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SIX SIGMA METRICS: APPLICATION ON ANALYTICAL PERFORMANCE OF BIOCHEMICAL PARAMETERS

Dr Gayathri Chelamkuri — Assistant Professor, Department of Biochemistry, Govt Medical College and Hospital, Kadapa.

Dr. M.Venkateswarulu* — Professor and Head, Department of Biochemistry, Govt Medical College and Hospital, Kadapa.*Corresponding Author

ABSTRACT **INTRODUCTION:** The principles of quality management, assurance and control have become the foundation by which clinical laboratories are managed and operated. Maintaining a quality performance is no longer confined to private laboratories; with a mission to make public health care system more efficient, there is a dire necessity to improve the quality performance of the clinical laboratories in public sector as well to optimize the use of available resources cost effectively. Six Sigma is a quality management tool evaluating process performance and improvement. Six Sigma in Total Quality Management (TQM) implies performance goals of 6 Sigmas or 6 SD of process variation should fit within tolerance limits of the process [6]. Its unique approach uses both internal and external quality control data as a self-assessment tool. Sigma metrics performance also guides the QC design and protocol of the laboratory. A 3 Sigma zone is regarded as marginal performance and anything below it are labeled unacceptable. **OBJECTIVE:** The objective of the present study is to evaluate laboratory performance in terms of Sigma metrics **MATERIALS AND METHODS:** Six Sigma of 7 chemistry parameters analyzed on Beckman Coulter AU 480 over a period of 6 months i.e., May 2021 to October 2021, is computed for two levels I and II. The quality requirements viz Coefficient of Variation and % Bias, for calculating the Six Sigma are drawn from the Internal Quality Control values and the External Quality Assurance Scheme. Allowable Total Error (TEa) is adapted from Clinical Laboratories Improvement Act (CLIA) guidelines. Six Sigma was calculated for 7 chemistry parameters using TEa, Coefficient of Variation (CV) and % Bias. **RESULTS:** In the present study, Sigma metric values >3 for both levels of Internal quality controls is observed for Total bilirubin, AST, ALT, Alkaline phosphatase. Parameters like Glucose, Total Proteins, Albumin, sigma values were found below 3. **CONCLUSION:** Six Sigma serves as inexpensive tool to evaluate the laboratory performance employing both internal and external quality control data at a time. Six sigma also serves as a guide to design the QC protocol in the laboratory.

KEYWORDS : Six Sigma, %CV, TEa, Bias, IQC, EQAS

INTRODUCTION:

The scope of clinical laboratories on patient health care is multifarious; physicians depend on laboratory results in carrying out the diagnosis, treatment and management of patients. Despite the constant challenges clinical laboratories face in terms of workload and limited resources, they ought to produce quality laboratory results that are significant for addressing medical and public health needs. Quality is defined as conformance with the requirements of users or customers. Commonly, this is assessed in terms of accuracy, precision, sensitivity and specificity. The contribution of precision and accuracy to analytical uncertainty is substantial. The degree of imprecision is reflected in terms of random analytical errors and the amount of inaccuracy is given by systematic errors.

Six Sigma is an evolution in quality management that dates back to early 1990 Motorola approach to TQM [6]. Since then it has been applied widely in business and industry to reduce the cost of products, eliminate defects and decrease variability in processing. It consists of five steps: Define, Measure, Analyze, Improve and Control[1]. Computing Six Sigma serves a dual purpose of evaluating both process performance and improvement. Sigma metrics is calculated by using total allowable error (TEa), bias, and precision. Imprecision is expressed as Co-efficient of Variation (CV %), while Bias signifies accuracy problem. The corresponding data can be obtained from the Internal Quality Controls (IQC) run routinely and through External Quality Assurance Scheme (EQAS) or Peer Group programs respectively. Total allowable error (TEa) indicates allowable difference from the true values [8]. Thus, Six Sigma assimilates Internal and External Quality together under one roof. A process performance in terms of sigma metric scale can be approached either by measuring outcomes or measuring variation. The outcomes can be counted as defects or errors, expressed as defects per million (DPM) and then converted to a sigma metric scale as below [1].

1σ	6,90,000 errors/million reports
2σ	3,08,000 errors/million reports
3σ	66,800 errors/million reports
4σ	6,210 errors/million reports
5σ	230 errors/million reports
6σ	3.4 errors/million reports

For laboratory measurements, it is straight forward to calculate the sigma performance from CV, Bias and TEa[6]. Six Sigma Scale defines how many sigma fits within tolerance limits [5] and varies from 0 to 6; with a performance less than 3 not considered acceptable. If the Six Sigma value is more than 3 then the performance of the laboratory is satisfactory [5]. A Six Sigma performance is considered world class quality [5]. Further, measuring process variation in sigma units help in selecting appropriate QC rules, designing and implementing QC procedures.

OBJECTIVE OF THE STUDY:

The objective of the present study is to evaluate the six sigma of 7 chemistry parameters analyzed on Beckman Coulter AU 480 for a period of 6 months from May 2021 to October 2021 in the department of Clinical Biochemistry.

MATERIALS AND METHODS:

The present observational study is a retrospective analysis of the data taken from Internal Quality Controls (Levels I and II) and the External Quality Assurance Scheme for a period of 6 months from May 2021 to October 2021 in the Department of Clinical Biochemistry, Government General Hospital, Kadapa. Chemistry parameters analyzed on automated analyzer, AU 480: Glucose, Total Bilirubin, Total Protein, Albumin, Aspartate Transaminase (AST), Alanine Transaminase (ALT) and Alkaline Phosphatase are included in the study.

1. Sigma Metric is calculated using the equation: (TEa% – Bias) / CV, where TEa is allowable total error and CV is Coefficient of Variation[3].

2. CV, Coefficient of Variation, is calculated as (Standard Deviation / Mean) multiplied by 100. Mean and Standard Deviation are derived from the Internal Quality Controls levels I and II (Randox) run in the laboratory on daily basis.

3. Bias is derived from the External Quality Assurance Scheme (under aegis of CMC Vellore) run once a month as per the formula:

(Laboratory EQAS result − peer group mean / peer group mean) X 100[3]

4. TEa is followed as per Clinical Laboratory Improvement Amendment (CLIA) guidelines[8].

5. The mean of Six Sigma for individual parameter for both levels I and II over a period of 6 months is calculated and a cumulative sigma is derived for the complete period.

ETHICAL APPROVAL: Obtained from the Institutional Ethics Committee (IEC)

Month, Year	Parameters						
	Total Bilirubin	Total Protein	Albumin	AST / SGOT	ALT / SGPT	Alkaline phosphatase	Glucose
May, 21	3.24	3.10	2.72	3.54	4.72	4.04	2.36
June, 21	1.53	1.42	1.29	2.66	2.25	3.48	3.20
July, 21	2.01	0.16	0.89	2.52	3.39	5.59	2.47
Aug, 21	3.36	2.91	3.79	5.20	2.28	7.91	3.72
Sept, 21	4.51	2.94	2.80	3.02	3.98	8.16	3.75
Oct, 21	3.13	2.02	0.70	2.54	3.77	8.18	1.42

RESULTS:

Quality is assessed on the Sigma scale, with 3 sigma as the minimum allowable sigma for routine performance and Sigma of being 6 the world class quality goal. Six Sigma was calculated for

		Parameters					
	Total Bilirubin	Total Protein	Albumin	AST / SGOT	ALT / SGPT	Alkaline phosphatase	Glucose
May, 21	3.91	3.05	2.70	3.22	3.33	4.15	2.89
June, 21	1.99	1.46	1.09	2.76	2.57	2.83	3.48
July, 21	1.52	0.16	0.73	2.36	3.43	4.90	3.08
Aug, 21	6.34	3.08	3.69	6.67	5.25	7.62	4.17
Sept, 21	1.93	3.97	1.89	2.79	2.26	3.22	3.57
Oct, 21	5.07	1.92	0.63	2.01	2.74	6.53	1.46

7 chemistry parameters for two levels (I and II) of quality control in the laboratory. Table 1 shows the mean CV of all the parameters for levels I and II. Tables No 2 &3 shows the Six Sigma values of all the parameters month wise for levels I and II separately. Table 4 shows the cumulative sigma for all the parameters.

Table 1 Mean Co-efficient of Variation (CV) for parameters level –I and level-II

	Mean CV	
Parameter	Level-I	Level-II
Glucose	2.18	1.96
Total Bilirubin	4.84	4.26
Total Protein	2.84	2.81
Albumin	2.46	2.92
AST / SGOT	4.63	3.80
ALT / SGPT	4.85	4.50
Alkaline Phosphatase	5.60	6.01

Table: 2 Six Sigma values for the control level-I

Table: 3 Six Sigma values for the control level-II

Table: 4 Cumulative Six Sigma values for parameters level-I and II

	Cumulative Six Sigma	
	Level-I	Level-II
Glucose	2.60	2.92
Total Bilirubin	3.33	4.11
Total Protein	2.14	2.15
Albumin	1.89	1.54
AST / SGOT	3.27	4.01
ALT / SGPT	3.12	3.55
Alkaline Phosphatase	4.78	4.24

Table :5 Sigma Metric performance of various biochemical analytes

QC levels	Performance on Sigma values		
	< 3 unacceptable	3 to 4 Fair	4 to 5 Good
Level-I	Glucose, Total Protein, Albumin	Total Bilirubin, AST, ALT,	ALP
Level-II	Glucose, Total Protein, Albumin	ALT	Total Bilirubin, AST, ALP
QC: Quality control, AST: Aspartate Transaminase, ALT: Alanine Transaminase, ALP: Alkaline Phosphatase			

DISCUSSION:

Laboratory testing processes are complex and prone to errors. Systematic errors are related to calibration problem that affect the accuracy and may be resulting from i) impure calibration materials, ii) improper preparation of calibrating solutions, iii) erroneous set point and assigned values, iv) unstable calibrating solutions, v) contaminated solutions, vi) inadequate calibration techniques, vii) nonlinear or unstable calibration functions, viii) unstable reagent blanks and ix) inadequate sample blanks [6]. Random errors implies precision problem arising due to i) lack of reproducibility in the pipetting of samples and reagents ii) dissolving of reagent tablets and mixing of sample and reagents iii) lack of stability of temperature baths, timing regulation and photometric and other sensors [6]. Stringent quality control is an essential requisite to ensure and deliver consistent results and contribute toward improved patient care. It is imperative to optimize the rational use of the resources without compromising the quality of the laboratory. Quality control in medical laboratory is a statistical process to monitor and evaluate the analytical process. Sigma Metric application serves as a simple and inexpensive tool that gives a combined impact of both internal and external quality data on a single equation, albeit retrospectively.It takes into consideration the measures of imprecision in terms of CV and inaccuracy in terms of Bias. On a prospective front, Six Sigma helps us to choose or redefine the QC protocol and design. Sigma metrics in the laboratory provides a more quantitative work frame for assessing process performance and creates a scientific basis for designing an appropriate QC strategy [6].

Quality is assessed on the sigma scale, with 3 sigma as the minimum allowable sigma for routine performance and sigma of 6 being the world class quality goal. Six Sigma measures outcomes in terms of Defects or Errors that can be translated as Non-conformances as per to International Organization for Standardization, ISO. Six sigma values are inversely related to the defects or errors.

Our laboratory currently analyses two levels of Internal Quality controls every day. In the present study, the parameters that showed a sigma values above 3 include Total Bilirubin, AST, ALT, Alkaline Phosphatase [Table:5]. For parameters Glucose, Total Proteins and Albumin, sigma values were found below 3 [Table:5]. The sigma performance of the various analytes is categorized as < 3 (unacceptable) and 3 to 4 (Fair) and 4 to 6 (Good). Based on the Six Sigma Performance, a corrective action will be initiated to redefine the QC protocol of the laboratory based on selection of appropriate Westgard rules, total number of control measurements per Statistical QC (SQC) event (N) and frequency of SQC events (Run size-R of patient samples between SQC events) as follows[7]:

Sigma of analytes	Westgard rules	Number of control levels(N) Run size (R)
< 3	$1_{3S}/2_{2S}/R_{4S}/4_{1S}$ / 6x / 8x	N6 and R45
3 to 4	$1_{3S}/2_{2S}/R_{4S}/4_{1S}$ / 6x	N4 and R45
4 to 5	$1_{3S}/2_{2S}/R_{4S}/4_{1S}$	N4 and R200

In addition, various aspects of laboratory quality management associated with Methodology, Standard Operating Procedures (SOP), QC and calibrating materials reconstitution and storage, equipment maintenance, working conditions, laboratory staff training were also scrutinized to minimize the errors.

CONCLUSION:

Six Sigma approach makes use of the information on precision and accuracy that laboratories acquire initially during method validation studies and have available on continuing basis from internal and external quality control. A calculation of Six Sigma makes it straightforward to select the right control rules and the right number of control measurements depending on the run size Six Sigma serves as

inexpensive tool to evaluate the laboratory performance employing both internal and external quality control data at a time.

CONFLICTS OF INTEREST: None declared

REFERENCES:

1. Kirankumar P. Chauhan, Jatin D Patel, Amit Trivedi Six Sigma in Clinical Biochemistry: It matters, measure it International Journal of Clinical Biochemistry and Research, July-September 2017; 4(3): 270-274
2. Lakshman M Reddy, Bhulaxmi P, Malathi K, Salma M, Prakasham S E. "Evaluation of sigma metrics in a Medical Biochemistry lab" International Journal of Biomedical Research 2015; 69 (3): 164-171
3. Lokesh Kumar Sharma, Rashmi Rasi Datta, Neera Sharma Sigma Metric Evaluation of Drugs in a Clinical Laboratory: Importance of Choosing Appropriate Total Allowable Error and a Troubleshooting Roadmap https://doi.org/ 10.1055s-0041-1726572
4. Nitinkumar G et al Application of Six Sigma for the Quality Assurance in Clinical Biochemistry Laboratory-A retrospective study Int J Res Med. 2013; 2(3);17-20
5. Ramya KR, Vijetha Shenoy Belle, Pravesh Hegde, Sushma Jogi, Krishnananda Prabhu RV. Assessment of six sigma metrics applications of quality control in clinical biochemistry laboratory. International Journal of Biochemistry. September 2019, 11(3): 100-103
6. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 5 th Edition, Carl A. Burtis, Edward R Ashwood, David E Bruns
7. Trupti Diwan Ramteke , Anita Shivaji Chalak , Shalini Nitin MaksaneSigma Metrics: A Powerful Tool for Performance Evaluation and Quality Control Planning in a Clinical Biochemistry Laboratory- Journal of Clinical and Diagnostic Research. 2021 Mar, Vol-15(3): BC20-BC23
8. Xuehui Mao, Jing Shao, Bingchang Zhang, Yong Wang Evaluating analytical quality in clinical biochemistry laboratory using Six Sigma Biochem Med (Zagreb) 2018;28(2):020904