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USING SIX SIGMA TO EVALUATE ANALYTICAL PERFORMANCE OF HEMATOLOGY ANALYZER

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ABSTRACT

Many medical decisions in the hospital based on hematology examination results, must be aware of their method performance. Sigma-metric is an excellent way to evaluate analytical performance quality. The performance analysis of laboratory hematology analyzer and Cell Dyne Ruby can use Sigma-metric. This study aimed to evaluate the analytical performance of Abbott Cell Dyne Ruby hematology analyzer, by Six Sigma in Clinical Pathology Laboratory of the Dr. Soetomo Hospital Surabaya, Indonesia. Sigma analysis was calculated by a formula, sigma = (TEa – CV)/ Bias. The CLIA proficiency testing criteria specified Total Error Allowable (TEa). The Coefficient of Variant (CV) and bias data were supplied from analyzer running three levels of control Low (L), Normal (N), and High (H) include following analytes: hemoglobin (Hb), Red Blood Cell count (RBC), Hematocrit (HCT), White Blood Cell count (WBC), and Platelet count (PLT). Sigma-value as follows Hb(L:4.33 N:6.68 H:2.62), RBC(L:3.43 N:3.84 H:3.46), HCT(L:2.52 N:1.73 H:2.27), WBC (L:7.14 N:8.44 H:6.38), and PLT (L:2.46 N:8.75 H:7.84). Average Sigma-value for all parameters was 4.75. Minimum Sigma-value for any business or manufacturing process was three. More than Six Sigma-value was a world-class performance. Hematology analyzer Cell Dyne Ruby provides "Good" performance by Sigma-metric.

Key words: Sigma-metric, cell dyne ruby, total error allowable, the coefficient of variant, bias

INTRODUCTION

Many medical decisions are based on clinical laboratory results. These include admission, discharge, even therapies such as transfusion, medication, radiotherapy, chemotherapy, and operation procedure. Almost 60-70% important medical decisions need these, to diminish laboratory error to minimize medical error.[1,2]

There are three classic phases in laboratory process: pre-analytical, analytical, and post-analytical phase. Errors could happen in any stage of the process. Many studies show that most frequent errors occur in the pre-analytical phase.[2,3] Errors rarely happen in the analytical phase. Automation, improved laboratory technology, assay standardization, and better-trained staff have a significant role in this. But errors can occur due to minimal internal quality control that is applied by laboratories. This phenomenon is just like an iceberg. Not many errors can be detected by minimal quality control procedure.[4]

Analytical performance is evaluated by internal and external quality assessment. Internal laboratory quality can be assessed by calculating the coefficient of a variant that expresses the precision of each quantitative laboratory parameter. External laboratory quality for quantitative parameters can be assessed by calculating variant index score in laboratory external quality program. By Six Sigma, it will optimize statistical control rule for individual assays based on their inherent quality (bias and precision) and the accuracy required for their intended clinical use.[5-7]

Six Sigma is a quality indicator that can be used to evaluate a process. It was first described by Motorolla company in the 1980s. Implementation of Six Sigma has expanded in many manufacturers, especially in flight industries where safety is their priority. Recently, many laboratories apply Six Sigma as a quality indicator in their process. Laboratories can improve quality system and especially improve patient safety by using Six Sigma.[8-11]

Hematology analyzer is an automatic instrument to perform a Complete Blood Count (CBC) test. This examination includes counts number of hematology cells: erythrocyte, leukocyte, and platelet measures hemoglobin and hematocrit level, and also identify differential leukocyte numbers in absolute and percentage. The instrument also counts many other

parameters related to blood cells.[12,13] CBC is one of the most frequent laboratory tests that been requested in the hospital. It can be used for screening, diagnosis, and therapy monitoring for many diseases like anemia, infectious disease, hematologic malignancy or coagulation disorder.

The laboratory must ensure that instrument for laboratory test has good quality, including hematology analyzer. It must be avoided inaccurate laboratory result that can harm patients. This study aims to evaluate the analytical performance of Abbott Cell Dyne Ruby hematology analyzer, by Six Sigma in Clinical Pathology Laboratory of the Dr. Soetomo Hospital Surabaya, Indonesia.

METHODS

Data were analyzed from the routine CBC test results of assayed control material in July-August 2016. There were three control materials: Low, Normal, and High. Examination of the material was performed once daily with Abbot Cell Dyne Ruby hematology analyzer. Hemoglobin (Hb), Hematocrit (HCT), Red Blood Cell (RBC) Count, White Blood Cell (WBC) Count, and platelet (PLT) count were analyzed in CBC results. Data was consecutively collected in one lot number, that means it has the same control material.

Mean and standard deviation of the collected data were calculated with Microsoft Excel Software. The Coefficient of Variant (CV) was calculated with the formula:

(SD/Mean) X 100%

Data from the mean of control material results and the target value of control material to calculate the bias was used. The value was available in the insert kit. Bias was calculated with the formula:

Δ calculated mean and target value
difference/target value) X 100%

Total error allowance (TEa) of each parameter was adopted from Clinical Laboratory Improvement Amendments (CLIA) criteria. Then, Sigma-value was calculated in each parameter and each control level with the formula:

[(TEa – Bias)/CV] X 100%

CV, Bias, and Sigma calculation were performed with Microsoft Excel Software.

RESULT AND DISCUSSION

Researchers collected 42 control material CBC test results for 42 consecutive days by Abbott Cell Dyne Ruby hematology analyzer. There were three levels of controls with different values. It was low, normal, and high. Mean, SD, and the target value of material control are available in Table 1.

Bias and CV-value were calculated from data in Table 1. Sigma-value calculated from TEa form (CLIA criteria). Data of Sigma-value, Bias, CV, and TEa were available in Table 2.

The highest Sigma-value was achieved by platelet parameter in normal level (8.74789). Hematocrit at normal level was the lowest Sigma-value (1.727522). Parameters with Sigma-value more than six were

Table 1. The target value, mean, and SD of hematology control material CBC test

Parameter	Control material	Target value	Mean	SD
Hb (g/dL)	Low	7.6	7.37	0.079373
	Normal	12.2	12.03333	0.101653
	High	15.9	15.65714	0.327981
RBC	Low	2.91	2.940952	0.042415
(x 10^6/µL)	Normal	4.36	4.343333	0.063587
	High	5.34	5.359048	0.087459
Hematocrit	Low	20.9	20.74286	0.436545
(%)	Normal	33.2	32.37143	0.655853
	High	42.2	41.6619	0.865723
WBC	Low	4	4.002381	0.08372
(x 10^3/µL)	Normal	7.2	7.304286	0.117199
	High	17.1	17.0619	0.395571
Platelet	Low	74	82.79048	4.417002
(x 10^3/µL)	Normal	221	222.0952	6.220167
	High	528	507.1429	13.60987

Table 2. CV, Bias,TEa and Sigma-value

Parameter	Control material	CV (%)	Bias (%)	TEa (%): CLIA	Sigma-value
Hb	Low	1.076968	3.02	7	3.69556
	Normal	0.844762	1.36	7	6.676438
	High	2.094768	1,52	7	2.616041
RBC	Low	1.442226	1.06	6	3.425261
	Normal	1.464019	0.38	6	3.838749
	High	1.631985	0.35	6	3.462042
Hematocrit	Low	1.442226	1.06	6	3.425261
	Normal	2.026024	2.5	6	1.727522
	High	2.077973	1.28	6	2.271445
WBC	Low	2.091756	0.06	15	7.142323
	Normal	1.60453	1.45	15	8.44484
	High	2.318444	0.2	15	6.383592
Platelet	Low	5.335157	11.8	25	2.459159
	Normal	2.800675	0.5	25	8.74789
	High	2.683636	3.95	25	7.843835

achieved by hemoglobin in normal level (6.676438), WBC at low level (7.142323), normal level (8.74789), and high level (6.383592). Sigma-value less than three were hemoglobin at high level (2.616041), platelet in low level (2.459159), hematocrit in normal level (1.727522), and high level (2.271445)

Average Sigma-value for Hb: 4.329346, HCT: 2.474743, RBC: 3.575351, WBC : 7.323585, and PLT: 6.350295. Average Sigma for all parameters and all levels was 4.75. Minimum Sigma-value for any business or manufacturing process was three. More than Six Sigma-value was a world-class performance. There are some levels related to Sigma-value in clinical laboratory practice. The levels are world-class, excellent, good, marginal, weak, and unacceptable.[11] The relation between the levels and Sigma-value can be seen in Table 3. Higher Sigma-value could be achieved, and fewer defect opportunities could happen.[8,9]

Table 3. Sigma-value and the levels[9,14]

Sigma-value	Level	Defect per million opportunities
6	World-class	3.4
5	Excellent	233
4	Good	6,210
3	Marginal	66,807
2	Poor	308,537
1	Unacceptable	690,000

More than Six Sigma-value is world-class, and minimum Sigma-value for manufacturing is three.

There are two methods to implement Sigma-metric in clinical laboratory process: For pre-analytical and post-analytical phase: numbers of defects in a group were counted, then calculate defects per million. The standard table was utilized to convert defect per million in Sigma-value; For analytical phase: estimate imprecision and bias of the parameter performance and also define tolerance limit as total error allowance. Then we calculate Sigma-value by the formula.[8]

Imprecision is also called as the CV. Calculation of CV is based on control material test results data for the internal quality control process. Mean and SD is calculated by those data, and CV is calculated by the formula: SD/mean. Data of control material test results can be obtained by a cumulative CV from historical imprecision. Clinical & Laboratory Standards Institute (CLSI) recommends the data is obtained at least by 3-6 months routine internal quality control test; 20 days control test results that were performed twice daily; Two examination runs within a single day, each run consisting of 10-20 replicates control material. This process is also called as within-day or between-run imprecision; A single run with at least 20 replicates of control material. This process usually called as within-run imprecision or repeatability.[15]

In this study, data from daily control material examination for 42 consecutive days, were obtained and choose this method following our laboratory policy to perform control material test.

There are many methods to calculate bias. Data of bias can be obtained from reference material or reference method; The mean of a peer group; The all method means of a proficiency testing or external quality assessment survey; A comparative method.[15] This study, used bias from the mean of a peer group from data in the kit insert of control material. This method is the easiest way if use assayed control material.

The quality requirement is expressed by TEa in Sigma-metric. This data obtain by U.S. CLIA proficiency testing criteria, the Royal College of

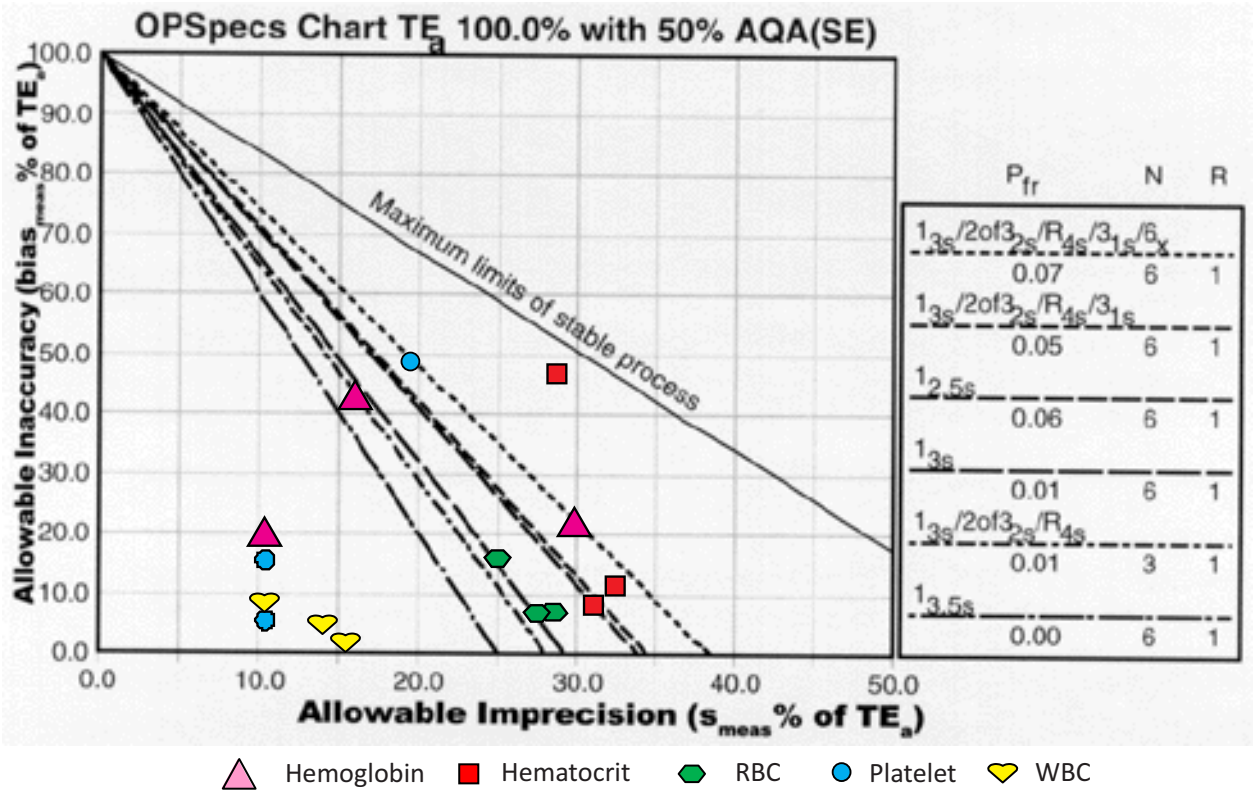

Figure 1. Normalized OPSpecs chart

Pathologists of Australasia (RCPA) guidelines, the Ricos *et al.* database on desirable specifications for total error based on within-subject biologic variation, an International Organization for Standardization (ISO) standard, a peer group specification, or even a locally determined specification.[15]

The design internal quality control procedure by Sigma-value so, need a normalized OPSpecs chart.

Data for TEa, CV, and bias must be obtained first to use normalized OPSpecs chart. Choose normalized OPSpecs charts, start with 90% Analytical Quality Assurance (AQA) and less control material numbers (N). In hematology analyzer control materials are usually available in three numbers, low, normal, and high. Whereas in clinical chemistry, it is usually available in two numbers, normal and abnormal. Then, select a control rule(s) whose operating limits are above your normalized operating point. Identify the control rule(s) from the key on the right side of the chart. If no QC procedure can be selected, try the 90% AQA & N=6 chart. Continue with 50% AQA & N=3 Chart and 50% AQA & N=6 Chart. Choose quality control (QC) procedures can be selected.[7]

In Figure 1, $1_{3,5S}$ rule for WBC and 1_{3S} for RBC can be selected. Considering medical decision levels for Hb are low and normal, a 1_{3S} rule can be chosen. It is ironic for PLT count, because it has less performance in low value, whereas it has world-class performance in high and normal value. Platelet count is important in low level because many medical decisions depend on it, especially in dengue infection disease and hemostatic disorders.[14] Multi-rules of $1_{3S}/2of3_{2S}/R_{4S}/3_{1S}/6_X$ can be chosen for PLT QC procedure.[16] Special attention must be given in HCT parameter because it has the worst Sigma-value. For now, multi-rules of $1_{3S}/2of3_{2S}/R_{4S}/3_{1S}/6_X$ must be chosen. The laboratory management must discuss with the instrument technician to improve HCT performance. QC procedure for the instrument is performed with 6 numbers control materials and a single run. Alternatively laboratory can use the rules with three numbers controls and double runs.[17]

The HCT is calculated from the RBC count and the Mean Cell Volume (MCV). The optical channel is used for the determination of RBC and PLT data. The RBC parameters are calculated using 0°, 10°, and 90° sensor data, while the PLT parameters are calculated using 0° and 10° sensor data. The MCV is derived from the RBC size distribution data on the 0°, 10°, and 90° histograms. The optical channel evaluation, especially by 90° sensor data replacement maybe can improve the Sigma-value of HCT and RBC of this instrument.[18]

CONCLUSION AND SUGGESTION

Sigma-metric can be used to evaluate the analytical performance of the laboratory instrument

and choose QC procedure. Cell Dyne Ruby hematology analyzer provides "Good" performance. QC procedure for the instrument is performed with multi-rule and a single run six numbers control materials or double runs three numbers control. Sigma value HCT and RBC parameters should be improved by optical channel evaluation.

REFERENCES

1. Plebani M. Errors in clinical laboratories or errors in laboratory medicine?. Clin Chem Lab Med. 2006; 44(6): 750–759.
2. Hammerling JA. A review of medical errors in laboratory diagnostics and where we are today. Laboratory Medicine. 2012; 43(2): 41-44.
3. Tiwari E, Pallipady A, Mishra S. Preanalytical, analytical and Post-analytical errors in a chemical laboratory. International Journal of Science and Research. 2015; 4(3): 2279-2281.
4. Plebani M. The detection and prevention of error in laboratory medicine, review article. Ann Clin Biochem. 2010; 47: 101–110.
5. Karkalousos P & Evangelopolous A. Quality control in clinical laboratories (internet). In Tech Europe. 2011(cited 30 August 2018). Available from http://www.intechopen.com/books/applications-and-experiences-of-quality-control/ quality -control-in-clinical-laboratories.
6. Yadav R, Bhartiya JP, Verma SK, Nandkeoliar MK. External quality assessment scheme. IJRRMS, 2013; 3(4): 1-4.
7. Westgard J & Westgard O. Six Sigma based quality control: Learning guide series. Abbott Laboratories, 2016.
8. Sawalakhe P, Desmukh S, Lakhe R. Evaluating performance of testing laboratory using Six Sigma. International Journal of Innovations in Engineering and Science. 2016; 1(1): 13-20.
9. Kalra J, Kopargaonkar A. Quality improvement in clinical laboratories: A Six Sigma concept. Pathology and Laboratory Medicine, 2016; 1(1): 11-20.
10. Maksane S, Parikh R, Vaswani L. Quantitative assessment of analytical phase quality of clinical biochemistry parameters using Sigma-metrics. International Journal of Medical Laboratory, 2017; 4(2): 81-90.
11. Al Muhareb TM, Jones JG. Using lean Six Sigma in the improvement of service quality at aviation industry: A case study at the departure area in KKIA. World Academy of Science, Engineering and Technology International Journal of Environmental and Ecological Engineering, 2014; 8(1): 145-151.
12. Turgeon M. Instrumentation in hematology in clinical hematology theory and procedure. Philadelphia USA, Lippincott Williams & Wilkins, 2012; 526-571.
13. Vajpayee N, Graham S, Bem S. Basic examination of blood and bone marrow. In Mcpherson RA, Pincus MR, editors. Henry's clinical diagnosis and management by laboratory method. Philadelphia USA, Elsevier Saunders, 2011; 509-535.
14. Westgard S. Six Sigma: Laboratory quality control in the healthcare ecosystem. Abbott Laboratories, 2016.
15. Westgard S. Quantitating quality: Best practices for estimating the Sigma-metric. Abbott Laboratories, 2016.
16. Deen J, Luum L, Martinez E, Huat Tan L. Clinical management and delivery of clinical services. In: Farrar J, Castelo Branco I, Dimaano E, Harris E, Hung N, Laksono IS, Martinez J, Pleites EB, Venancio R, Villegas E, Weber M, Wills B, advisers, and peer reviewers. Dengue: Guidelines for diagnosis, treatment, prevention, and control. France, WHO, 2009; 25-54.
17. Westgard J. Westgard rules and Multi rules (internet) Westgard rules. 2018 (cited 30 August 2018) available from website https://www.westgard.com/ mltirule.htm
18. Abbott Laboratories. CELL-DYN Ruby TM system operator's manual. Abbott Park (USA). 2006.