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Course Notes

DOI: 10.1515/rrlm-2016-0024

The use of quality indicators to improve the performance in the processes of pre-examination and post-examination by applying Six Sigma scale

Utilizarea indicatorilor de calitate pentru îmbunătăţirea performanţei pre- şi post-examinare, utilizând conceptul Six Sigma

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Received: 25th February 2016; Accepted: 22th May 2016; Published: 8th June 2016.

Introduction

One of the new requirements of the 2013 version of standard SR EN ISO 15189 is risk management (1) that identifies, analyzes and controls all potential sources of error that could affect results. With a view to continuous improvement, the medical tests laboratory documents the corrective actions and monitors in dynamics the quality indicators (QI) established on the basis of identified errors. In this regard errors should be defined taking into account all stages of the total examination process (from pre-examination to post-examination) in accordance with standard ISO 22367:2008(2).

In current practice, though over 60% of errors occur in pre- and post-examination stages and majorly affect end results (3), they do not receive appropriate attention. This material presents the manner of establishment and monitoring of QI as defects per million opportunities (DPMO) on the Six Sigma scale in the pre- and post-examination processes (1). We believe that by monitoring DPMO from the pre- and post-examination processes and converting them to Sigma values alongside with the use of Sigma metric equation in the examination process one can ensure continuous improvement of the quality of results in medical tests laboratories.

I. Quality indicators (QI)

QI are the measure of the degree to which a set of inherent characteristics meets particular requirements (1).

For example, in the case of blood count, one of the inherent features in the process is to receive blood specimens wholly collected on an-

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ticoagulant. The particular requirement in this case is that the specimens received by the laboratory must be non-hemolyzed. The measure of quality for the blood counts received may be the proportion of hemolyzed blood counts (that do not meet the specific requirements, namely with defects) of the total received.

The establishment of QI as a method of continuous improvement of the quality management system has been a concern of all medical laboratory professional societies. Since 2000, Nevalainen et al reported that implementing QI on a Six Sigma scale can support continuous improvement of the laboratory performance (4). Ricos et al (2004) communicated performance specifications for QI identified in extra-analytical phases (5), but the first study on these indicators of the overall process of examination of the 3 phases, pre-examination, examination and post-examination was communicated by Plebani et al (2006) (6). Since 2008, the scientific community recognized and attempted the harmonization of the 23rd QI in pre-examination, 6 QI in examination and 11th QI in post-examination (8). QI can be expressed in many ways: yield%, defects% DPMO (defects per million opportunities), PPM (parts per million) or on the Six Sigma scale (8). It is difficult to monitor each QI according to an own specification performance as it is much easier to establish QI as DPMO on a Six Sigma scale for each process (pre-examination, examination and post-examination). Performance analysis in this case is made against a single specification of performance, Sigma > 3).

According to SR EN ISO 15189 medical laboratories can establish QI after a thorough analysis of all sources of error in the total testing process (TTP) by applying risk management (1). The laboratory error is defined as any defect that occurs from test request until the reporting of result, including interpretation and reaction to this result (2).

Errors in laboratory practice should be divided into:
- Laboratory errors namely inconsistent results with "statistical effect", which are not due to human intervention,
- Mistakes, namely non-compliant results, without "statistical effect", due to human intervention.

The errors in pre- and post - examination are largely mistakes.

The quality of laboratory results must be defined as a guarantee that every stage of the total testing process is performed correctly. This can be achieved by implementing the risk management in the medical laboratory.

II. Risk Management

Risk is the combination between the likelihood of occurrence of a failure (something unacceptable) and the impact on the final outcome (severity of effect) (9). Risk management is a process that achieves: identification, analysis and evaluation of all risk situations, risk control and residual risk analysis. An important risk assessment technique is FMEA ("Failure Mode and Effects Analysis") (10). FMEA combines the likelihood of defects occurrence (often - once a week, probable occasional, isolated, improbable / in theory) with the degree of severity of each error (catastrophic - the patient's death, critical - permanent dysfunction or life-threatening injury, serious - lesion or dysfunction requiring medical intervention; minor – temporary lesion / dysfunction requiring no medical intervention, negligible - temporary discomfort) (2, 9).

III. Six Sigma

Six sigma is the most complete management system that aims to improve quality by eliminating defects (11). While in the analytical phase,

we can apply Six Sigma equation, in the pre-/ post-analytical stage we can implement the Six Sigma concept by counting defects followed by converting them into DPMO and by relating DPMO on the Six Sigma scale.

The Six Sigma concept is based on completing the five steps of the so-called algorithm **DMAIC** (Define-Measure-Analyze-Control). The first step (**D - Define**) aims to establish how many opportunities of defects appear for a certain type of primary sample (by applying FMEA, **Table 1**). We record the defects that appear for each method of measurement in case of samples received (in a given time) and we calculate DPMO (**M - measure**) and the results obtained will be converted into Sigma value using a conversion table. We analyze (**A - Analyze**) the Sigma value obtained considering that the acceptable performance means Sigma > 3. We search for causes of poor performance by means of Sigma < 3 and apply (**I - Improve**) corrective actions (e.g. training) to solve cases. The algorithm is permanently applied (**C - Control**) monitoring the performances obtained.

D - Define:

For the definition of QI in TTP (the first stage of DMAIC), it is important to establish significant errors (frequent and with major impact) that occur throughout the entire process of examination in the following stages (3, 5):

- selecting the test and preparing the referral note,
- preparing the patient for harvest,
- primary sample collection (hospital or outpatient),
- transportation to the laboratory,
- primary sample identification,
- processing of primary sample for analysis (or getting secondary sample),
- actual analysis,
- reporting/releasing results,
- interpretation and medical decision.

The responsibility of each laboratory is to eliminate errors likely to occur during TTP by the QI established after a FMEA analysis (**Table 1**).

IV. The pre-analytical phase includes (3):

A. The pre-pre-examination process begins with test selection and preparation of the referral

Table 1. Model of risk analysis by FMEA ("failure mode and effects analysis") in total testing process (TTP)

	Processes (Phases)	Process stages	Errors (defects)	Probability of a defect occurecce*	Effect on the result**	Establishing of QI (if applicable)	Monitoring of QI by DPMO (Six Sigma)	Corrective / preventive actions	Residual risk
Total testing process (TTP)	**Process of pre-pre-examination**								
	Process of pre-examination								
	Process of examination								
	Process of post-examination								
	Process of post-post-examination								

** Each laboratory establish its frequency of risk; ** Each laboratory specify the effect of the identified risk on the final result; DPMO - defects per million opportunities; QI - quality indicators.*

note and lasts up the receipt of samples in the laboratory.

B. ***The pre-examination process*** extends from receipt of samples in the laboratory to actual examination (receipt, identification, recording, centrifugation, and sub-sampling.

A. ***In the pre-pre-examination process*** the error-prone process stages are: selecting the test and preparing the referral note, patient preparation for harvesting, primary sample collection (hospital or outpatient), transportation to the laboratory.

A.1. *The referral note and test selection* must contain the following data:
- the unique and complete patient identification (which is a key indicator because the failure to observe it can cause serious consequences for the medical decision and patient safety),
- the name or other identification of the requesting doctor because failure to do so may result in the delay of sending an alert result,
- type of sample (blood, urine, other biological product),
- required tests.

To avoid the entry on the referral note of the wrong test we recommend making tests requests from electronic pre-configured lists.

Based on professional guidelines and consensus between the laboratory and clinician tests algorithms should be used for each suspected diagnostic to avoid multiple applications that provide the same information, decrease the efficiency of the laboratory and imply extra costs. For example, from the beginning of an investigation the clinician should require all thyroid endocrine markers (TSH, T4, FT4, FT3) instead of TSH.

Also, on the referral note one may mention relevant information for the interpretation of the results: sex, birth date, special physiological conditions, and medication habits (smoking, coffee etc.) diagnose presumptive etc.

A.2. Preparing the patient

In order to harvest the primary sample the patient is instructed on:
- coming at the time set for harvest "*a jeun*",
- low-protein diet the day before harvest,
- avoiding exercise at least 2 hours before harvesting the primary sample,
- providing information about the medication taken.

A.3. Primary sample collection

Since 2006, Plebani et al communicated significant differences regarding the registered defects as PPM in three laboratories in Italy for patients hospitalized and ambulatory patients (3).

Minimum requirements to avoid collection errors are:
- the hospital does not collect from catheter,
- in the ambulatory, before collection, requests are registered in the computer or in the register and the date and time of receipt, the identity of the person who receives the patient are noted,
- irrespective of the place of harvest (hospital or outpatient) before harvesting, the nurse must verify patient identity and traceability in the tests requests.

Compliance with minimum requirements does not exclude sources of error that may occur in primary sample collection stage due to:
- preparing the puncture site: insufficient removal (evaporation) of disinfectant may cause contamination and hemolysis of the sample collected,
- tourniquet application: do not apply more than a minute, it is removed after the blood begins to flow into the first tube. Prolongation of compression produces haemoconcentration on the puncture site (e.g. increases the potassium and lactic acid),
- choice of tube type and harvest order: each request requires the choice of certain tube in accordance with CLSI H5-A6 (12) guide, the correct order of tubes avoiding contamination of the blood with additives,

- labeling of tubes is a key indicator, the writing of patient data marker may lead to the erroneous identification of the sample, the correct solution being the use of bar code labels.

The sources of error that occur immediately after harvest can be determined by:
- mixture of blood with additives: for example, the tube without additives (with red plug) should not be mixed, but placed upright immediately after collection; the coagulation activator tube is mixed gently 5 times, so as the centrifuged specimen does not become jelly-like and the additives tube (heparin, EDTA or citrate) is mixed gently for 8-10 times, in order to avoid hemolysis,
- the volume of blood collected. Thus, in the expired tubes the vacuum decreases and the proportion additive / blood is modified or is insufficiently collected; the small needle diameter and the too large diameter of the tube can cause hemolysis; the number of tests required obliges to the harvest of a certain volume of blood.

The most common error in the collection stage is to obtain a primary hemolyzed sample. Among the possible causes of hemolysis, we can include:
- the collection with syringe, and then the transfer in the tubes (the degree of hemolysis is inversely proportional to the diameter of the needle),
- harvesting from the catheter or infused vein;
- use of traumatized veins after applied treatments,
- antiseptic used (pay attention to sanitary alcohol),
- puncture site (capillary puncture massaging the surrounding tissue),
- tube - the wide tube cause hemolysis,
- vigorously mix blood / anticoagulant,
- detachment of the clot formed on the inner side of the red plug.

A critical error for blood tests is the coagulation of primary samples because there was an insufficient mixture between blood and anticoagulant, the mixture was in optimal amount, it was done correctly, but late after the clotting began in the tube, or expired tubes were used.

A.4. Transport of material to the laboratory
For the transport of primary samples one must comply with European transport standard that establish conditions for potentially infectious materials (13) and SR EN ISO 15189: 2013 requirements (1) on the safety and security and of carrier and environment and sample integrity and stability. Clear rules for the stability of the sample can be found in CLSI guidelines (12) which state that blood samples must be transported by the laboratory within 2 hours of harvest at a temperature between 10-22 degrees Celsius and urine samples must be transported by the laboratory within maximum 2 hours at a temperature of 2-8 degrees Celsius (14).

Common sources of error frequent during the transport of primary samples are related to: the time from harvest until the receipt in the laboratory, packing and labeling type, transport temperature, light exposure, position of the tubes in the stand, tubes agitation, etc.

The pre-pre-examination phase involves several processes, most outside the laboratory, and quality indicators in the pre-pre-examination process must be set only in agreement with the requesting doctors and based on national and / or international professional guidelines.

B. The pre-examination covers
B.1. Receipt of primary sample in the laboratory.
B.2. The primary sample preparation for examination.

B.1. Checking the primary sample in the laboratory is a key indicator. The laboratory personnel checks each tube macroscopically (volume, appearance, integrity, appropriate tube) and traceability to analysis request, then records the requests in the computer (or regis-

ter). Mandatorily the electronic or paper record contains in addition to patient data and tests requested, the date and time of receipt and identification of the person receiving the biological material.

B.2. Primary sample preparation for testing involves centrifuging (length, speed), sampling, labeling secondary sample (ensuring primary sample traceability) and storage in stability conditions (time, temperature).

V. The post-analytical phase includes:

A. The post-examination process

A.1. Reporting results.

A.2. Releasing results.

B. The post-post-examination process

B.1. Interpretation of results.

B.2. The medical decision.

A.1. Errors in reporting results stage:

- incomplete tests report (no result),
- incomplete information for interpretation: we may lack data on the state of the sample, date and time of harvest, date and time of receipt, the method of analysis used, identification of the person who validated (name, signature) or the tests report contains erroneous data due to manual transcription of the results, inadequate reference interval,
- non-validated tests report.

A.2. Errors in the release of results stage refer to:

- delaying the release of the result (response time),
- late communication of alert values (in maximum 4 minutes for inpatients and 15 minutes for outpatients 15 minutes - as recommended by international professional guides) (5),
- non preserving data confidentiality when the laboratory must pay attention to the identity of the person receiving the result and to the call communication of the result.

B. The post-post-examination process comprises the steps of interpreting the results and the medical decision. Errors in the stages of interpretation of the results by the clinician and the medical decision can be much reduced through proper communication between the clinician and the laboratory.

M - Measure

Registration of defects must be carried out for each department by domain (hematology, chemistry) or measurement sub-domain (automatic blood count, ESR, coagulation tests) and by type of tube.

The errors related to the type of tube (without anticoagulant, with anticoagulant: EDTA, sodium citrate, separating gel, sterile containers for urine) would only influence the results of analytics that are determined in that tube. For example, the percentage of contaminated urine specimens received in the microbiology will not affect in any way the hematology results.

Therefore, registration of defects and calculation in DPMO must be made for each domain / sub-domain according to the measuring tube (**Table 2, Table 3, Table 4**) using the formula:

DPMO =	Total defects/(No. of requests *or* samples received x No. of opportunities)	x 1000000

where:

DPMO - defects per million opportunities;

Total defects - total number of defects counted in a given time;

No. of requests / samples received - total number of requests/samples received in a given time for each measurement domain (clinical chemistry, hematology, microbiology);

No. of opportunities - total number of types of defects (e.g., can be identified till 12 types of defects in clinical chemistry, hematology: incomplete applications, hemolysed specimens, coagulated specimens, etc. and also can be identified till 9 types of defects in microbiology).

Table 2. Model of quality indicators for the clinical chemistry

Date	Patient ID	Harvesting place: hospital (H) or outpatient (O)	TYPES OF DEFECTS										Total defects
			OF PRE-EXAMINATION PROCESS							OF POST-EXAMINATION PROCESS			
			Incomplete data requests	Haemolysated specimen	Inadequate tube	Insufficient specimen	Inadequate transport conditions (temperature, duration, position of the tube in stand)	Specimen collected postprandial (turbid)	Lack of tube traceability on request	Inadequate centrifugation(duration, speed)	Sampling without primary specimen traceability	Incomplet analysis bulletin (no test, no reference interval, lack of result of one or more tests, no opinions and interpretations)	Unvalidated analysis bulletin	Critical values unannounced on time	
1.01	01	H						X			X				2
1.01	02	O		X			X					X			3
1.01	44	H				X									1
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
31.03	53	O					X								1
Total defects in a given data range (1.01 - 31.03)															2442

Nota bene: the measurements of clinical chemistry are made in the same type of tube.

Figure 3. Model of quality indicators for the field of hematology

Data	Patient ID	Harvesting place: hospital (H) or outpatient (O)	TYPES OF DEFECTS										Total defects
			PRE-EXAMINATION							POST-EXAMINATION			
			Incomplete data requests	Coagulated specimen	Haemolysated specimen	Lack of tube traceability on request	Inadequate transport conditions (temperature, duration, position of the tube in stand)	Drawn Blood volume – too high	Drawn Blood volume – too low	Lack of collection tube	Incomplet analysis bulletin (no test, no reference interval, lack of result of one or more tests, no opinions and interpretations)	Unvalidated analysis bulletin	Critical values unannounced on time	Analysis bulletin – blood smear without opinion-s and interpretations	
...	...	H		X											1
...	...	O		X	X										2
...	...	O		X					X		X				3
...	...	H					X								1
...	...														
Total defects in a given data range															7

Nota bene: the measurements of hematology subdomains (blood count, hemostasis tests, erythrocyte sedimentation rate, imunohematological tests) are made in different tubes are different, all of them with anticoagulant (EDTA, sodium citrate, etc).

Table 4. Model of quality indicators for the field of microbiology

Data	Pacient ID	Harvesting place: hospital (H) or outpatient (O)	TYPES OF DEFECTS									Total defects
			PRE-EXAMINATION					POST-EXAMINATION				
			Incomplete data requests	Non sterile container	Contaminated urine specimen	Inadequat collection time (after administration of antibiotics)	Inadequate transport conditions (temperature, duration, position of the tube in rack)	Incorrect analysis bulletin (transfer of data from one patient to another)	Incorrect analysis bulletin (wrong data transfer from notebook to computer)	Unvalidated analysis bulletin	Reporting Delay	
...	...	H	x	x	x					x		4
...	...	O			x				x			2
Total defects in a given data range												6

We convert DPMO in Sigma value according to the conversion table (**Table 5**).

Table 5. Sigma Conversion Table (15)

DPMO (defects per million of opportunities)	Sigma level	Yield (%)
5000000	1	50%
308537	2	65%
66807	3	93.3%
6210	4	99.4%
233	5	99.976%
3.4	6	99.9997%

A - Analysis

Depending on the Sigma value obtained, we analyze the results for each measurement domain knowing that an acceptable performance means Sigma > 3 and a target performance is of 6 Sigma.

For example, using **Table 2**, where we noted defects from pre- and post-examination of the requests received in case of clinical chemistry in a given period (we chose as an example the first three months of the year) we obtained a total number of defects of 2442 for 12 opportunities for defects identified per primary samples received in the given time frame. If during this period we received a total number of requests / primary samples for clinical chemistry of 2246, then DPMO = [2442 / (2246 x 12)] x 1000000 = 90605 which corresponds in the conversion table (**Table 5**) to a Sigma level < 2. The result obtained shows an unacceptable performance for which the laboratory must take corrective measures to solve cases.

The same steps are completed for the other measuring domains (on hematology – example **Table 3**, on microbiology - example **Table 4**, etc.).

I - Improves

In case of low performance (below 3 Sigma), the laboratory identifies the causes and applies the appropriate corrective actions which in most

cases consist of retraining the staff involved. We envisage the process / sub-process where errors occur and their frequency and severity.

C - Control

After implementation of corrective actions, the process of recording all defects and the continuous improvement is monitored by reducing errors that occurred out of the pre- and post-examination processes.

Conclusion

Implementation of the Six Sigma concept in the process of testing by establishing the quality indicators for the pre- and post-examination processes along with the use of Sigma metric Equation in the examination process represents the guarantee of quality of the results obtained in medical tests laboratories.

References

1. SR EN ISO 15189:2013. Medical laboratories - Requirements for quality and competence. ASRO, Romania; 2013.
2. International Organisation for Standardization/ Technical Specification ISO/TS 22367:2008. Medical laboratories - reduction of error through risk management and continual improvement. Geneva, Switzerland: International Organization for Standardization: 2008.
3. Plebani M. Errors in clinical laboratories or errors in laboratory medicine? Clin Chem Lab Med. 2006;44(6):750-9 DOI: 10.1515/CCLM.2006.123.
4. Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L, Morgan T. Evaluating laboratory performance on quality indicators with the six sigma scale. Arch Pathol Lab Med. 2000;124(4):516-9.
5. Ricós C, García-Victoria M, de la Fuente B. Quality indicators and specifications for the extra-analytical phases in clinical laboratory management. Clin Chem Lab Med. 2004;42(6):578-82. DOI: 10.1515/CCLM.2004.100.
6. Plebani M, Ceriotti F, Messeri G, Ottomano C, Pansini N, Bonini P. Laboratory network of excellence: enhancing patient safety and service effectiveness. Clin Chem Lab Med. 2006;44(2):150-60. DOI: 10.1515/CCLM.2006.028.
7. Sciacovelli L, Plebani M. The IFCC Working Group on laboratory errors and patient safety. Clin Chim Acta. 2009;404(1):79-85. DOI: 10.1016/j.cca.2009.03.025.
8. Westgard JO, Westgard SA. Developing a Scientific Quality System. Chapter 8. In: Basic Quality Management Systems: Essential for Quality Management in the Medical Laboratory, Westgard QC, Inc., 2014, 105-130.
9. International Organization for Standardization. ISO 14971:2007: Medical devices - Application of risk management to medical devices.
10. Jiang Y, Jiang H, Ding S, Liu Q. Application of failure mode and effects analysis in a clinical chemistry laboratory. Clin Chim Acta. 2015;448:80-5. DOI: 10.1016/j.cca.2015.06.016.
11. Schweikhart SA, Dembe AE. The applicability of Lean and Six Sigma techniques to clinical and translational research. J Investig Med. 2009;57(7):748-55. DOI: 10.2310/JIM.0b013e3181b91b3a.
12. Clinical Laboratory Standards Institute (CLSI). Procedures for the Collection of Diagnostic Blood Specimens by. Venipuncture; Approved Standard - Sixth Edition (Vol. 27 No. 26). CLSI document H3-A6. Clinical Laboratory Standards Institute; Wayne, Pennsylvania, USA: 2007.
13. ADR 2015. European Agreement concerning the International Carriage of Dangerous Goods by Road. http://www.unece.org/trans/danger/publi/adr/adr2015/15contentse.html (accessed on 05.01.2016).
14. Clinical Laboratory Standards Institute (CLSI). Urinalysis; Approved Guideline - Third Edition. (Vol. 29, No. 4) CLSI document GP16-A3. Clinical Laboratory Standards Institute; Wayne, Pennsylvania, USA: 2009.
15. Ehrlich BH. Transactional Six Sigma and Lean Servicing: Leveraging Manufacturing Concepts to Achieve World-Class Service. Boca Raton: St. Lucie Press, 2002. DOI: 10.1201/9781420000337.