

Opinion Paper

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Performance criteria and quality indicators for the pre-analytical phase

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Abstract: The definition, implementation and monitoring of valuable analytical quality specifications have played a fundamental role in improving the quality of laboratory services and reducing the rates of analytical errors. However, a body of evidence has been accumulated on the relevance of the extra-analytical phases, namely the pre-analytical steps, their vulnerability and impact on the overall quality of the laboratory information. The identification and establishment of valuable quality indicators (QIs) represents a promising strategy for collecting data on quality in the total testing process (TTP) and, particularly, for detecting any mistakes made in the individual steps of the pre-analytical phase, thus providing useful information for quality improvement projects. The consensus achieved on the developed list of harmonized QIs is a premise for the further step: the identification of achievable and realistic performance targets based on the knowledge of the state-of-the-art. Data collected by several clinical laboratories worldwide allow the classification of performances for available QIs into three levels: optimum, desirable and minimum, in agreement with the widely accepted proposal for analytical quality specifications.

Keywords: harmonization; performance criteria; pre-analytical phase; quality indicators; quality specifications; total testing process.

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Introduction

Quality specifications, frequently referred to as performance criteria, represent “the level of performance required to facilitate clinical decision-making” [1]. Several strategies to set analytical quality specifications have been promulgated for more than 30 years, and finally a consensus on the hierarchy of models has been achieved as a result of the Stockholm Conference [2]. Analytical quality specifications represent fundamental criteria for measuring, assuring and maximizing the reliability of laboratory results. However, at the Stockholm Conference, Walter G. Guder presented a lecture on the influence on analytical quality specifications of pre-analytical factors, underlining that “despite the documented quality of analytical process, results are sometimes distrusted because of non-compliance with the clinical case or previous results from the same or other laboratories. When these cases were analyzed in a quality assurance project, it turned out that non-analytical errors explained more than 60% of the cases, of which variables in the pre-analytical phase contributed to more than half of the cases” [3].

In the last 14 years a growing body of evidence has been accumulated on the relevance of the pre-analytical phase, its vulnerability and impact on the overall quality of laboratory information. Although the seminal concept of the brain-to-brain laboratory loop was described more than four decades ago, awareness and consensus on the importance of extra-analytical aspects in laboratory quality are a recent achievement. In fact, a wide consensus has been achieved in the last few years on the need to assure quality and safety in the so-called “brain-to-brain loop”, in view of the fact that the quality of laboratory information is strongly affected by the coordinated and correlated management of all procedures and processes of the total testing process (TTP). Under this perspective, quality in laboratory medicine should be defined as “the guarantee that each and every step in the TTP is correctly performed, thus ensuring valuable decision making and effective patient care” [4]. Achieving consensus for the comprehensive definition of errors in laboratory testing

has been a milestone in the effort to reduce errors and improve patient safety in laboratory medicine [5]. According to this concept, all phases and activities of the testing cycle should be assessed, monitored and improved in order to decrease the total error rates and thereby improve patient safety. Most laboratory-related diagnostic errors are due to defects in extra-analytical phases, including inappropriate test request and/or result acknowledgment and interpretation. Therefore, in the interests of patients, any direct or indirect negative consequence related to a laboratory test must be considered, irrespective of which step is involved and whether the error depends on a laboratory professional (e.g., calibration or testing error) or a non-laboratory operator (e.g., inappropriate test request, error in patient identification and/or blood collection).

Errors in the pre-analytical phase

While the frequency of laboratory errors varies greatly, depending on the study design and TTP steps investigated, a series of papers published between 1989 and 2007 drew the attention of laboratory professionals to the pre- and post-analytical phases, which currently appear to be more vulnerable to errors than the analytical phase [6, 7]. In particular, two papers published in 1997 and 2007 [8, 9] using one study design allowed us to investigate most TTP steps in the same clinical context. In both studies, the pre-analytical phase had the highest error rate, the most frequent problems arising from mistakes in tube filling, inappropriate containers, and requesting procedures. Identification errors were noted too, while the appropriateness of test request was not considered in the study design. Further studies confirmed these data, and currently pre-analytical errors are estimated to account for up to 70% of all mistakes made in laboratory diagnostics, most of which arise from problems in patient preparation, and sample collection, transportation, preparation for analysis and storage [10]. Several technological, informatic and computer science advances introduced in the pre-analytical phase have the potential to decrease the risk of errors [11], but the complexity of the process, the evidence of different owners and mutual responsibilities at the boundaries of several steps requires an adequate governance based on reliable measures and indicators. In fact, the development and utilization in clinical laboratories of pre-analytical robotic workstations have significantly reduced errors in the “conventional” pre-analytical steps that are needed

to make a sample suitable for analysis: centrifugation, aliquoting, diluting and sorting the specimens into batches for their introduction into automated analyzers [12, 13]. A careful exploration of the pre-analytical phase has revealed that it consists of a pre-pre-analytical phase and “true” pre-analytical phase. The *pre-pre-analytical phase* is the processes of selecting and ordering appropriate tests, as well as collecting, identifying, labeling, handling, and transporting biological samples. These processes are neither performed by, nor usually under the control of, laboratory staff. Evidence has been collected to demonstrate a significant higher error rates with clinical ward rather than laboratory staff performing the collection, identification, labeling, handling and transport of samples [14–16]. The pre-analytical phase, in turn, is: the process of accepting samples by the laboratory, centrifuging, aliquoting, diluting, and sorting the biological samples. This categorization is not only of “taxonomic” value, but also underlines the responsibilities and duties of non-laboratory personnel, most of the processes being performed by other healthcare operators (nurses, medical doctors, etc.). This, in turn, represents a key issue in defining strategies and methods for reducing the risk of errors in the pre-analytical phase.

Quality specifications in the extra-analytical phases

The significant decrease of the error rates in the analytical phase experienced in the last three decades is the result of several improvements such as automation, standardization and optimization of reagents, improved training of the laboratory staff but, first and foremost, by the development and implementation of valuable analytical quality specifications and their utilization in setting objective goals in routine practice, and particularly in measuring, recording and improving laboratory performances in internal quality control and external quality assurance programs [7]. The hierarchy of models to establish analytical quality specifications defined in the Stockholm Conference was the fruit of years of work, publications and scientific debate, while for extra-analytical phases only some preliminary proposals are available. In particular, the establishment of valuable quality indicators (QIs) seems to be a promising strategy for collecting data on quality and any mistakes made in the individual steps of the pre-analytical phase. This, in turn, may yield data on the state-of-the-art and on possible goals to attain for improvement to be made.

Quality indicators

According to the approach of the Institute of Medicine (IOM) to quality in healthcare, the identification of reliable QIs is a crucial step in enabling users to quantify the quality of a selected aspect of care by comparing it against a defined criterion. A quality indicator (QI) is thus “an objective measure that potentially evaluates all critical care domains as defined by the IOM (patient safety, effectiveness, equity, patient-centeredness, timeliness and efficiency), is based on evidence associated with those domains, and can be implemented in a consistent and comparable manner across settings and over time” [17]. According to the International Standard for medical laboratories accreditation (ISO 15189: 2012) “The laboratory shall establish QIs to monitor and evaluate performance throughout critical aspects of pre-examination, examination and post-examination processes” and “The process of monitoring QIs shall be planned, which includes establishing the objectives, methodology, interpretation, limits, action plan and duration of measurement” [18]. Therefore, the establishment of QIs covering the entire testing process should be considered “a must” for complying with the requirements of the International Standard and achieving accreditation. The IFCC Working Group “Laboratory Errors and Patient Safety” has developed a Model of Quality Indicators available on www.ifcc-mqi.com and collected data from several laboratories at an international level. Other programs on QIs have been organized and implemented in several countries [19–21]. Therefore, in order to harmonize both the list of QIs and reporting system, a conference was organized to achieve a preliminary consensus and to design further steps of the project [22]. In addition to the list of “harmonized” QIs, also the system for data collection and reporting should be harmonized to allow the comparison of data between different laboratories. Here we report on the data collected by a series of clinical laboratories attending the project on pre-analytical QIs with very high priority, as they: 1) evaluate fundamental steps of the pre-analytical phase; and 2) may be implemented by all laboratories, irrespective of their size and geographic area [22]. The number of participating laboratories changed over time, involving a total of 75 clinical laboratories. However, the number may differ from a specific QI to another QI as any clinical laboratory may select some QIs and is not obliged to collect data for the entire list. In addition to the traditional expression of data in a percentage (%), the Six Sigma metric has been introduced as it is widely recognized as “a metric for measuring defects and improving quality” [23, 24].

Preliminary results

Table 1 reports the data collected for all QIs of very high priority: errors are reported as a median value calculated on all percentage results and sigma values. As an example, we also report data showing the dispersion of results around the median level (Figures 1–3). The variability and changes in data over time can be explained by the heterogeneity and progressive increase in the number of clinical laboratories participating in the program. In addition, some laboratories have changed the type and/or increased the number of QIs to be implemented on an annual basis. Figure 1 shows the data collected on “*misidentification errors*”, a category that considers both misidentified samples (on total number of samples) and patients (on total number of requests), as well as unlabeled samples (on total number of samples) and errors concerning patient identification. On the left-hand side are data collected by all laboratories involved in the program, while the right-hand side shows data from one clinical laboratory (Lab 1). Figure 2 shows the data on “*requests with erroneous data entry*” (on total number of requests), only for the errors concerning the tests erroneously added but not requested namely “added tests”. Finally, Figure 3 shows the data on “*hemolyzed samples*” (on total number of samples). Some differences occurred over time, in both the group of all laboratories (left-hand side of the figure), and in the single laboratory (right-hand side). On investigating the reasons for the increase in errors in 2011 for Lab 1, it was found that the method employed to identify hemolysis had changed from visual detection to the use of the automated serum index; some corrective measures taken led to a significant decrease in the subsequent 2-year period. Likewise, the wide variability observed in the group of all laboratories may have been due to differences in methods used for identifying hemolysis, namely visual detection and automated serum index. On the basis of this evidence, it was decided to split the data collected by laboratories using visual detection and those using automated serum index. Finally, Table 2 provides as an example the proposed quality specifications for three QIs based on the data collected, and according to the proposal by Fraser et al. [25] that they should be classified into three levels: optimum, desirable and minimum. As a minimum and maximum value, we adopted the 25° and 75° percentile, respectively. The decision to propose three performance levels, although they are based on the state-of-the-art, and not on biological variability as originally suggested by Fraser, was made in order to encourage laboratories to gradually improve their performance and that no more 25% of the laboratories results have an unsatisfactory performance.

Table 1 QIs results collected from 2009 to 2013.

Quality indicators	Year	Results, % (median)	Sigma value (median)
Misidentification errors	2009	0.083	4.576
Errors concerning patient identification	2010	0.040	4.739
Misidentified samples	2011	0.057	4.656
Misidentified patients	2012	0	5.040
Unlabelled samples	2013	0.010	5.040
Test transcription errors	2009	0.220	4.248
Requests with erroneous data entry (test name, missed test, added test)	2010	0.140	4.429
	2011	0.130	4.512
	2012	0.050	4.536
	2013	0.101	4.411
Incorrect sample type	2009	0.050	4.791
Wrong container	2010	0.040	4.853
Inappropriate sample type	2011	0.020	5.027
	2012	0.020	4.932
	2013	0.038	4.860
Incorrect fill level	2009	0.100	4.583
Inappropriate sample-anticoagulant volume ratio	2010	0.041	4.849
With insufficient sample volume	2011	0.074	4.667
	2012	0.050	4.734
	2013	0.140	4.468
Unsuitable sample for transportation and storage problems	2009	0.010	5.054
Damage during transportation	2010	0.013	5.015
Under inappropriate temperature condition or/and time	2011	0.010	4.338
Lost-not received	2012	0.010	4.966
Not properly stored	2013	0.020	4.500
Contaminated sample	2013	0	3.258
	2014	0.150	4.429
Sample hemolyzed	2009	0.850	3.887
Hematology/coagulation	2010	0.660	3.949
Chemistry	2011	0.630	3.975
Immunology	2012	0.270	4.175
	2013	0.440	4.093
Samples clotted	2009	0.206	4.293
Hematology/coagulation	2010	0.050	4.739
Chemistry	2011	0.060	4.739
Immunology	2012	0.090	4.429
	2013	0.179	4.378

Median value calculated on all percentage results and sigma values provided by all participating laboratories to the IFCC “Laboratory Errors and Patient Safety” project on Quality Indicators, from 2009 to 2013.

Discussion

The identification, implementation and monitoring of QIs represent a fundamental tool for complying with

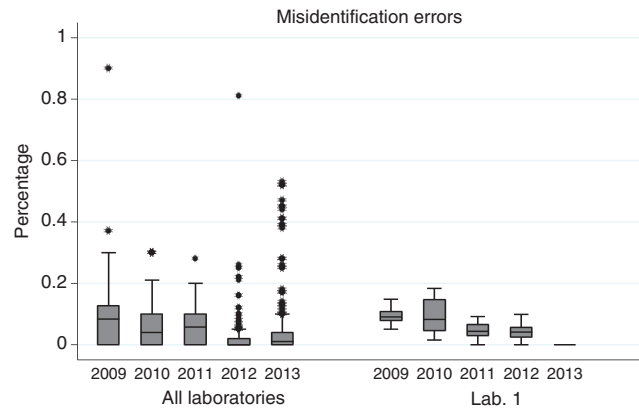


Figure 1 Misidentification errors (included: errors concerning patient identification, misidentified samples, misidentified requests, unlabeled samples): graph showing statistical measures (median, upper and lower quartiles, minimum and maximum data values).

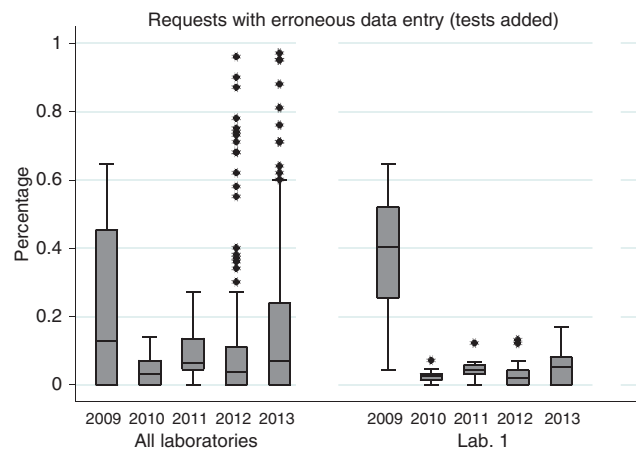


Figure 2 Requests with erroneous data entry (test added but not requested): graph showing statistical measures (median, upper and lower quartiles, minimum and maximum data values).

the requirements of the International Standard for the accreditation of medical laboratories, as well as serving as an indicator for internal quality improvement strategies and allowing reliable benchmarking between different laboratories [26]. The consensus achieved on the list of harmonized QIs is a preliminary to a further step: the identification of achievable and realistic performance targets. The acceptability of a performance indicator should be based on observed and/or expected outcomes in relation to the purpose for which it is to be used. As an example, for misidentification errors, the final goal is a zero-defect standard, as the consequences of patient misidentification can be dangerous and harmful. Few data are available on the impact of errors in the pre-analytical phase on clinical outcomes. The identification of quality specifications

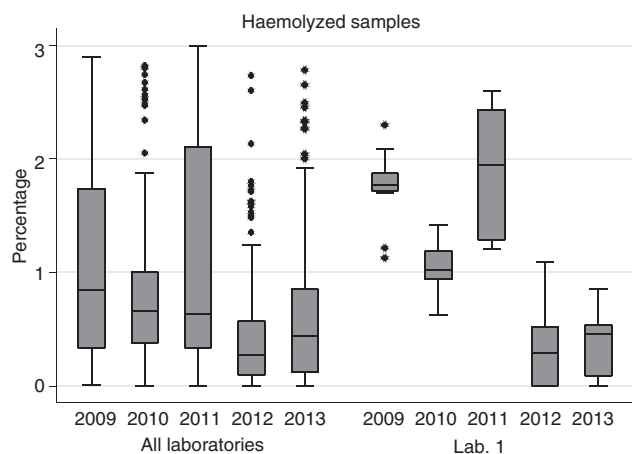


Figure 3 Hemolyzed samples: graphical representation of statistical measures (median, upper and lower quartiles, minimum and maximum data values).

Table 2 Quality specifications for three QIs.

Quality indicators	Value	Quality specifications		
		Minimum (25th percentile)	Desirable (Median)	Optimum (75th percentile)
Misidentification errors	Percentage	0	0.010	0.040
	Sigma	4.54	5.04	5.25
Test transcription errors (added tests)	Percentage	0	0.070	0.240
	Sigma	4.26	4.59	4.74
Sample hemolyzed	Percentage	0.120	0.440	0.852
	Sigma	3.84	4.09	4.39

Proposal of quality specifications based on percentiles values calculated on laboratories results (expressed as percentage and sigma) collected in the last year (2013).

based on the state-of-the-art should therefore be considered an essential preliminary step in arousing the awareness in clinical laboratories of the need to measure and improve their performances in extra-analytical QIs. The data collected from several laboratories worldwide have provided valuable insight on the state-of-the-art both, especially as they were obtained using a harmonized list of QIs and with a homogeneous reporting system. The expression of the data as both a percentage and in sigma metrics may allow clinical laboratories enhance their appreciation of the quality level for each indicator and prioritize corrective actions and improvement initiatives. The classification of the quality specifications for available QIs into three levels, optimum, desirable and minimum represents the translation to the pre-analytical phase of a proposal already adopted for evaluating analytical performances

in EQA/PT schemes. Well known and widely accepted by laboratory professionals, this criterion has proved effective in improving the analytical quality and reducing the analytical error rates.

Conclusions

The identification of harmonized QIs and the preliminary definition of quality specifications based on the state-of-the-art represents an essential step in assuring quality in TTP and patient safety. In particular, as available literature emphasizes the vulnerability of the pre-analytical phase, the implementation and monitoring of valuable QIs is a formidable tool for identifying the most critical steps and reducing the risk of errors in the initial phase of the testing cycle.

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