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An Excel Visual Basic for Application worksheet for automatic selection of a sigma statistical quality control procedure, facilitating quality management for laboratories

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KEYWORDS
Sigma metric; Statistical quality control; QC plan tool; Quality management.

ABSTRACT
Defining the proper statistical quality control (SQC) procedure and designing the quality control plan provide the analytical quality management (QM) that is essential in laboratory practice, ensuring that reported test results achieve the quality required for medical decisions. The Westgard sigma rules with run size, one of the popular quality control planning tools, is an effective tool for evaluating measurement performance and simplifying an appropriate selection of SQC. To achieve QM, the author established an Excel Visual Basic for Application (VBA) worksheet for automatic sigma scale calculation and automatic selection of SQC procedures. This file applied the Westgard sigma rules with run size concept, developed for a convenient multistage SQC design. In addition, there are more functions for monitoring QC results, documenting, and compiling the corrections utilized to improve QC design. Of 23 assays from our laboratory, only one-fifth of the tests (22%) achieved an optimal level of performance (≥ 6 sigma). Analytes with the highest sigma performance were triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), magnesium (Mg) and creatine phosphokinase (CK). In contrast, one-third of the tests (35%) had a sigma scale of less than 4, requiring them to be solved, improved and have rigorous QC monitoring by primary following in the Data Analysis sheet. Thus, this Excel VBA worksheet is an alternative tool for simplifying analytical QM that is effectively controlled and convenient, with multistage SQC designs.

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Introduction

Statistical quality control (SQC) is an essential laboratory practice to ensure reported test results achieve the quality required for medical decisions. Laboratories need the optimal SQC to provide a procedure to detect performance changes, potentially causing medically important errors. SQC practice is the evaluation of analytical quality control as a part of quality management. Sigma-metric is the popular quality control planning tool employed for process improvement. In 1986 Bill Smith was the person who applied the six sigma statistic for quality improvement methodology to the Motorola company[1]. Westgard JO is developing QC design and planning tools to support laboratory efforts to select SQC procedures, such as the "Westgard sigma rule for QC design and Run size"[2].

Rosenbaum MW et al carried out a survey about quality control practices for chemistry and immunochemistry in a cohort of 21 large academic medical centers in America in 2018, which revealed that most hospitals (76%) used a rule such as 2 SD to monitor QC results, which is not recommended because of causing a high probability a false rejection, and only 10% used multi-Westgard rules based on the performance of an assay[3]. Westgard JO discusses that this survey is a disappointing finding, but not entirely unexpected because there may be a variety of explanations, such as the guideline is too expensive, does not provide a practical methodology to implement the recommended principles and approach, is too difficult to understand because of the statistical and theoretical nature of the subject, or laboratories are not interested in a quantitative SQC planning methodology. They are still making available new graphical tools and worksheets that are simple recommendations for running QC[4].

In 2021 Westgard et al announced the report of the Global QC Practice survey, which was used in more than 600 laboratories from more than 100 countries. Most laboratories still used 2 SD as the primary rule for QC techniques and Westgard rules for observing QC that utilized those limits for all assays. For determining the control limit, the majority of laboratories calculated the actual mean and the actual SD to create Levey-Jennings control charts, which is the proper procedure. However, the others perform using the manufacturer's range, which is quite wide for detecting the error. In determining control material, most laboratories use the controls provided by manufacturers. Although the recommendation from CLSI is a third-party process, it is the second most popular control type. Concerning the frequency of running QC, most laboratories follow the standard from CLSI, which is once-a-day QC, followed by running twice a day, and three times a day. Even though more frequent running QC has earlier error detection, it comes with a higher budget in the process[5].

From a survey in 2018 to the Global QC practices survey in 2021, Westgard opined that "Laboratories know they should do the right thing, whereas they are unable to utilize them routinely. We think one the reason for this gap between theory and practice is the complexity of the theory and the lack of practical tools to help laboratories apply the evidence-based approach". The author took up this challenge to create practical tools, such as an Excel VBA worksheet, to simplify the theory for alternative implementation customizing the QC for each assay's sigma performance, thus improving QC planning as a part of the quality management system (QMS).

Materials and methods

Materials

In this study, control results were analyzed with Mindray ClinChem Multi Control level 1 and level 2 by Mindray BS-800 analyzer that was used to perform 23 routine biological assays: sodium (Na), potassium (K), chloride (Cl), glucose (Glu), urease (Urea), creatinine (Crea), uric acid (UA), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein

(LDL), total protein (TP), albumin (ALB), total bilirubin (T-Bili), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), calcium (Ca), magnesium (Mg), phosphorus (P), amylase (AMY), creatine kinase (CK), and lactate dehydrogenase (LDH). The protocol was approved by the Ethics Committee of Prasat Hospital (PSH REC No. 004/2023).

Study design and participants

Brew6sigma, an implementation of an Excel VBA worksheet that is used in this study, used Microsoft Excel 2016, integrated with the Westgard sigma rule for QC design and Run size, which provides simplicity of sigma metric calculation and the design of statistic quality control (SQC) tools to support analytical quality management (Figure 1). The SQC procedure selects the optimized control rules and the number of control measurements to detect medically important errors. Designing a QC plan to integrate SQC is needed to monitor failure modes in analytical methods or instrument systems. Brew6sigma is the alternative of the practical tool with the PDCA cycle concept, to help laboratories apply the complicated six sigma quality management system that adheres to the Thai medical technology standard 2022, corresponding to ISO 15189 standards. The components of a Brew6sigma VBA worksheet include the Index sheet, typically serving as a table of contents for the program, Data Analysis sheet, Summarize sheet, Control level 1 sheet, Control level 2 sheet, Bias sheet, Corrective Action sheet, and Test sheet.

The Data Analysis sheet asks the user to enter the data of TEa, defined from three source recommendations for setting a quality goal or quality requirement, CLIA CAP and Rico, and fill up in-house data that consists of mean, SD and bias in each test for sigma metric calculation. From in-house data, mean and SD are determined on a replication experiment. The CV refers to the "coefficient of variation", which describes the standard deviation as a percentage of the mean, as shown in the following equation:

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

The CLSI guideline defines the criteria for acceptable CV from the repeatability that the experimental product has at least 20 replicates collected over 20 days (between-runs) and should be less than or equal to thirty-three percent of TEa[6].

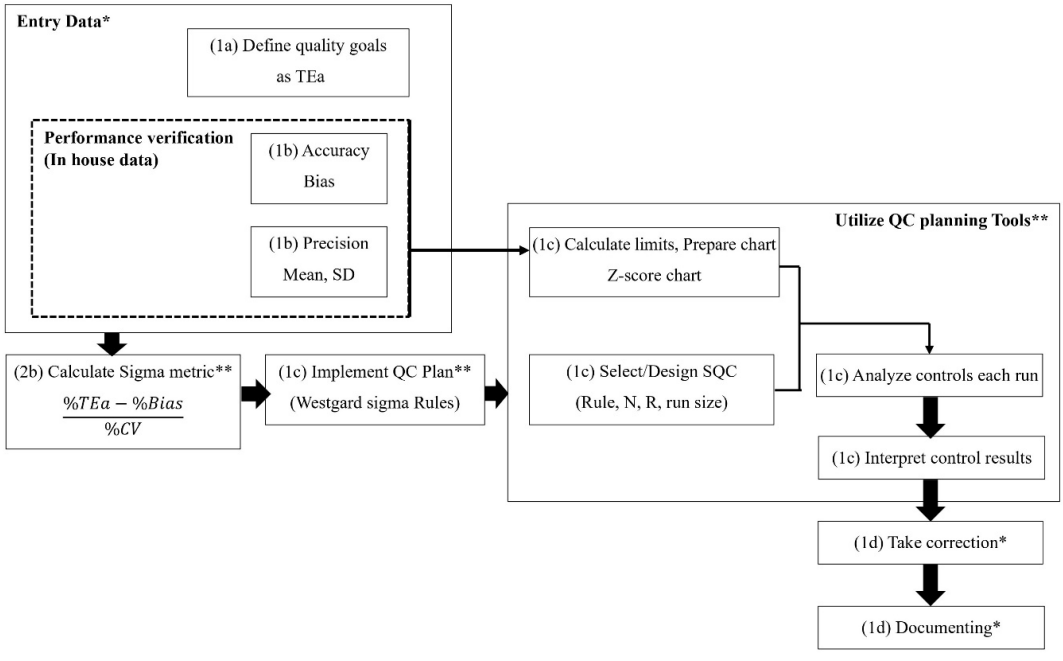


Figure 1 Flow diagram illustration of how the automatic SQC selection process works.
Note: * The part for the user to enter data and documentation of correction, ** The part of the Excel VBA worksheet that automatically calculates the sigma metric and automatically selects the proper SQC procedure.

In this program, the sigma metric was calculated with the following equation:

$$SM = (TEa\% - Bias\%) / (CV\%)$$

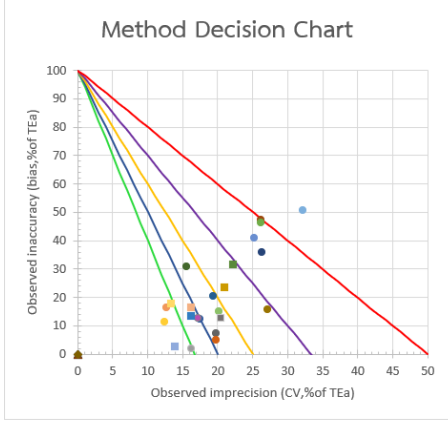
Where TEa represents the allowable total error. Bias and CV represent systemic and random errors, respectively. Thus, the Excel VBA will select an appropriate SQC from the calculated sigma metric or sigma scale, referenced from the Westgard sigma rule for QC design and run size performance of method decision level, Westgard rules, run size (number of patients), number of control measurements and frequency of runs (Table 1). In addition, if the sigma scale is less than six, which may result in more defects, the program will calculate the quality goal index (QGI) by evaluating the root of causing errors, by the following expression:

$$QGI = Bias / 1.5\ CV$$

The QGI ratio represents bias or precision that achieves its quality goals. The quality goals chosen for use are 1.5*TEa/6 for bias and TEa/6 for precision. A high QGI ratio means that bias exceeds its accuracy goal, while imprecision meets its precision goal. On the contrary, a low QGI ratio means that bias meets its accuracy goal while imprecision exceeds its precision goal. The criteria are for interpreting QGI when the sigma metric is less than six, as the calculated QGI is less than 0.8 and more than 1.2, presenting the cause of the problem by imprecision and inaccuracy, respectively, while QGI between 0.8-1.2 presents the cause of the problem by both imprecision and inaccuracy[7].

The Summarize sheet performs the individualized sigma metric, method decision level, and optimal SQC procedure (consisting of the control rules, number of controls, and run size of patient

needed) in each test along with an automatic pie chart of sigma proportion. The user will provide the individual normalized method decision chart by filling in the test name in the field (Figure 2). In the Control level 1 and Control level 2 sheets, the user must input control data to prepare to create Levey-Jennings control charts. In addition, this Excel VBA calculates the cumulative mean, SD and CV. The cumulative CV is a long-term estimate of the central tendency observed for a control material, based on a large number of control measurements collected over a long period (≥ 6 months). Comparing the monthly CV to the cumulative CV, if the monthly CV is more than twice the cumulative CV, then it should be investigated and documented. Any significant change may indicate a change in instrument calibration or a fault in its function.



test_name	%CV of TEa	%Bias of TEa
Na	26.22	46.40
K	26.32	36.00
Cl	26.24	47.40
Glucose	19.74	7.25
Urea	27.16	15.67
Creatinine	19.39	20.50
Uric Acid	15.64	30.80
Cholesterol	25.27	41.00
Triglyceride	12.70	16.40
HDL	16.28	2.05
LDL	12.50	11.30
Total Protein	32.16	50.50
Albumin	20.24	15.00
Total Bilirubin	17.47	12.30
AST	19.75	4.80
ALT	17.24	12.80
ALP	21.04	23.45
Ca	16.28	13.20
P	22.30	31.60
Mg	13.92	2.53
Amylase	16.29	16.25
LDH	20.43	12.73
CK	13.33	17.70

Figure 2 The automatically plotted operating point when entering the named test in the table.
Note: "Normalized" Method decision chart observed inaccuracy is calculated as 100*bias/TEa and imprecision is calculated as 100*CV/TEa, where original parameters are all in units of %.

The Bias sheet collects monthly bias data and is convenient for summary and usage. Bias, inaccuracy, trueness or systemic error is determined during method validation studies from method experiment comparison. The laboratories should perform experiments to verify a manufacturer's claim after installation. After initial validation, laboratories require monitoring bias using EQA/PT samples with target values or assigned values, established by reference methods or the mean of the survey group (peer group). The user must fill up this sheet with their results and the assigned result, which is measured by the same method and instrument for bias calculation. In the calculation

of the sigma metric, this worksheet calculates bias with the following equation:

$$\%Bias = (Your\ result - Assigned\ result)/(Assigned\ result \times 100)$$

To establish the corrective action, the Corrective Action sheet documents and collects corrections that solve the error or are out of control from all the operating tests.

Test sheets specify the standard quality control chart or the Levey-Jennings chart, which is computed from the mean and SD determined in the laboratory by a method operating under stable conditions. The Levey-Jennings chart provides monitored and interpreted control results under the right SQC. This sheet presents a control chart as a z-score chart in which individual control results are calculated for the z-score and plotted on the y-axis versus time on the x-axis. The z-score shows the standard deviation of a control result from the expected mean value, which is determined by the following expression:

$$z\text{-}score = (value - mean) / SD$$

A z-score chart is typically created as the mean (z-score is 0) plus or minus a certain multiple of the SD, commonly ± 3SD, ± 2SD or and ± 1SD. It is expected that 99.7% (i.e. almost all) control results fall within the mean ± 3 SD limits, whereas about 95% are expected within the mean ± 2 SD limits, and 67% within the mean ± 1 SD[8]. As a result, this worksheet interprets control results using optimal SQC procedure from the calculated data in the Data Analysis sheets (as shown beside the z-score chart). In addition, it can interpret control results as violations based on the fully cataloged number of ways that can break the "Westgard rules"[9] and record corrections to establish corrective action. Doing the proper SQC observation and monitoring control results are components of the quality control plan, which is helpful for quality management.

Results

The performances, sigma values and right SQC of the 23 assays in the Mindray BS800 analyzer are used in the Excel VBA worksheet for automatic calculation of the sigma scale and automatic selection of the SQC procedure presented by in-house data of the laboratory at Prasat Hospital, as shown in the Data Analysis sheet (Table 1).

The summarized sigma metric in each test is divided by class, performed in table 2, and shown as a pie chart from the proportion of sigma in the supplement part. Only one-fifth of the test (22%) achieved an optimal level of performance (≥ 6 sigma). Analytes with the highest sigma performance were triglyceride, HDL, LDL, Mg and CK. The assays with sigma ≥ 5 (17.39%) are excellent, and sigma ≥ 4 (26.09%) are good. In contrast, one-third of the tests (35%) with a sigma scale of less than 4 need to be fixed, improved and have rigorous QC monitoring by primarily following the Data Analysis sheet (Table 1).

Table 1 In-House data, individual calculated sigma metric and optimal SQC display in Data Analysis sheet

Test	TEa	33%TEa	mean_1	SD_1	CV1*	mean_2	SD_2	CV2*	Precision check	bias	Sigma1*	Sigma2*	Six Sigma*	Normalized** Method Decision	N, R**	Rules**	Run Size ** (Patient samples)	QGI1***	QGI2***	Problem
Na	5	1.65	114.4	1.5	1.31	137.5	1.8	1.31	/	2.32	2.04	2.05	2.04	Poor	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	1.18	1.18	Imprecision & Inaccuracy
K	6	1.98	3.80	0.06	1.58	6.978	0.11	1.58	/	2.16	2.43	2.44	2.43	Poor	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	0.91	0.91	Imprecision & Inaccuracy
Cl	5	1.65	92.8	1.14	1.23	109	1.43	1.31	/	2.37	2.14	2.00	2.00	Poor	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	1.29	1.20	Inaccuracy
Glucose	8	2.64	101	1.44	1.43	245	3.87	1.58	/	0.58	5.20	4.70	4.70	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200	0.27	0.24	Imprecision
Urea	9	2.97	19.8	0.46	2.32	58.5	1.43	2.44	/	1.41	3.27	3.11	3.11	Marginal	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	0.40	0.38	Imprecision
Creatinine	10	3.3	0.877	0.017	1.94	3.52	0.065	1.85	/	2.05	4.10	4.31	4.10	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200	0.70	0.74	Imprecision
Uric Acid	10	3.3	5.14	0.07	1.36	10.87	0.17	1.56	/	3.08	5.08	4.42	4.42	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200	1.51	1.31	Inaccuracy
Cholesterol	10	3.3	91	2.3	2.53	182	3.17	1.74	/	4.10	2.33	3.39	2.33	Poor	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	1.08	1.57	Imprecision & Inaccuracy
Triglyceride	15	4.95	113	1.6	1.42	210	4	1.90	/	2.46	8.86	6.58	6.58	World Class	N;2,R;1	13s	1000			
HDL	20	6.6	27.65	0.9	3.26	60	1.5	2.50	/	0.41	6.02	7.84	6.02	World Class	N;2,R;1	13s	1000			
LDL	20	6.6	58	1.3	2.24	120	3	2.50	/	2.26	7.91	7.10	7.10	World Class	N;2,R;1	13s	1000			
Total Protein	8	2.64	4.68	0.12	2.56	8.55	0.22	2.57	/	4.04	1.54	1.54	1.54	Unacceptable	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	1.05	1.05	Imprecision & Inaccuracy
Albumin	8	2.64	3.03	0.046	1.52	5.25	0.085	1.62	/	1.20	4.48	4.20	4.20	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200	0.53	0.49	Imprecision
Total Bilirubin	20	6.6	1.15	0.04	3.48	4.58	0.16	3.49	/	2.46	5.04	5.02	5.02	Excellent	N;2,R;1	13s; 22s; R4s	450	0.47	0.47	Imprecision
AST	15	4.95	51	1.5	2.94	162	4.8	2.96	/	0.72	4.86	4.82	4.82	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200	0.16	0.16	Imprecision
ALT	15	4.95	58	1.5	2.59	144	3.7	2.57	/	1.92	5.06	5.09	5.06	Excellent	N;2,R;1	13s; 22s; R4s	450	0.49	0.50	Imprecision
ALP	20	6.6	84.5	3.5	4.14	202	8.5	4.21	/	4.69	3.70	3.64	3.64	Marginal	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45	0.75	0.74	Imprecision

Table 1 In-House data, individual calculated sigma metric and optimal SQC display in Data Analysis sheet (Cont.)

Test	TEa	33%TEa	mean_1	SD_1	CV1*	mean_2	SD_2	CV2*	Precision check	bias	Sigma1*	Sigma2*	Six Sigma*	Normalized** Method Decision	N, R**	Rules**	Run Size ** (Patient samples)	QGI1***	QGI2***	Problem
Ca	10	3.3	8.6	0.14	1.63	12.9	0.17	1.32	/	1.32	5.33	6.59	5.33	Excellent	N;2,R;1	13s; 22s; R4s	450	0.54	0.67	Imprecision
P	10	3.3	4.30	0.09	2.09	8.07	0.18	2.23	/	3.16	3.27	3.07	3.07	Marginal	N;6,R;1	13s; 22s;	45	1.01	0.94	Imprecision
															(N;2,R;3)	R4s; 41s; 8x				& Inaccuracy
Mg	15	4.95	2.03	0.04	1.97	3.35	0.07	2.09	/	0.38	7.42	7.00	7.00	World Class	N;2,R;1	13s	1000			
Amylase	20	6.6	85.7	2.5	2.92	221	7.2	3.26	/	3.25	5.74	5.14	5.14	Excellent	N;2,R;1	13s; 22s; R4s	450	0.74	0.67	Imprecision
LDH	15	4.95	149	4	2.68	261	8	3.07	/	1.91	4.88	4.27	4.27	Good	N;4,R;1	13s; 22s;	200	0.47	0.42	Imprecision
															(N;2,R;2)	R4s; 41s				
CK	20	6.6	150	4	2.67	258	5.7	2.21	/	3.54	6.17	7.45	6.17	World Class	N;2,R;1	13s	1000			

Note: * The automatically calculated values from in-house data are presented by CV and the sigma metric, ** The automatic functions used to select the optimal SQC are established from individual sigma metrics and presented by normalized method decision, number of controls (N), number of runs (R), rules and the number of patient samples (Run size), *** If sigma scale is less than 6, the calculated value from CV and bias is presented by the QGI ratio defining the root of the error.

Table 2 Summary number of sigma metric classifications by the decision method

Sigma	Test (n)	%	Test
6	5	21.74	Triglyceride, HDL, LDL, Mg, CK
5	4	17.39	Total-bilirubin, ALT, Ca, Amylase
4	6	26.09	Glucose, Creatinine, Uric, Albumin, AST, LDH
< 4	8	34.78	Sodium, Potassium, Chloride, Urea nitrogen, Cholesterol, Total protein, ALP, P

A summary bias table in the Bias sheet supports collecting and monitoring accuracy or frequency of EQA/PT in each test. There are user-editable bias value choices for sigma scale calculation. The Corrective Action sheet performs all of the corrections from all of the tests that utilize implementation and records the violation of QC results in each test sheet by the user for improving QC. Summarized corrections are shown as a table for creating owner laboratory guidelines to solve the problem.

Each test sheet presents a z-score chart and summary data, including mean, SD, CV, bias, sigma metric, method decision, rules, N, R and Run size from table 1, to interpret the QC result for monitoring precision or detecting random error. The QC results as 2 levels are documented in the Control level 1 sheet and Control level 2 sheet for creating a z-score chart and calculating cumulative CV that monitors the shift or drift of control results (Figure 3).

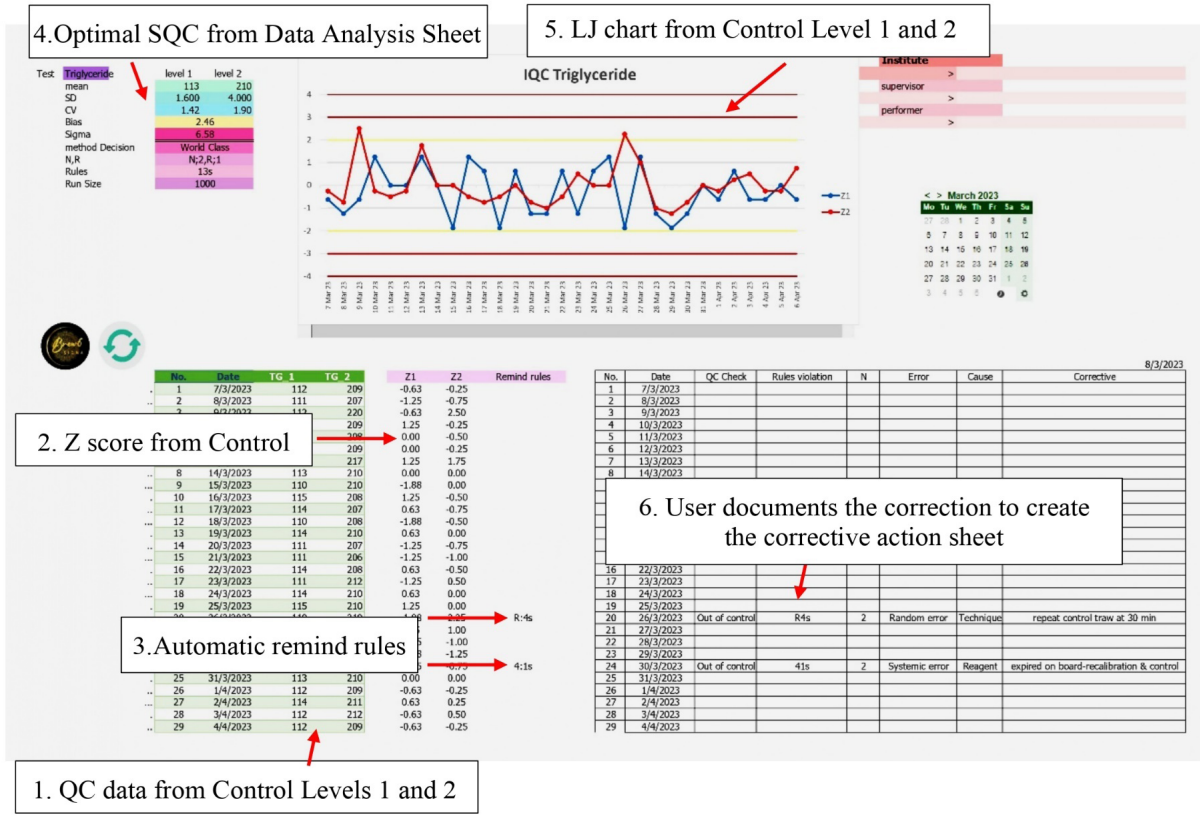


Figure 3 The display of the triglyceride sheet (test sheet).

Discussion

There are several main reasons to explain the differences in sigma metric found in this research, such as 1) the difference of source selected for the TEa target, 2) the difference between the algorithms used to evaluate CV and bias, and 3) the different selection sigma metric between 2 or more control levels.

For the Sigma metric, determining the TEa goals should be made carefully, as neither standardization nor harmonization of the existing resources for TEa goals exists[10]: Clinical Laboratory Improvement Amendments (CLIA), College of America Pathologists Participant (CAP), Royal College of Pathologists of Australasia and the Australasian Clinical Biochemist Association Quality Assurance Program (RCPA), Ricos' biological variability. Each TEa has a direct impact on the sigma metric.

The coefficient of variation (CV%) describes the variation of a test that is expressed as a percentage of the mean and calculated as CV% = (SD/mean) x100. When the SD increases in proportion to concentration, the CV will increase. Likewise, the level of concentration relates to CV as in lower concentrations the CV may be higher, and at higher concentrations, the CV may be lower[11]. Thus, the right target values or mean concentrations should be close to medical decision levels (MDLs), and the right sigma metric should be calculated from the CV at the concentration that hits the MDLs[12]. However, multianalyte controls with 20 or more analytes will be unlikely to hit the MDLs for all of them. In addition, the real concentration of control will be less or over the MDLs. The guideline for choosing the CV to calculate the sigma metric is if all of the controls in each test have a concentration near MDLs, the mean of all CV is used, and if any value is nearest to MDLs, then its CV concentration is used.

Considering the selection sigma metric between 2 or more control levels, for example, Peng S et al calculated the sigma metric and selected the optimal SQC for each control level, then monitored the quality control following each optimal SQC. It is difficult and complicated for the operator because of the differences in sigma value between the levels of control[13]. From Kumar and Mohan, the CV of individual control level used in the sigma metric was from the average CV value in 12 months. They calculated the sigma metric of each control level with the different sigma metrics. The introduction should be evaluated with discretion, which strictly complies with Westgard multi-rules to abolish discrepancy[14]. In conclusion, this study calculated the sigma metric in each test from all concentration levels, then chose the least sigma metric for the strongest criteria to monitor QC.

Lastly, The traditional error model as the Plan-Do-Check-Act (PDCA) cycle described by Deming[15] provides the basic process for developing, implementing and operating a quality management system (QMS). The Excel VBA worksheet can facilitate the PDCA cycle concept and sigma metric tools for analytical quality management as shown in figure 1.

Plan: (1a) Define quality goals as an allowable total error (TEa). TEa guides the selection of analytic measurement procedures, or examination procedures in ISO terminology.

Do: (1b) Validate safety characteristics (precision and bias) using experimental studies and statistical data analysis. Acceptable performance can be evaluated by determining quality on a Sigma scale using the method decision chart. (2b) Assuming the sigma metric indicates acceptable performance (that is greater than 3, preferably at least 4 and, better yet, 5 or 6) proceed to implement the analytical method.

Check: (1c) The SQC procedure optimizes the control rules, number of controls, number of runs, and number of patient samples (Run size) to detect medically important errors. Design a QC plan to integrate SQC with other control mechanisms that are needed to monitor specific failure modes that may occur with a particular analytic method or instrument system.

Act: (1d) Monitor the quality of the testing process over time to characterize performance, identify failures, and improve the QC plan[16].

Conclusion

The Excel VBA worksheet, which employs Westgard sigma rules with run size, is an alternative tool simplifying analytical QM, including specifying quality goals, judging the acceptability of performance of examination procedures, designing statistical quality control (SQC) procedures to detect significant medical errors that are effectively controlled and convenient with multistage SQC designs. Moreover, this file has a function for monitoring QC results, evaluating quality from external quality assessment and proficiency testing surveys, and establishing corrective action for improving the QC plan.

Take home messages

This Excel VBA worksheet is suitable for any hospital starting to apply the sigma SQC designs for analytical QM.

Conflicts of interest

The author declares no conflict of interest.

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Supplementary

Program interface

The components of a Brew6sigma VBA worksheet include the Index sheet, typically serving as a table of contents for the program, Data Analysis sheet, Summarize sheet, Control level 1 sheet, Control level 2 sheet, Bias sheet, Corrective Action sheet, and Test sheet. When the user clicks each button, the program will run to that page (sheet).

Input the in-house data for the Data Analysis sheet, click the “Fill up” button, and then pop up the entry data window.

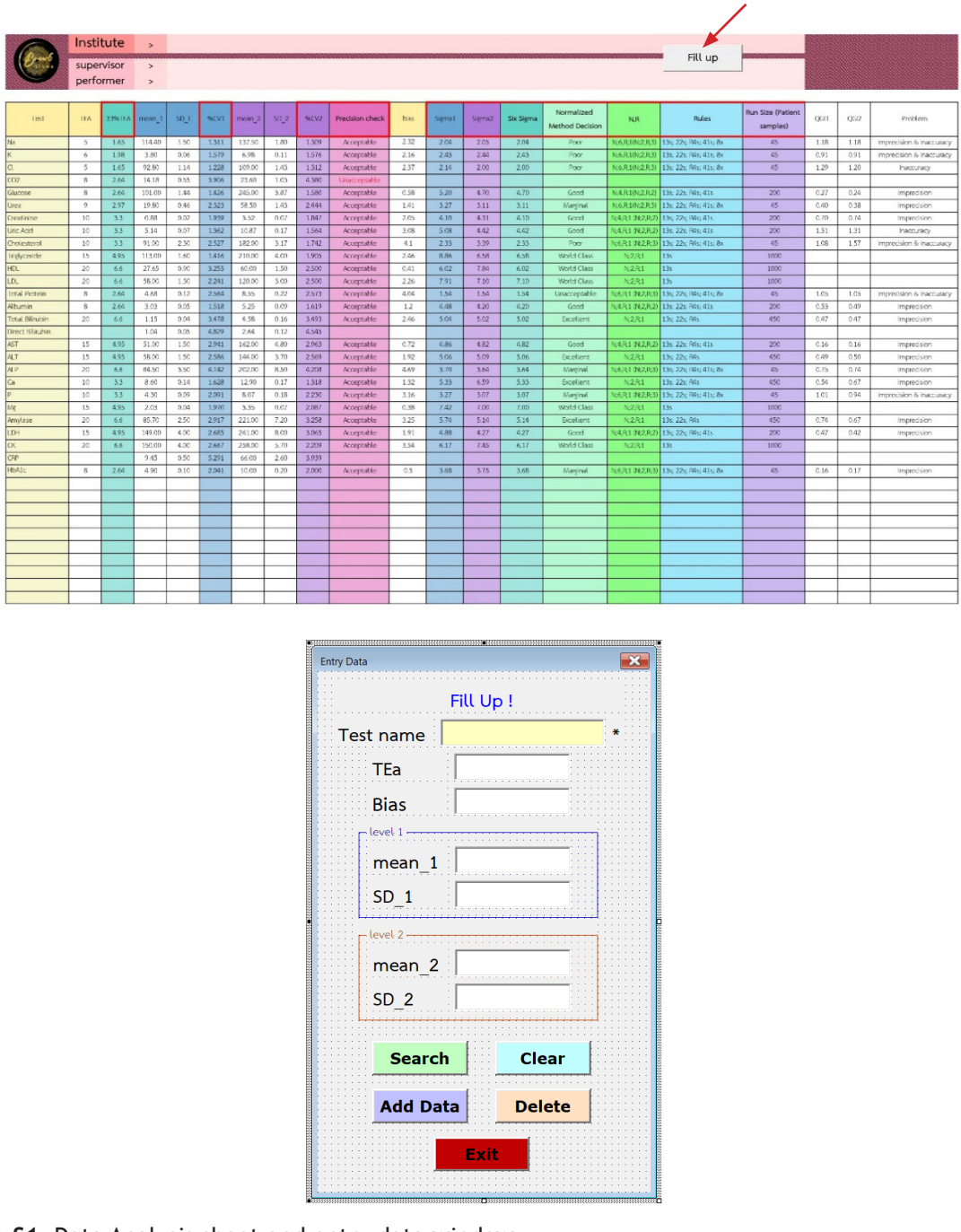


Figure S1 Data Analysis sheet and entry data window.

Click the “Add Data” button for the calculation sigma metric. Thus, the Excel VBA will select an appropriate SQC from the calculated sigma metric or sigma scale, referenced from the Westgard sigma rule for QC design and run size performance of method decision level, Westgard rules, run size (number of patients), number of control measurements and frequency of run.

The Summarize sheet calculates the individualized sigma metric, method decision level and optimal SQC procedure (consisting of the control rules, number of control results, and run size of patients needed) in each test along with a pie chart of sigma proportion. The user will provide the individual normalized method decision chart by filling in the test name in the field.

Test	Six Sigma ammari:	Normalized Method Decision	N,R	Rules	Run Size (Patien
Na	2.04	<4	Poor	N;6,R;1(N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
K	2.43	<4	Poor	N;6,R;1(N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Cl	2.00	<4	Poor	N;6,R;1(N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Glucose	4.70	4	Good	N;4,R;1(N;2,R;2)	13s; 22s; R4s; 41s	200
Urea	3.11	<4	Marginal	N;6,R;1(N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Creatinine	4.10	4	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200
Uric Acid	4.42	4	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200
Cholesterol	2.33	<4	Poor	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Triglyceride	6.58	6	World Class	N;2,R;1	13s	1000
HDL	6.02	6	World Class	N;2,R;1	13s	1000
LDL	7.10	6	World Class	N;2,R;1	13s	1000
Total Protein	1.54	<4	Unacceptable	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Albumin	4.20	4	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200
Total Bilirubin	5.02	5	Excellent	N;2,R;1	13s; 22s; R4s	450
AST	4.82	4	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200
ALT	5.06	5	Excellent	N;2,R;1	13s; 22s; R4s	450
ALP	3.64	<4	Marginal	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Ca	5.33	5	Excellent	N;2,R;1	13s; 22s; R4s	450
P	3.07	<4	Marginal	N;6,R;1 (N;2,R;3)	13s; 22s; R4s; 41s; 8x	45
Mg	7.00	6	World Class	N;2,R;1	13s	1000
Amylase	5.14	5	Excellent	N;2,R;1	13s; 22s; R4s	450
LDH	4.27	4	Good	N;4,R;1 (N;2,R;2)	13s; 22s; R4s; 41s	200
CK	6.17	6	World Class	N;2,R;1	13s	1000

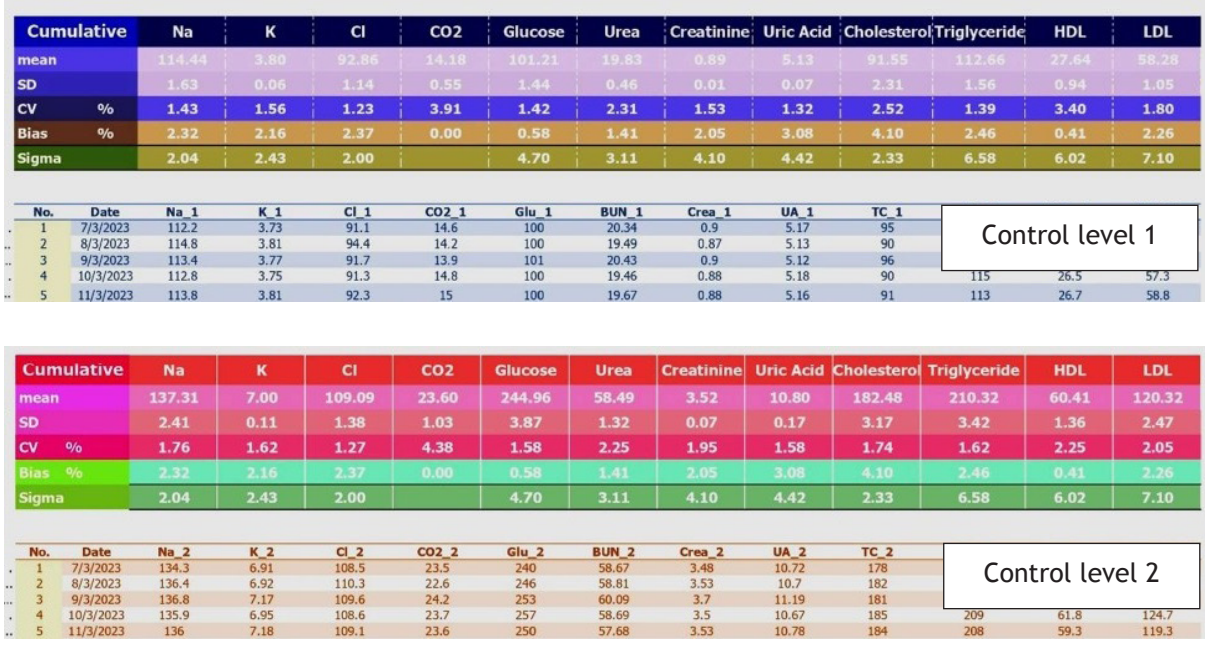
Sigma	Test (n)	%
6	5	22%
5	4	17%
4	6	26%
<4	8	35%
Σ	23	100%

test_name	%CV of TEa	%Bias of TEa
Na	26.22	46.40
K	26.32	36.00
Cl	26.24	47.40
Glucose	19.74	7.25
Urea	27.16	15.67
Creatinine	19.39	20.50
Uric Acid	15.64	30.80
Cholesterol	25.27	41.00
Triglyceride	12.70	16.40
HDL	16.28	2.05
LDL	12.50	11.30
Total Protein	32.16	50.50
Albumin	20.24	15.00
Total Bilirubin	17.47	12.30
AST	19.75	4.80
ALT	17.24	12.80
ALP	21.04	23.45
Ca	16.28	13.20
P	22.30	31.60
Mg	13.92	2.53
Amylase	16.29	16.25
LDH	20.43	12.73
CK	13.33	17.70

Figure S2 The Summarize sheet and the Westgard sigma rule for QC design and run size.

In the Control level 1 and Control level 2 sheets, the user must input control data to prepare to create Levey-Jennings control charts. In addition, this Excel VBA calculates the cumulative mean, SD and CV. The cumulative CV is a long-term estimate of the central tendency observed for a control material based on a large number of control measurements collected over a long period (≥ 6 months). Comparing the monthly CV to the cumulative CV, if the monthly CV is more than twice the cumulative CV, then it should be investigated and documented. Any significant change may indicate a change in instrument calibration or a fault in its function.

The Bias sheet collects monthly bias data and is convenient for summary and usage. The Corrective Action sheet is a document that collects corrections that solve the error or are out of control from all the operating tests.



Cumulative	Na	K	Cl	CO2	Glucose	Urea	Creatinine	Uric Acid	Cholesterol	Triglyceride	HDL	LDL
mean	114.44	3.80	92.86	14.18	101.21	19.83	0.89	5.13	91.55	112.66	27.64	58.28
SD	1.63	0.06	1.14	0.55	1.44	0.46	0.01	0.07	2.31	1.56	0.94	1.05
CV %	1.43	1.56	1.23	3.91	1.42	2.31	1.53	1.32	2.52	1.39	3.40	1.80
Bias %	2.32	2.16	2.37	0.00	0.58	1.41	2.05	3.08	4.10	2.46	0.41	2.26
Sigma	2.04	2.43	2.00		4.70	3.11	4.10	4.42	2.33	6.58	6.02	7.10

No.	Date	Na_1	K_1	Cl_1	CO2_1	Glu_1	BUN_1	Crea_1	UA_1	TC_1			
1	7/3/2023	112.2	3.73	91.1	14.6	100	20.34	0.9	5.17	95			
2	8/3/2023	114.8	3.81	94.4	14.2	100	19.49	0.87	5.13	90			
3	9/3/2023	113.4	3.77	91.7	13.9	101	20.43	0.9	5.12	96			
4	10/3/2023	112.8	3.75	91.3	14.8	100	19.46	0.88	5.18	90	115	26.5	57.3
5	11/3/2023	113.8	3.81	92.3	15	100	19.67	0.88	5.16	91	113	26.7	58.8

Control level 1

Cumulative	Na	K	Cl	CO2	Glucose	Urea	Creatinine	Uric Acid	Cholesterol	Triglyceride	HDL	LDL
mean	137.31	7.00	109.09	23.60	244.96	58.49	3.52	10.80	182.48	210.32	60.41	120.32
SD	2.41	0.11	1.38	1.03	3.87	1.32	0.07	0.17	3.17	3.42	1.36	2.47
CV %	1.76	1.62	1.27	4.38	1.58	2.25	1.95	1.58	1.74	1.62	2.25	2.05
Bias %	2.32	2.16	2.37	0.00	0.58	1.41	2.05	3.08	4.10	2.46	0.41	2.26
Sigma	2.04	2.43	2.00		4.70	3.11	4.10	4.42	2.33	6.58	6.02	7.10

No.	Date	Na_2	K_2	Cl_2	CO2_2	Glu_2	BUN_2	Crea_2	UA_2	TC_2			
1	7/3/2023	134.3	6.91	108.5	23.5	240	58.67	3.48	10.72	178			
2	8/3/2023	136.4	6.92	110.3	22.6	246	58.81	3.53	10.7	182			
3	9/3/2023	136.8	7.17	109.6	24.2	253	60.09	3.7	11.19	181			
4	10/3/2023	135.9	6.95	108.6	23.7	257	58.69	3.5	10.67	185	209	61.8	124.7
5	11/3/2023	136	7.18	109.1	23.6	250	57.68	3.53	10.78	184	208	59.3	119.3

Control level 2

Bias

test	Date	Month	Year	Your value	Assigned value	%Bias	Bias
ALB	28/2/2023	กุมภาพันธ์	2023	4.70	4.63	1.51	1.51
ALP	28/2/2023	กุมภาพันธ์	2023	213.00	225.41	5.51	5.51
ALT	28/2/2023	กุมภาพันธ์	2023	40.00	38.06	5.10	5.10

Year: 2023

Month: กุมภาพันธ์ | มีนาคม | เมษายน

Bias.	year			
	2023			
test	กุมภาพันธ์	มีนาคม	เมษายน	
ALB	1.51	1.19	1.20	1.30
ALP	5.51	3.52	5.05	4.69
ALT	5.10	17.58	1.92	8.20

Bias sheet

Date	Name	Rules violation	N	Error	Cause	Corrective
9 Mar 23	from_Amy	13s	2	Random error	Technique	Repeat control
9 Mar 23	from_P	41s	2	Systemic error	Reagent	Calibrate and Repeat control
9 Mar 23	from_Ca	13s	2	Random error	Technique	repeat control traw at 30 min
10 Mar 23	from_ALP	8x	2	Systemic error	Reagent	Calibrate and Repeat control
10 Mar 23	from_Glu	13s	2	Random error	Technique	repeat control traw at 30 min
10 Mar 23	from_DirectBili	41s	2	Systemic error	Control material	calibrate and repeat control
10 Mar 23	from_CRP	8x	2	Systemic error	Reagent	Calibrate and Repeat control
11 Mar 23	from_DirectBili	41s	2	Systemic error	Reagent	calibrate and repeat control

Cause event	Error (n)		
test name	RE	SE	sum
from_BUN		4	4
Control material		2	2
Technique		1	1

Corrective Action sheet

Figure S3 The Control level 1, level 2, Bias and Corrective Action sheet.