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ORIGINAL ARTICLE

Pre-Analytical Components of Risk in Four Branches of Clinical Laboratory in Romania - Prospective Study

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SUMMARY

Background: **Development of quality measurement principles is a strategic point for each clinical laboratory. Pre-examination process is the most critical and the most difficult to be managed. The aim of this study is to identify, quantify, and monitor the nonconformities of the pre-analytical process using quality indicators that can affect the patient's health safety in four different locations of a Romanian private clinical laboratory.**
Methods: **The study group consisted of all the analysis requests received by the departments of biochemistry, hematology, and coagulation from January through March 2015. In order to collect the pre-analytical nonconformities, we created a "Risk Budget", using the entries from the "Evidence notebook - non-conform samples" from the above mentioned departments. The laboratory established the quality indicators by means of the risk management technique in order to identify and control the sources of errors, FMEA (Failure Modes and Effects Analyses), which had been implemented and monitored for its purposes and special needs. For the assessment of the control level over the processes, the results were transformed on the Six Sigma scale, using the Westgard calculation method and being obtained in this way the frequency with which an error may occur. (https://www.westgard.com/six-sigma-calculators.htm).**
Results: **The obtained results prove that the quantification and monitoring of the indicators can be a control instrument for the pre-analytic activities. The calculation of the Six Sigma value adds extra information to the study because it allows the detection of the processes which need improvement (Sigma value higher than 4 represents a well controlled process). The highest rates were observed for the hemolyzed and the lipemic samples, in the department of biochemistry and hemolyzed, insufficient sample volume, or clotted samples for the department of hematology and coagulation. Significant statistical differences between laboratories participating in the study have been recorded for these indicators.**
Conclusions: **The elaborated study between the four branches of a Romanian private clinical laboratory was a challenge, and it helped in choosing strategic decisions regarding the improvement of the patient's health safety in the institution, corresponding to the accreditation requirements in accordance with ISO 15189:2013.**
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KEY WORDS

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INTRODUCTION

Risk management strategies in the clinical laboratory to ensure the patient's health safety aim to prevent, identify, and decrease the number of unwanted events by ana-

lyzing the errors [1]. The development of quality measurement principles is a strategic task of each clinical laboratory. Without analysis of errors, the performance cannot be assessed objectively [2]. In the clinical laboratory, all the errors must be measured and controled by means of quality indicators, which ensure an objective assessment of the context in which errors occur and, when appropriate, by comparisons between the laboratories at different periods of time [1]. ISO 15189:2013, "Medical Laboratories - Particular requirements for quality and competence", section 4.14.7, states that laboratory directors "must establish quality indicators to monitor and evaluate the performance of all critical aspects of the pre-examination, examination, and post-examination processes" [3]. According to the clinical laboratory principles that were found in the quality control plan, the laboratory should decide what is important to be measured, how to collect and analyze the data, to establish the thresholds of performance and also the way this data is used and reported [2].

Considering these aspects, ISO/TS 22367, "Technical Specifications - Medical Laboratories. Reduction of error through risk management and continual improvement", shows how risk management can be implemented in the structure, organization, functioning, and quality management of the clinical laboratory, focusing on the pre-analytical and post-analytical processes. In the clinical laboratory, the analytical process is the most standardized, having well defined and internationally accepted quality indicators [1]. Many specialists in the field of quality management state that extra-analytical processes record the highest number of errors, particularly the pre-analytical process. The pre-examination and post-examination processes are the most critical and the most difficult to be managed. The laboratory should also select the quality indicators to evaluate the processes which extend beyond the laboratory activity. In this situation, it is more difficult to measure the process performance, but it promotes more effectively the process of improving which is described in the quality standards [1,2].

Various legislative regulations, standards or international organizations may influence the clinical laboratory in choosing the quality indicators. The indicators selected by each laboratory should cover all the aspects of the measurement process (pre-examination, examination and post-examination). It is ideal to monitor all the aspects of the laboratory processes, but it is not practical. Thus, the laboratory management must be sure that the selected indicators are able to measure a wide variety of non-conformities [2].

Risk management of the pre-analytical phase in Romanian laboratories is a relatively new concept, which became mandatory in 2014, when ISO 15189:2013 was adopted.

Our aim was to identify, define, analyze, and estimate the pre-analytical quality indicators, in four branches of the Romanian laboratory, in the period from January through March 2015, classifying errors according to their criticality for the patient's health safety.

MATERIALS AND METHODS

The study group consisted of all the requests for analysis received by the clinical laboratory (no exclusion criteria were applied). The laboratories from this study use the same system of quality management, since all of them are accredited according to ISO 15189. Clinical laboratories are equipped with hematology, biochemisttry, and coagulation analyzers, without any pre-analytical automation.

Quality indicators were established by the means of a risk management technique in order to identify and control the sources of errors in the laboratory, FMEA (Failure Modes and Effects Analysis), an integral part of the pre-analytical process. Due to this technique it was possible to define the critical stages in the collecting and processing of blood samples, which can lead to errors. In this technique of risk management, the errors were classified by RPN (Risk Priority Number), so we could pay attention to those errors that were monitored [1]. This number was obtained by multiplying the awarded scores in order to assess the probability of the error's occurence, severity, and detectibility.

- The laboratory has established a scale for assessing the probability of the error's occurence (the scale was from 1 to 5, where 1 represented the least frequent errors, and 5 represented the errors with the highest probability of occurence; Table 1) [4,5]. The laboratory decided what the significance is for each term of the scale, and it may be different for different tests. In this study, the scale we used for the probability of the error's occurence was the one shown in Table 1.
- The consequences of an error in the clinical laboratory can be: an incorrect result, a result received by the clinician with delay or the lack of the result for the required test. These situations can influence the patient's health safety because the result of the test can lead to misdiagnosis and to an inappropriate treatment or even the lack of it. For each analyzed error, the laboratory assessed the severity of the harm that occurs from it, using a scale from 1 to 5 (Table 2) [4,5]. The scale setting was performed after brainstorming between laboratory specialists, but also between the specialists and clinicians who in fact use the tests' results.
- The detectability was expressed as being the probability that the control process implemented by the laboratory can detect an error and it was quantified using a scale from 1 to 5 (1 represented a high probability of detection, and 5 represented low probability of detection, meaning ineffective control measures; Table 3) [4,5]. (Note: It is important to be aware of the detection process, because it may be

similar to the accuracy of the diagnosis using a medical test).

- Criticality was considered as being "the product of severity times and probability (FMEA) or frequency of occurence (FRACAS)" [4]. According to SR EN ISO 14971:2011, a matrix of the risk acceptability was drawn up (Table 4) [5]. Each cell within the risk matrix indicated if the criticality or the risk (according to SR EN ISO 14971:2011, the two terms are synonymous) was acceptable or unacceptable based on the combination of the two factors. The interpretation of the results from this matrix was performed by the staff of the laboratory together with the clinicians, to determine if they can be applied. (Note: FMEA - Failure Modes and Effects Analysis; FRACAS - Failure Reporting and Corrective Action System)
- The laboratory correlated the fixed data, by multiplying the scores given to assess the criticality and the probability of the errors detection and obtained risk priority numbers - RPN.
  Relying on the RPN three main categories for errors were identified:

1. Critical errors (RPN: 24 - 75) - errors resulting from the type of analysis request (electonic or manual) and the means used to provide or record it. These errors could have serious consequences for the patient safety in case they were not detected early and quickly corrected [1].
2. Major errors (RPN: 12 - 18) - errors resulting from the non-conformity of specimens (icterus, hemolysis, lipemia) or non-conformities of the specimens' presentation (insufficient sample volume, samples collected in inappropriate containers, inadequate sample-anticoagulant for the requested test).
3. Minor errors (RPN: 2 - 8) - errors with low probability of their occurrence, high probability of detection or no severity. These errors are taken into account in order to review the procedure and the technical training [1].

This matrix of risk has its limits in medical practice, because it was designed for industrial use before a product was marketed. Nevertheless, in laboratory, any error should be noticed, regardless of its risk priority number (RPN).

Defining the selected indicators by FMEA

1. Misidentification errors (critical errors) (QI_1), indicator of pre-analytical process, could occur when the staff with less laboratory experience may be less likely to understand the potential for error from manual data entry. Critical errors may affect the patient's health safety. These kind of errors may come from outside the laboratory (misidentified samples detected before release of results or after issuing results, misidentified or inappropriate requests) or from the laboratory (misidentification of sample aliquots may occur when "a sample is divided into one or more parts and placed into a separate tube or container" [6]).
   The calculation formula: misidentification errors
   - percentage of "number of misidentified samples/ total number of samples"
   - percentage of "number of misidentified requests/ total number of requests"
   - percentage of "number of inapropriate requests/ total number of requests"
   - percentage of "number of unlabeled samples/total number of samples" [1,7-10]
2. Hemolysed samples (QI_2), both plasma and serum samples, were considered the samples with any degree of hemolysis, from "mild hemolysis" to "intense hemolysis".
   The calculation formula: hemolysed samples = percentage of "number of hemolysed samples/total number of samples" [1,7-10].
3. Clotted samples (QI_3), were considered the samples collected in containers with an anticoagulant (EDTA or citrate) and they showed clots at the pre-analytical inspection.
   The calculation formula: clotted samples = percentage of "number of clotted samples/total number of samples with an anticoagulant" [1,7-10].
4. Insufficient sample volume (QI_4) refers to any type of sample. Our study took into consideration only the samples with insufficient sample volume for the determinations of coagulation and hematology. Issues related to the insufficient sample volumes can be discussed also for the biochemistry determinations, paying attention to the pediatrics department. The clinical laboratories included in this study do not currently serve the pediatrics department [11].
   The calculation formula: insufficient sample volume = percentage of "number of samples with insufficient sample volume/total number of samples" [1,7-10].
5. Icteric samples (QI_5)
   The calculation formula: icteric samples = percentage of number of icteric samples/total number of samples.
6. Lipemic samples (QI_6)
   The calculation formula: lipemic samples = percentage of lipemic samples/total number of samples.
7. Total incidents of samples (QI_7)
   The calculation formula: total incidents of samples = percentage of total number of samples quality incidents/total number of samples [1,7-10].

Note: The terms "sample" and "specimen" are used with the same meaning (e.g., "hemolysed samples/specimens", "lipemic samples/specimens").

Data collecting

In order to collect data concerning the errors of the pre-analytical process, a standard form was designed and called "Form of data collection for risk budget from the…department" and applied in biochemistry, hematology and coagulation departments.

For the critical errors such as misidentification samples,

data collection could be done in the following situations: 1) the physician or the patient demands an analysis report, which could not be found; or 2) the laboratories specialists cross check the analysis reports and the lists of the patients for whom there were analysis demands in LIS (Laboratory Information System).
The second method for data collecting was initiated by checking the conformity of the specimens (mentioning "nonconform specimen"). These kinds of errors could be identified by the staff responsible with the processing of blood specimens in the laboratory and also by the staff responsible for the analysis and validation, by noticing that the results of the required analysis do not correspond with the clinical data provided to the laboratory, or does not correlate with other previous results from the same patient, if they exist.
In order to evaluate the control level of the processes, the results were transformed according to the Six Sigma scale, using the Westgard calculation (https://www.westgard.com/six-sigma-calculators.htm), obtaining in this way the frequency with which an error is likely to occur per million opportunities (DPM).
Descriptive and inferential statistics were used to prove the objectives of the present work. Nominal qualitative variables were sumarized by absolute and relative frequencies (percentages). The assessment of the significant differences in frequencies of the studied quality indicators, for the analyzed periods, was performed by Chi-square test.
In all two-sided tests, it was considered that a significant result is given by an estimated significance level, $p < 0.05$.
For the statistical processing we used IBM SPSS Statistics for Windows, version 20.0 (IBM Corp, Armonk, NY, USA).

RESULTS

From January through March 2015, the following numbers of medical analysis requests, were recorded by: A laboratory (Lab A) - 32,820; B laboratory (Lab B) - 45,921; C laboratory (Lab C) - 20,850; D laboratory (Lab D) - 16,775. For this period of the study, data collected were for all the proposed quality indicators, excepting critical errors concerning the patients' identification.
The distribution of the studied indicators from the four laboratories was summarized in a descriptive way using the absolute and relative frequencies for each analyzed period of time (Table 5).

Biochemistry Department: Total incidents of samples

There were statistically significant differences between A laboratory and each of the B, C and D laboratories in January 2015, February 2015, and March 2015 for the quarter, related to the total incidents of samples (Chi-square test, $p = 0.0001$). In January 2015, there was an increase in frequency of the total incidents of samples in comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0.02% versus Lab B: 1.14%; versus Lab C: 0.43% versus Lab D: 1.46%). In February 2015, there was an increase in frequency of the total incidents of samples in comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0.01% versus Lab B: 0.86%; versus Lab C: 0.86% versus Lab D: 2.02%). In March 2015, there was an increase in frequency of the total incidents of samples in comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0.03% versus Lab B: 0.59%; versus Lab C: 0.81% versus Lab D: 1.93%). Quarterly, there was an increase in frequency of the total incidents of samples in comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0.02% versus Lab B: 0.85%; versus Lab C: 0.72% versus Lab D: 1.82%).
Between B laboratory and C laboratory there were statistically significant differences only in January 2015 (Chi-square test, $p = 0.0001$), with a higher frequency of the total incidents of samples obtained from B laboratory (1.14% versus 0.43%). There were no significant differences in February 2015 (Chi-Square test, $p = 0.93$), March 2015 (Chi-square test, $p = 0.07$) or quarterly (Chi-square test, $p = 0.10$). There were no statistically significant frequencies between B laboratory and D laboratory in January 2015 (Chi-square test, $p = 0.12$, 1.14% versus 1.46%), but in February 2015, March 2015, and quarterly there were statistically significant differences (Chi-square test, $p = 0.0001$). It was noticed that in all the analyzed periods of time, differences existed between the frequencies of C laboratory and D laboratory (Chi-square test, $p = 0.0001$).

Biochemistry Department: Hemolysed samples/specimens

There were statistically significant differences between frequencies of hemolyzed specimens obtained in A laboratory and each of the B, C and D laboratories in January 2015, February 2015, March 2015, and quarterly (Chi-square test, $p = 0.0001$). Thus, in January 2015, there was an increase in frequency of the hemolyzed specimens in comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0% versus Lab B: 1.05%; versus Lab C: 0.32% versus Lab D: 0.44%). In February 2015, there was an increase in frequency of the hemolyzed specimens in comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0% versus Lab B: 0.77%; versus Lab C: 0.19% versus Lab D: 0.95%). In March 2015, there was an increase in frequency of the hemolyzed specimens in comparison with A laboratory and the B and D laboratories (Table 5) (Lab A: 0% versus Lab B: 0.51%; versus Lab D: 0.84%). Quarterly, there was an increase in frequency of the hemolyzed specimens comparison with A laboratory and the other laboratories (Table 5) (Lab A: 0% versus Lab B: 0.76%; versus Lab C: 0.15% versus Lab D: 0.76%).
There were statistically significant differences between

Table 1. The scale of the probability of the error's occurrence.

Terms	Assessment	Description
Frequent	5	Once/day
Probable	4	2 - 10/week
Ocasional	3	Once/week
Isolated	2	Once/month
Improbable	1	Once/year

Note: Fixing the scale for the probability of the error's occurence was difficult because the time unit was not the best reference in predicting the occurence of the error. Observing an error/day may have a different meaning depending on the work. For this reason, the defect rate or the DPM (defects per million opportunities) provided a better perspective for estimating the error's occurence, because it pays attention to the laboratory's workload.

Table 2. The scale of severity.

Terms	Assessment	Description
Catastrophic	5	Patient died
Critical	4	Harm that damages the quality of life
Severe	3	Harm that requires medical intervention
Minor	2	Harm that does not require medical intervention
Negligible	1	Temporary discomfort

Note: The scale provided enough levels to comprise the range of the possible severity degrees. Too many levels can lead to an inappropriate assessment of the harm's severity.

Table 3. Scale of probability for error's detection (detectability).

Assessment	Description
5	The control is ineffective
4	It is unlikely that the control measures detect the errors
3	Control measures may or may not detect the errors
2	Control measures almost always detect the errors
1	Control measures can detect errors

Table 4. Risk matrix.

Risk matrix	The severity of the error				
The probability of the error's occurence	1 (negligible)	2 (minor)	3 (severe)	4 (critical)	5 (catastrophic)
5 (frequent)	NA (5 x 1 = 5)	NA (5 x 2 = 10)	NA (5 x 3 = 15)	NA (5 x 4 = 20)	NA (5 x 5 = 25)
4 (probable)	A (4 x 1 = 4)	NA (4 x 2 = 8)	NA (4 x 3 = 12)	NA (4 x 4 = 12)	NA (4 x 5 = 20)
3 (occasionally)	A (3 x 1 = 3)	A (3 x 2 = 6)	A (3 x 3 = 9)	NA (3 x 4 = 12)	NA (3 x 5 =15)
2 (isolated)	A (2 x 1 = 2)	A (2 x 2 = 4)	A (2 x 3 = 6)	NA (2 x 4 = 8)	NA (2 x 5 = 10)
1 (improbable)	A (1 x 1 = 1)	A (1 x 2 = 2)	A (1 x 3 = 3)	A (1 x 4 = 4)	A (1 x 5 = 5)

Note: A - acceptable, NA - unacceptable.

Table 5. The relative and absolute frequences of the indicators of the pre-examination process from the biochemistry department.

Biochemistry Department Evaluated period	Total requests	Hemolysed samples n (%)	Lipemic samples n (%)	Icteric samples n (%)	Total incidents of samples n (%)
Laboratory A					
January 2015	8,376	0 (0)	2 (0.02) [&] [^]	0 (0)	2 (0.02)
February 2015	9,201	0 (0)	1 (0.01)	0 (0)	1 (0.01)
March 2015	10,279	0 (0)	3 (0.03) [&]	0 (0)	3 (0.03)
Quarterly	27,856	0 (0)	6 (0.02)	0 (0)	6 (0.02)
Laboratory B					
January 2015	12,604	132 (1.05)	12 (0.09) [&] [#]	0 (0)	144 (1.14) [*]
February 2015	13,259	102 (0.77) [*]	12 (0.09)	0 (0)	114 (0.86) [#]
March 2015	14,254	72 (0.51)	12 (0.08) [&]	0 (0)	84 (0.59) [#]
Quarterly	40,117	306 (0.76) [*]	36 (0.09)	0 (0)	342 (0.85) [#]
Laboratory C					
January 2015	5,534	18 (0.32) [$]	6 (0.11) [^] [#]	0 (0)	24 (0.43)
February 2015	6,272	12 (0.19)	36 (0.57)	6 (0.1) [$]	54 (0.86) [#]
March 2015	7,386	0 (0)	54 (0.73) [$]	6 (0.08) [$]	60 (0.81) [#]
Quarterly	19,192	30 (0.15)	96 (0.50)	12 (0.06)	138 (0.72) [#]
Laboratory D					
January 2015	4,106	18 (0.44) [$]	30 (0.73)	12 (0.29)	60 (1.46) [*]
February 2015	5,052	48 (0.95) [*]	48 (0.95)	6 (0.12) [$]	102 (2.02)
March 2015	4,972	42 (0.84)	48 (0.96) [$]	6 (0.12) [$]	96 (1.93)
Quarterly	14,130	108 (0.76) [*]	126 (0.89)	24 (0.16)	258 (1.82)

Note: n - absolute frequencies, comparisons without statistically significant differences: [&] - A versus B, [^] - A versus C, [#] - B versus C, [*] - B versus D, [$] - C versus D.

Table 6. Sigma values (DPM) for the selected indicators of the pre-examination process from the biochemistry department.

Biochemistry Department Evaluated period	Total requests	Hemolyzed samples Six Sigma (DPM)	Lipemic samples Six Sigma (DPM)	Icteric samples Six Sigma (DPM)	Total incidents of samples Six Sigma (DPM)
Laboratory A					
January 2015	8,376	ND	5 (239)	ND	5 (239)
February 2015	9,201	ND	4.8 (652)	ND	4.8 (652)
March 2015	10,279	ND	4.8 (584)	ND	4.8 (584)
Quarterly	27,856	ND	5.1 (215)	ND	5.1 (215)
Laboratory B					
January 2015	12,604	3.9 (10,473)	4.4 (952)	ND	3.8 (11,425)
February 2015	13,259	4 (7,693)	4.7 (905)	ND	3.9 (8,598)
March 2015	14,254	4.1 (5,051)	4.7 (842)	ND	4.1 (5,893)
Quarterly	40,117	4 (7,628)	4.7 (897)	ND	3.9 (8,525)
Laboratory C					
January 2015	5,534	4.3 (3,253)	4.6 (1,084)	ND	4.2 (4,337)
February 2015	6,272	4.4 (1,913)	4.1 (5,740)	4.7 (6,272)	3.9 (8,610)
March 2015	7,386	ND	4 (7,311)	4.7 (812)	4 (8,123)
Quarterly	19,192	4.5 (1563)	4.1 (5,002)	4.8 (625)	4 (7,190)
Laboratory D					
January 2015	4,106	4.2 (4,384)	4 (7,306)	4.3 (2,923)	3.7 (14,613)
February 2015	5,052	3.9 (9,501)	3.9 (9,501)	4.6 (1,188)	3.6 (20,190)
March 2015	4,972	3.9 (8,447)	3.9 (9,654)	4.6 (1,207)	3.6 (19,308)
Quarterly	14,130	4 (7,643)	3.9 (8,917)	4.5 (1,699)	4.2 (4,105)

Note: ND - not determined.

Table 7. The relative and absolute frequences of the indicators of the pre-examination process from the hematology department.

Hematology Department Evaluated period	Total requests	Hemolysed samples n (%)	Lipemic samples n (%)	Insufficient samples volume n (%)	Clotted samples n (%)	Total incidents of samples n (%)
Laboratory A						
January 2015	1,010	0 (0)	0 (0)	0 (0)	1 (0.1) $^{\&\ +}$	1 (0.1) $^{\&\ \wedge\ +}$
February 2015	1,147	0 (0)	0 (0)	0 (0)	1 (0.09) $^{\&\ \wedge\ +}$	1 (0.09) $^{\&\ \wedge\ +}$
March 2015	1,173	0 (0)	0 (0)	0 (0)	1 (0.08) $^{\&\ +}$	1 (0.08) $^{\&}$
Quarterly	3,330	0 (0)	0 (0)	0 (0)	3 (0.09) $^{\&\ +}$	3 (0.09) $^{\&}$
Laboratory B						
January 2015	1,341	0 (0)	0 (0)	0 (0)	1 (0.07) $^{\&\ \#\ *}$	1 (0.07) $^{\&\ \#\ *}$
February 2015	1,427	0 (0)	0 (0)	0 (0)	1 (0.07) $^{\&\ \#\ *}$	1 (0.07) $^{\&\ \#}$
March 2015	1,541	0 (0)	0 (0)	0 (0)	1 (0.06) $^{\&\ *}$	1 (0.06) $^{\&}$
Quarterly	4,309	0 (0)	0 (0)	0 (0)	3 (0.07) $^{\&\ *}$	3 (0.07) $^{\&}$
Laboratory C						
January 2015	616	0 (0)	0 (0)	1 (0.16)	0 (0) $^{\#\ \$}$	1 (0.16) $^{\wedge\ \#\ \$}$
February 2015	675	0 (0)	0 (0)	0 (0)	1 (0.15) $^{\wedge\ \#\ \$}$	1 (0.15) $^{\wedge\ \#\ \$}$
March 2015	802	0 (0)	0 (0)	0 (0)	8 (0.99) $^{\$}$	8 (0.99) $^{\$}$
Quarterly	2,093	0 (0)	0 (0)	1 (0.4)	9 (0.43) $^{\$}$	10 (0.47) $^{\$}$
Laboratory D						
January 2015	467	0 (0)	0 (0)	0	1 (0.24) $^{+\ *\ \$}$	1 (0.24) $^{+\ *\ \$}$
February 2015	533	0 (0)	0 (0)	3 (0.56)	1 (0.19) $^{+\ *\ \$}$	4 (0.75) $^{+\ \$}$
March 2015	550	0 (0)	1 (0.18)	2 (0.36)	1 (0.18) $^{+\ *\ \$}$	4 (0.72) $^{\$}$
Quarterly	1,550	0 (0)	1 (0.06)	5 (0.32)	3 (0.19) $^{+\ *\ \$}$	9 (0.58) $^{\$}$

Note: n - absolute frequencies; comparisons without statistically significant differences: $^{\&}$ - A versus B, $^{\wedge}$ - A versus C, $^{\#}$ - B versus C, * - B versus D, $^{\$}$ - C versus D.

B laboratory and C laboratory in January 2015, February 2015, March 2015, and quarterly, regarding hemolyzed specimens (Chi-square test, p = 0.0001). There were no significant differences between B laboratory and D laboratory in February 2015 (Chi-square test, p = 0.26), and quarterly (Chi-square test, p = 0.95). Excepting January 2015 (p = 0.43), there were statistically significant differences between C laboratory and D laboratory (Chi-square test, p = 0.0001).

Biochemistry Department: Lipemic samples/specimens

There were statistically significant differences between frequencies of lipemic specimens obtained from A laboratory and each of the C and D laboratories in February 2015, March 2015, and quarterly (Chi-square test, p = 0.0001). Thus, in February 2015, there was an increase in frequencies of the lipemic specimens compared to A laboratory and the C and D laboratories (Table 5) (Lab A: 0.01% versus Lab C: 0.57% versus Lab D: 0.95%). In March 2015, there was an increase in frequency of the lipemic specimens compared to A laboratory and the C and D laboratories (Table 5) (Lab A: 0.03% versus Lab C: 0.73% versus Lab D: 0.96%). Quarterly, there was an increase in frequency of the lipemic specimens in comparison with A laboratory and the C and D laboratories (Table 5) (Lab A: 0.02% versus Lab C: 0.50% versus Lab D: 0.89%).

Between B laboratory and C laboratory, excepting January 2015 (p = 0.88), there were significant differences in February 2015, March 2015, and quarterly (Chi-square test, p = 0.0001). There were similar statistically significant frequencies between B laboratory and D laboratory in January 2015, February 2015, March 2015, and quarterly (Chi-square test, p = 0.0001). Thus, there was an increase in lipemic specimens for D laboratory compared to B laboratory (Table 5) (January 2015: 0.73% versus 0.09%; February 2015: 0.95% versus 0.09%, March 2015: 0.96% versus 0.08%, quarterly: 0.89% versus 0.09%).

Both in January 2015 and quarterly, there were differences between the frequencies of C laboratory and D laboratory (Chi-square test, p = 0.0001).

In the final stage, the obtained values for the selected quality indicators were converted to Six Sigma Scale in order to determine the control level of the processes. For values of Six Sigma higher than 4, it was considered that the process was correctly controlled.

Table 8. Six Sigma Index for the selected quality indicators of the pre-analytical process from the hematology department.

Hematology Department Evaluated period	Total requests	Hemolyzed samples Six Sigma (DPM)	Lipemic samples Six Sigma (DPM)	Insufficient samples Six Sigma (DPM)	Clotted samples Six Sigma (DPM)	Total incidents of samples Six Sigma (DPM)
Laboratory A						
January 2015	**1,010**	**ND**	**ND**	**ND**	**4.6 (990)**	**4.6 (990)**
February 2015	**1,147**	**ND**	**ND**	**ND**	**4.7 (872)**	**4.7 (872)**
March 2015	**1,173**	**ND**	**ND**	**ND**	**4.6 (990)**	**4.6 (990)**
Quarterly	**3,330**	**ND**	**ND**	**ND**	**4.7 (901)**	**4.7 (901)**
Laboratory B						
January 2015	**1,341**	**ND**	**ND**	**ND**	**4.7 (746)**	**4.7 (746)**
February 2015	**1,427**	**ND**	**ND**	**ND**	**4.7 (701)**	**4.7 (701)**
March 2015	**1,541**	**ND**	**ND**	**ND**	**4.8 (619)**	**4.8 (619)**
Quarterly	**4,309**	**ND**	**ND**	**ND**	**4.7 (696)**	**4.7 (696)**
Laboratory C						
January 2015	**616**	**ND**	**ND**	**4.5 (1,623)**	**ND**	**4.5 (1,623)**
February 2015	**675**	**ND**	**ND**	**ND**	**4.5 (1,481)**	**4.5 (1,481)**
March 2015	**802**	**ND**	**ND**	**ND**	**3.8 (11,222)**	**3.8 (11,222)**
Quarterly	**2,093**	**ND**	**ND**	**4.9 (478)**	**4.2 (4,300)**	**4.1 (4,778)**
Laboratory D						
January 2015	**467**	**ND**	**ND**	**ND**	**4.4(2,141)**	**4.4 (2,141)**
February 2015	**533**	**ND**	**ND**	**4.1 (5,629)**	**4.4 (1,876)**	**4 (7,505)**
March 2015	**550**	**ND**	**4.5 (1,818)**	**4.2 (3,636)**	**4.5 (1,818)**	**4 (7,273)**
Quarterly	**1,550**	**ND**	**4.8 (645)**	**4.3 (3,226)**	**4.4 (1935)**	**4.1 (5,806)**

Note: ND - not determined.

Hematology Department: Total incidents of samples
There were statistically significant differences between A laboratory and C laboratory in March 2015, and quarterly related to the total incidents of samples (Chi-square test, $p = 0.008$, $p = 0.01$). Thus, in March 2015, there was an increase in frequency of the total incidents of samples for C laboratory compared to A laboratory (Table 5) (0.99% versus 0.08%) as well as quarterly, (0.47% versus 0.09%). Between B laboratory and each of C and D laboratories there were differences only in March 2015 and quarterly (Chi-square test, $p = 0.0001$), with a higher frequency of the total incidents of samples for C and D laboratories compared to B laboratory (March 2015: 0.99% versus 0.06%, respectively 0.72% versus 0.06%; quarterly: 0.47% versus 0.07%, respectively 0.58% versus 0.07%). There were no statistically significant differences between B laboratory and each of the C and D laboratories in January 2015 (Chi-square test, $p = 0.85$, respectively $p = 0.88$). Similarly, there were statistically significant frequencies between C laboratory and D laboratory in all the analyzed periods (January 2015 $p = 0.68$, February 2015 $p = 0.58$, March 2015 $p = 0.62$, and quarterly $p = 0.24$).

Hematology Department: Clotted samples
There were statistically significant differences between A laboratory and C laboratory in January 2015 (Chi-square test, $p = 0.01$), March 2015 (Chi-square test, $p = 0.008$), and quarterly (Chi-square test, $p = 0.01$) related to the clotted samples. Between B laboratory and C laboratory there were statistically significant differences in March 2015 and quarterly (Chi-square test, $p = 0.0001$), with a higher frequency of the clotted samples obtained from C laboratory (March 2015: 0.06% versus 0.99%, quarterly 0.07% versus 0.43%). There were no statistically significant differences in January 2015 (Chi-square test, $p = 0.45$) and February 2015 (Chi-square test, $p = 0.63$).

Coagulation Department
Concerning the mentioned periods of time for the selected indicators, there were no statistically significant differences between all the laboratories from this study ($p > 0.05$).

Table 9. The relative and absolute frequences of the indicators of the pre-examination process from coagulation department.

Coagulation Department Evaluated period	Total requests	Hemolyzed samples n (%)	Lipemic samples n (%)	Insufficient samples n (%)	Clotted samples n (%)	Total incidents of samples n (%)
Laboratory A						
January 2015	546	4 (0.73) $^{\&\ \wedge\ +}$	0 (0)	2 (0.37) $^{\&\ \wedge\ +}$	1 (0.18) $^{+}$	7 (1.28) $^{\&\ \wedge\ +}$
February 2015	533	1 (0.18) $^{\&\ \wedge\ +}$	0 (0)	3 (0.56) $^{\&\ \wedge\ +}$	1 (0.18) $^{\&\ \wedge}$	5 (0.93) $^{\&\ \wedge\ +}$
March 2015	555	1 (0.18) $^{\&\ +}$	0 (0)	0 (0) $^{\&}$	1 (0.18) $^{\&}$	2 (0.36) $^{\&\ +}$
Quarterly	1,634	6 (0.36) $^{\&\ \wedge\ +}$	0 (0)	5 (0.3) $^{\&\ \wedge\ +}$	3 (0.18) $^{\&\ \wedge\ +}$	14 (0.84) $^{\&\ +}$
Laboratory B						
January 2015	503	1 (0.20) $^{\&\ \#\ *}$	0 (0)	0 (0) $^{\&}$	0 (0) *	1 (0,20) $^{\&\ *}$
February 2015	446	2 (0.45) $^{\&\ \#\ *}$	0 (0)	2 (0.45) $^{\&\ \#\ *}$	1 (0.22) $^{\&\ \#}$	5 (1.12) $^{\&\ \#\ *}$
March 2015	546	3 (0.55) $^{\&\ \#\ *}$	0 (0)	4 (0.73) $^{\&\ \#\ *}$	1 (0.18) $^{\&}$	8 (1.45) $^{\&\ \#\ *}$
Quarterly	1,495	6 (0.40) $^{\&\ \#\ *}$	0 (0)	6 (0.40) $^{\&\ \#\ *}$	2 (0.13) $^{\&\ \#\ *}$	14 (0.93) $^{\&\ \#\ *}$
Laboratory C						
January 2015	460	4 (0.86) $^{\wedge\ \#\ \$}$	3 (0.65)	0 (0) $^{\wedge}$	0 (0)	7 (1.52) $^{\wedge\ \$}$
February 2015	400	1 (0.25) $^{\wedge\ \#\ \$}$	0 (0)	3 (0.75) $^{\wedge\ \#\ \$}$	1 (0.25) $^{\wedge\ \#\ \$}$	5 (1.25) $^{\wedge\ \#\ \$}$
March 2015	505	7 (1.38) $^{\#\ \$}$	6 (1.19)	0 (0) $^{\#}$	0 (0)	13 (2.57) $^{\#}$
Quarterly	1,365	12 (0.88) $^{\wedge\ \#\ \$}$	9 (0.6)	3 (0.2) $^{\wedge\ \#\ \$}$	1 (0.07) $^{\wedge\ \#\ \$}$	25 (1.83) $^{\#}$
Laboratory D						
January 2015	364	3 (0.82) $^{+\ *\ \$}$	0 (0)	0 (0) $^{+}$	1 (0.27) $^{+\ *}$	4 (1.1) $^{+\ *\ \$}$
February 2015	354	1 (0.28) $^{+\ *\ \$}$	1 (0.28)	1 (0.28) $^{+\ *\ \$}$	0 (0) $^{\$}$	3 (0.85) $^{+\ *\ \$}$
March 2015	377	2 (0.53) $^{+\ *\ \$}$	0 (0)	0 (0) *	0 (0)	2 (0.53) $^{+\ *}$
Quarterly	1,095	6 (0.54) $^{+\ *\ \$}$	1 (0.1)	1 (0.1) $^{+\ *\ \$}$	1 (0.1) $^{+\ *\ \$}$	9 (0.82) $^{+\ *}$

Note: n - absolute frequencies; comparisons without statistically significant differences: $^{\&}$ - A versus B, $^{\wedge}$ - A versus C, $^{\#}$ - B versus C, * - B versus D, $^{\$}$ - C versus D.

Table 10. Six Sigma Index/(DPM) for the selected indicators of the pre-examination process from coagulation department.

Coagulation Department Evaluated period	Total requests	Hemolyzed samples Six Sigma (DPM)	Lipemic samples Six Sigma (DPM)	Insufficient samples Six Sigma (DPM)	Clotted samples Six Sigma (DPM)	Total incidents of samples Six Sigma (DPM)
Laboratory A						
January 2015	546	4 (7,326)	ND	4.2 (3,663)	4.5 (1,832)	3.8 (12,831)
February 2015	533	4.4 (1,876)	ND	4.1 (5,629)	4.4 (1,876)	3.9 (9,381)
March 2015	555	4.5 (1,802)	ND	ND	4.5 (1,802)	4.2 (3,604)
Quarterly	1,634	4.2 (3,672)	ND	4.3 (3,060)	4.5 (1836)	3.9 (8,568)
Laboratory B						
January 2015	503	4.4 (1,988)	ND	ND	ND	4.4 (1,988)
February 2015	446	4.2 (4,484)	ND	4.2 (4,484)	4.4 (2,242)	3.8 (11,211)
March 2015	546	4.1 (5,495)	ND	4 (7,326)	4.5 (1,832)	3.7 (14,652)
Quarterly	1,495	4.2 (4,013)	ND	4.2 (4,013)	4.6 (1,338)	3.9 (9,365)
Laboratory C						
January 2015	460	3.9 (8,696)	4 (6,522)	ND	ND	3.7 (15,217)
February 2015	400	4.4 (2,500)	ND	4 (7,500)	4.4 (2,500)	3.8 (12,500)
March 2015	505	3.8 (13,861)	3.8 (11,881)	ND	ND	3.5 (25,743)
Quarterly	1,365	3.9 (8,791)	4 (6,593)	4.4 (2,198)	4.7 (733)	3.6 (18,315)
Laboratory D						
January 2015	364	3.9 (8,242)	ND	ND	4.3 (2,747)	3.8 (13,736)
February 2015	354	4.2 (2,825)	4.2 (2,825)	4.2 (2,825)	ND	3.9 (8,475)
March 2015	377	4.1 (5,305)	ND	ND	ND	4.1 (5,305)
Quarterly	1,095	4.1 (5,479)	4.7 (913)	4.7 (913)	4.7 (913)	3.9 (8,219)

Note: ND - not determined.

Table 11. The frequency of total errors from the four laboratories.

Clinical Laboratory	Evaluated period	Frequencies (%)
Laboratory A	January 2015	1.4
	February 2015	1.02
	March 2015	0.47
	Quarterly	0.96
Laboratory B	January 2015	1.21
	February 2015	2.05
	March 2015	2.11
	Quarterly	1.79
Laboratory C	January 2015	2.11
	February 2015	2.26
	March 2015	4.37
	Quarterly	2.91
Laboratory D	January 2015	2.8
	February 2015	3.62
	March 2015	3.19
	Quarterly	3.20

DISCUSSION

This study evaluated the quality indicators by using the risk management technique - FMEA, according to the values obtained for RPN, regardless of any pre-analytical event recorded in the working notebooks.

The purpose of the quality indicators' evaluation was to monitor the possible errors occuring at the collecting and preparation of the specimens for the analysis phase. The lack of a specimen in the laboratory or the rejection of a specimen by the laboratory can lead to a delayed diagnosis but also to delayed treatment [12]. Among the reasons for rejecting a specimen, we can list the presence of clots when the blood is collected in containers with anticoagulant and the staff did not mix the specimens well immediately after phlebotomy; insufficient sample volume that leads to inadequate rates between blood and anticoagulant; misidentification and/or unlabeled samples; samples collected in an inappropriate container; samples of wrong or inappropriate type (e.g., whole blood instead of plasma). In general, these errors can be considered phlebotomy errors. Although, all the above mentioned reasons concerning rejection are acceptable, the specimens can show inherent nonconformities: hemolysis, lipemia or icterus [13]. Each quality indicator takes into account the impact of the evaluated processes over laboratory management. A study performed between 2004 and 2008 analyzed the quality indicators for the extra-analytical processes in the clinical laboratory, and it had as a final purpose for each laboratory of the working group, to assess the main analytical processes and to implement corrective measures when the results did not correspond to the suggested specifications. The results we obtained were similar to the results of the mentioned study. The working group considered that the indicators, whose impact on the patient's health safety is higher, should be considered as "sentinel" indicators; these indicators are able to identify events that require supplementary actions to ensure that those actions will not be repeated [14].

Biochemistry Department

The values obtained by all the laboratories included in the study for QI_2 were lower, corresponding to the Six Sigma value of 3.9 and 4.4. A Sigma value higher than 4 represents a well controlled process. A Sigma value lower than 4 means that the process needs to be improved; moreover, the QI_2 results can reflect different methodologies of identification and determination of the hemolysis degree. Therefore, for the improvement of QI_2, the laboratories will have to specify how to determine the hemolysis (objectively - by determining the hemolysis index in automatic systems, or subjectively - by visual inspection), to determine the threshold at which to reject a specimen. The laboratory staff needs to be well trained to be able to identify by direct inspection, as much as possible of the serum/plasma quality issues, but also to be able to decide if the test result requested by the physician can be influenced by the specimen non-conformity noticed at the visual inspection [15].

The values obtained by all the laboratories for QI_5 and

QI_6 were lower, corresponding to a Six Sigma value of 3.9 - 5. A Sigma value lower than 4 for QI_5 indicates that the process can be improved by better collaboration with the clinicians and the nurses, who need to inform the patients about the collecting time and the factors that can influence the serum/plasma conformity.
Hemolysis, lipemia, and icterus can interfere with some laboratory tests, either through optical mechanism (example of methods that are not influenced by the color of the serum are ion selective electrode, electrophoresis), or through chemical mechanism (for example, the hemoglobin interference in the PCR method, used in determining nucleic acids, can have an inhibitory effect). The magnitude of the interference can vary according to the concentration of the interferent, the number of the existing interferents, the analyte concentration, the testing method, and also the quantity of the specimen from the chemical reaction [15].
Nevertheless, in the laboratory's activity there is not always time for a detailed visual inspection of the specimens nor for a complete and correct analysis of each non-conformity that appeared. Besides these, the lack of experience of the laboratory staff and/or the tiredness of the operator can be included.

Hematology Department
The values obtained by the majority of the laboratories for QI_3, QI_4, QI_6, and QI_7 were lower, corresponding to a Six Sigma value between 4 and 4.8. In March 2015, C laboratory obtained a Six Sigma value of 3.8 for QI_3, indicating that the process needs improvement by training and monitoring of the staff responsible for the blood collection. The data of each laboratory were checked monthly, including the period after the study, with the purpose of taking corrective actions when errors exceeded the suggested specifications. Only D laboratory reported results for QI_6, and this was possible because the evaluation of lipemia for the hematology specimens is not a common practice.

Coagulation Department
The values obtained by the laboratories included in the study for QI_2, QI_3, QI_4, QI_6, were lower, corresponding to a Six Sigma value between 3.8 and 4.5, meaning that in time an improvement is necessary.
The automation in the clinical laboratories can represent a great benefit, because it can eliminate some routine steps in the laboratory and therefore improve the quality and the patient's safety. The process of automation was previously applied to the sorting, transporting, centrifugation, and storage phases, leading to the current trend to apply it to the specimens' inspection. The first public reference of the specimens' inspection automation from the pre-analytical process was patented in 1996 by Cadell and Samsoondar [13].
Compared to the visual inspection, the most favorable aspect of automated determination of hemolysis, lipemia, and icterus is the objectivity and the possibility to estimate the interferences, and more than this, it increases the accuracy of the patients' test results. The automation of the pre-analytical process allows the shortening of the response time. In 2005, Vermmer et al. reported an improvement of the patients' results using automated determination, and they also noticed that the number of the specimens with hemolysis, lipemia, and icterus was much higher compared to the number obtained using the routine visual inspection [15].
In addition to the mentioned benefits of the pre-analytical process automation, the limits of the automation must be taken into consideration. Icterus and lipemia show real physiologic conditions, while hemolysis is often the result of an error of collecting, processing, transporting or storing. Hemolyzed serum/plasma can appear in pathological conditions associated with hemolytic anemia or other clinical conditions in which the content of erythrocytes is poured into the blood. For this reason, the causes of hemolysis must be completely investigated and must be correlated to the clinical data or to other specimens or previous results from the same patient [15].
Indeed, the measuring and the management of the errors of the pre-examination process continues to be a major challenge for the clinical laboratories. The main difficulty is to establish an efficient, systematic project to ensure that the risk management procedures from the pre-analytical process are correctly implemented. The accreditation standards require specific documents, easy to comprehend, regarding the type of container used for each test, the collecting procedure, the processing, and transporting of the specimens. These procedures must be distributed to all the involved staff [1,12].
A high percent of errors is the result of an insufficient specialty documentation, which represents the basis of operational procedures or their poor implementation. The staff responsible for the implementation of the operational procedures must be properly trained, so that they understand the importance of these procedures in the laboratory and their effect on the laboratory management and on the patient's safety [12]. The procedures that ensure the specimens' traceability during transportation and processing are well developed and used.
Many factors affect the patient's safety and many variables affect each of the sub-processes, services, and medical staff involved in the pre-examination process [1]. This complexity makes the errors from the pre-analytical process difficult to be manage, focusing more on the frequency estimation and maintaining the errors at a clinically acceptable level. It is essential to learn from the mistakes, and for this reason, the indicators' results are communicated to the quality manager and to the CEO [1,16]. These activities, - together with the laboratory's policy to reject the nonconform specimens, requiring a new collection - can lead to the idea of creating a "cult" of patient's safety and errors' acknowledgement [1].
The use of clear, understandable, and appropriate procedures, as well as a well trained laboratory staff, should

reduce the number of errors [12].
After implementing FMEA, with the purpose of selecting the quality indicators suitable to the processes, Six Sigma methodology can be used as a statistical indicator to quantify the results as DPM, to evaluate the training efficiency based on quality improvement in the clinical laboratory [3,4].

CONCLUSION

The continuous changing of the improvement targets for the quality procedures in the clinical laboratory leads to the improvement of the patient's health safety. The study performed in the four branches of the national clinical laboratory was a challenge, and it can be an aid in making strategic decisions regarding the patient's health safety, thus responding to the accreditation requirements. We consider that the study achieved the main goal, and it can be extended to other branches of the national clinical laboratory. The success of the study depends on the involvement and collaboration of laboratories and the training and experience of the staff responsible for collecting the data in order to define the best practices that will ensure performance improvement.

Declaration of Interest:
Authors declared no conflict of interests.

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Additional material:

Table 12. Biochemistry Department: Total incidents of specimens - Chi square test, p-values.

Total incidents of specimens	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D p
January 2015	-	0.0001	0.0001	0.0001
February 2015	-	0.0001	0.0001	0.0001
March 2015	-	0.0001	0.0001	0.0001
Quarterly	-	0.0001	0.0001	0.0001
Note: "-" reference laboratory with which were compared the other laboratories				
Total incidents of specimens	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.0001	0.12 *	
February 2015	-	0.93 #	0.0001	
March 2015	-	0.07 #	0.0001	
Quarterly	-	0.10 #	0.0001	
Note: "-" reference laboratory with which were compared the other laboratories				
Total incidents of specimens	Laboratory C	Laboratory D p		
January 2015	-	0.0001		
February 2015	-	0.0001		
March 2015	-	0.0001		
Quarterly	-	0.0001		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: # - B versus C, * - B versus D.

Table 13. Biochemistry Department: Hemolysed specimens - Chi square test, p-values.

Hemolysed specimens	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D p
January 2015	-	0.0001	0.0001	0.0001
February 2015	-	0.0001	0.0001	0.0001
March 2015	-	0.0001	0.0001	0.0001
Quarterly	-	0.0001	0.0001	0.0001
Note: "-" reference laboratory with which were compared the other laboratories				
Hemolysed specimens	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.0001	0.0001	
February 2015	-	0.0001	0.26 *	
March 2015	-	0.0001	0.01	
Quarterly	-	0.0001	0.95 *	
Note: "-" reference laboratory with which were compared the other laboratories				
Hemolysed specimens	Laboratory C	Laboratory D p		
January 2015	-	0.43 $		
February 2015	-	0.0001		
March 2015	-	0.0001		
Quarterly	-	0.0001		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: * - B versus D, $ - C versus D.

Table 14. Biochemistry Department: Lipemic specimens - Chi square test, p-values.

Lipemic specimens	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D p
January 2015	-	0.08 [&]	0.06 [^]	0.0001
February 2015	-	0.02	0.0001	0.0001
March 2015	-	0.18 [&]	0.0001	0.0001
Quarterly	-	0.0005	0.0001	0.0001
Note: "-" reference laboratory with which were compared the other laboratories				
Lipemic specimens	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.88 [#]	0.0001	
February 2015	-	0.0001	0.0001	
March 2015	-	0.0001	0.0001	
Quarterly	-	0.0001	0.0001	
Note: "-" reference laboratory with which were compared the other laboratories				
Lipemic specimens	Laboratory C	Laboratory D p		
January 2015	-	0.0001		
February 2015	-	0.02		
March 2015	-	0.19 [$]		
Quarterly	-	0.0001		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: [&] - A versus B, [^] - A versus C, [#] - B versus C, [$] - C versus D.

Table 15. Biochemistry Department: Icter specimens - Chi square test, p-values.

Icteric specimens	Laboratory C	Laboratory D p
January 2015	-	0.0001
February 2015	-	0.97 [$]
March 2015	-	0.68 [$]
Quarterly	-	0.008
Note: "-" reference laboratory with which were compared the other laboratories		

Note: comparisons without statistically significant differences: [$] - C versus D.

Table 16. Hematology Department: Total incidents of specimens - Chi square test, p-values.

Total incidents of specimens	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D p
January 2015	-	0.63 [&]	0.69 [^]	0.93 [+]
February 2015	-	0.59 [&]	0.72 [^]	0.06 [+]
March 2015	-	0.58 [&]	0.008	0.05
Quarterly	-	0.91 [&]	0.01	0.003
Note: "-" reference laboratory with which were compared the other laboratories				
Total incidents of specimens	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.85 [#]	0.88 [*]	
February 2015	-	0.63 [#]	0.03	
March 2015	-	0.0001	0.0001	
Quarterly	-	0.0001	0.0001	
Note: "-" reference laboratory with which were compared the other laboratories				
Total incidents of specimens	Laboratory C	Laboratory D p		
January 2015	-	0.68 [$]		
February 2015	-	0.58 [$]		
March 2015	-	0.62 [$]		
Quarterly	-	0.24 [$]		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: [&] - A versus B, [^] - A versus C, [+] - A versus D, [#] - B versus C, [*] - B versus D, [$] - C versus D.

Table 17. Hematology Department: Cloted samples - Chi square test, p-values.

Cloted samples	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D p
January 2015	-	0.63 [&]	0.01	0.93 [+]
February 2015	-	0.59 [&]	0.72 [^]	0.16 [+]
March 2015	-	0.58 [&]	0.008	0.14 [+]
Quarterly	-	0.91 [&]	0.01	0.11 [+]
Note: "-" reference laboratory with which were compared the other laboratories				
Cloted samples	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.45 [#]	0.88 [*]	
February 2015	-	0.63 [#]	0.53 [*]	
March 2015	-	0.0001	0.51 [*]	
Quarterly	-	0.0001	0.42 [*]	
Note: "-" reference laboratory with which were compared the other laboratories				
Cloted samples	Laboratory C	Laboratory D p		
January 2015	-	0.79 [$]		
February 2015	-	0.45 [$]		
March 2015	-	0.14 [$]		
Quarterly	-	0.30 [$]		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: [&] - A versus B, [^] - A versus C, [+] - A versus D, [#] - B versus C, [*] - B versus D, [$] - C versus D.

Table 18. Coagulation Department: Total incidents of specimens - Chi square test, p-values.

Total incidents of specimens	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D p
January 2015	-	0.09 &	0.61 ^	0.45 +
February 2015	-	0.25 &	0.74 ^	0.44 +
March 2015	-	0.11 &	0.005	0.85 +
Quarterly	-	0.82 &	0.02	0.47 +
Note: "-" reference laboratory with which were compared the other laboratories				
Total incidents of specimens	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.05	0.22 *	
February 2015	-	0.83 #	0.41 *	
March 2015	-	0.28 #	0.31 *	
Quarterly	-	0.72 #	0.55 *	
Note: "-" reference laboratory with which were compared the other laboratories				
Total incidents of specimens	Laboratory C	Laboratory D p		
January 2015	-	0.69 $		
February 2015	-	0.55 $		
March 2015	-	0.03		
Quarterly	-	0.05		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: & - A versus B, ^ - A versus C, + - A versus D, # - B versus C, * - B versus D, $ - C versus D.

Table 19. Coagulation Department: Hemolysed specimens - Chi square test, p-values.

Hemolysed specimens	Laboratory A	Laboratory B p	Laboratory C p	Laboratory D P
January 2015	-	0.45 &	0.41 ^	0.62 +
February 2015	-	0.22 &	0.32 ^	0.47 +
March 2015	-	0.11 &	0.05	0.85 +
Quarterly	-	0.72 &	0.22 ^	0.37 +
Note: "-" reference laboratory with which were compared the other laboratories				
Hemolysed specimens	Laboratory B	Laboratory C p	Laboratory D p	
January 2015	-	0.054 #	0.32 *	
February 2015	-	0.33 #	0.38 *	
March 2015	-	0.28 #	0.93 *	
Quarterly	-	0.52 #	0.45 *	
Note: "-" reference laboratory with which were compared the other laboratories				
Hemolysed specimens	Laboratory C	Laboratory D p		
January 2015	-	0.89 $		
February 2015	-	0.85 $		
March 2015	-	0.39 $		
Quarterly	-	0.45 $		
Note: "-" reference laboratory with which were compared the other laboratories				

Note: comparisons without statistically significant differences: & - A versus B, ^ - A versus C, + - A versus D, # - B versus C, * - B versus D, $ - C versus D.