-40. doi: 10.1515/cclm-2014-0914.

- 8. Coskun A, Inal TC, Serteser M. Six Sigma Projects and Personal Experiences. Croatia: InTech; 2011. http://dx.doi.org/10.5772/679
- Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L, Morgan T. Evaluating laboratory performance on quality indicators with the six sigma scale. Archives of Pathology & Laboratory Medicine. 2000;124(4):516– 519. https://doi.org/10.5858/2000-124-0516-elpoqi
- 10. Thomas V, Desai PB, Mithrason AT. Evaluation of clinical biochemistry laboratory performance using sigma metrics. Int J Clin Bio chem Res. 2018;5(4):604. http://dx.doi.org/10.18231/2394-6377.2018.0128
- 11. Sten Westgard, Hassan Bayat, James O Westgard. AnalyticalSigmametrics: A review of Six Sigma implementation tools for medical laboratories. BiochemMed (Zagreb) 2018;28(2):020502. https://doi.org/10.11613/bm.2018.020502
- Neufassung der "Richtlinie der Bundesärztekammer zur Qualitätssicherung labor medizinischer Untersuchungen – Rili-BÄK". Dt Aerzteblatt 2014;111:A1583–618.

- Westgard JO, Westgard SA. Establishing evidence-based statistical quality control practices. Am J Clin Pathol. 2019;151:364-70https:// doi.org/10.1093/ajcp/aqy158
- Kumar BV, Mohan T. Sigmametrics as a tool for evaluating the performance of internal quality control in a clinical chemistry laboratory. J Lab Physicians. 2018;10(2):194-99. https://doi. org/10.4103/jlp.jlp_102_17
- Koshy JS, Raza A. Sigma metrics in quality control- An innovative tool. Int J Clin Biochem Res 2021;8(4):253-259. https://doi. org/10.18231/j.ijcbr.2021.055
- Ustundag-Budak Y, Huysal K. Application of Sigma Metrics and Performance Comparison Between Two Biochemistry Analyser and a Blood Gas Analyser for the Determination of Electrolytes. J Clin Diagn Res. 2017 Feb;11(2):BC06-BC09. doi: 10.7860/ JCDR/2017/23486.9259.
- 17. Xia Y, Xue H, Yan C, Li B, Zhang S, Li M, et al. Risk analysis and assessment based on Sigma metrics and intended use. Biochem Med (Zagreb). 2018;28:020707 DOI: 10.11613/BM.2018.020707