

## QUALITY INDICATORS OF THE PRE-ANALYTICAL PHASE INDIKATORI KVALITETA PREANALITIČKE FAZE

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**Summary:** *Quality indicators* are tools that allow the quantification of quality in each of the segments of health care in comparison with selected criteria. They can be defined as an objective measure used to assess the critical health care segments such as, for instance, patient safety, effectiveness, impartiality, timeliness, efficiency, etc. In laboratory medicine it is possible to develop quality indicators or the measure of feasibility for any stage of the total testing process. The total process or cycle of investigation has traditionally been separated into three phases, the pre-analytical, analytical and post-analytical phase. Some authors also include a »pre-pre« and a »post-post« analytical phase, in a manner that allows to separate them from the activities of sample collection and transportation (pre-analytical phase) and reporting (post-analytical phase). In the year 2008 the IFCC formed within its Education and Management Division (EMD) a task force called *Laboratory Errors and Patient Safety (WG-LEPS)* with the aim of promoting the investigation of errors in laboratory data, collecting data and developing a strategy to improve patient safety. This task force came up with the Model of Quality Indicators (MQI) for the total testing process (TTP) including the pre-, intra- and post-analytical phases of work. The pre-analytical phase includes a set of procedures that are difficult to define because they take place at different locations and at different times. Errors that occur at this stage often become obvious later in the analytical and post-analytical phases. For these reasons the identification of quality indicators is necessary in order to avoid potential errors in all the steps of the pre-analytical phase.

**Keywords:** quality indicators, health care, patient safety, laboratory medicine, pre-analytical phase, errors

**Kratak sadržaj:** *Indikatori kvaliteta* su alatke pomoću kojih je moguće kvantifikovati kvalitet svakog segmenta zdravstvene službe u poređenju sa odabranim kriterijumima. Indikatori kvaliteta mogu da se definišu kao objektivno merilo za procenu kritičnih zdravstvenih segmenata kao što su npr. sigurnost pacijenata, efektivnost, nepristrasnost, pravovremenost, efikasnost itd. Kada je reč o laboratorijskoj medicini moguće je razviti indikatore kvaliteta ili meru izvodljivosti za bilo koji stupanj ukupnog laboratorijskog procesa. Ukupan proces ili ciklus ispitivanja tradicionalno obuhvata tri faze, pre-analitičku, analitičku i post-analitičku. Neki autori uvode i »pre-pre« i »post-post« analitičku fazu kako bi se identifikovale aktivnosti koje prate inicijalni izbor neophodnih analiza i njihovog tumačenja od strane kliničara, na koji način se razdvajaju od aktivnosti uzimanja i transporta uzoraka (pre-analitička faza) i izveštavanja (post-analitička faza). Godine 2008. IFCC je u okviru svog Komiteta za edukaciju i menadžment (EMD) formirao radnu grupu »*Laboratory Errors and Patient Safety*« (WG-LEPS) sa ciljem da promoviše ispitivanje grešaka u laboratorijskoj medicini, sakuplja podatke i razvija strategiju radi poboljšanja sigurnosti pacijenata. Ova radna grupa sačinila je *Model of Quality Indicators (MQI)* za celokupni laboratorijski proces (TTP) uključujući pre-, intra- i post-analitičku fazu rada. Pre-analitička faza obuhvata niz procesa koje je teško definisati s obzirom na to da se odvijaju na različitim mestima i u različito vreme. Greške koje mogu da se dese u ovom procesu često postaju očigledne u analitičkoj ili post-analitičkoj fazi. Kako bi se moguće greške u navedenim fazama izbegle potrebno je identifikovati indikatore kvaliteta pomoću kojih je moguće otkrivati greške u svakom stupnju pre-analitičke faze.

**Ključne reči:** indikatori kvaliteta, zdravstvena služba, sigurnost pacijenta, laboratorijska medicina, pre-analitička faza, greške

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## Introduction

According to the ISO 9001 Standard, *quality* is always relative to requirements. This means that the quality of something can be determined by comparing the sum of related characteristics with the sum of necessary requirements. If the characteristics meet all the requirements, high or excellent quality is achieved. If this is not the case, low or poor quality is reached. *Quality* is, therefore, a matter of degree, that is, the *quality* of something depends on a set of related characteristics and the necessary requirements defined accordingly.

Besides this, there are many other definitions of *quality*. One of them, for example, is the definition of quality offered by the Institute of Medicine (IOM) of the National Academies that states: »The degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge« (1).

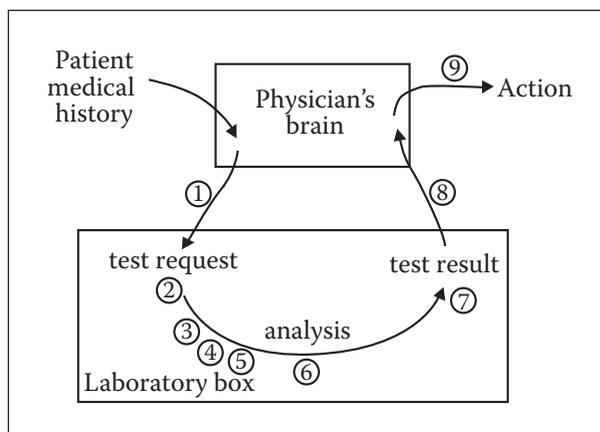
To ensure large-scale total quality, it is necessary for the employees in a health or other organization to work constantly on quality improvement. Quality is also a function of trust, in medicine generally, but especially in laboratory medicine.

*Quality indicators* are tools that allow the quantification of quality in each of the segments of health care in comparison with selected criteria (2). Quality indicators can be defined as an objective measure used to assess the critical health care segments such as, for instance, patient safety, effectiveness, impartiality, timeliness, efficiency, etc. The criteria for the choice of quality indicators have been widely accepted by health organizations, and can be grouped into three conceptual areas: 1) significance, 2) scientific base, and 3) the possibility of measurement, which are elaborated in detail depending on where they are applied.

## Quality Indicators in Laboratory Medicine

When it comes to laboratory medicine, it is possible to develop quality indicators or the measure of feasibility for any stage of the total testing process. The total process or cycle of investigation is based on the original brain-to-brain loop concept, described by Lundberg (3, 4). He sketched a series of activities, beginning with the clinical question in accordance with the doctor's opinion, followed by test selection, sample collection, transportation to the laboratory, analysis, reporting back to the doctor, interpretation and decision making by the clinician (5).

These activities have traditionally been separated into three phases, the pre-analytical, analytical and post-analytical phase. Some authors also include a »pre-pre« and a »post-post« analytical phase, in order to identify the activities that follow the initial choice of necessary analyses and their interpretation by the clini-



**Figure 1** Brain-to-brain information loop by George D. Lundberg (3, 4).

cian, in a manner that allows to separate them from the activities of sample collection and transportation (pre-analytical phase) and reporting (post-analytical phase) (6).

Considering the total testing process, quality indicators can be defined for each of these phases, divided into six categories according to the IOM:

- 1) test requirement
- 2) patient identification and sample collection
- 3) sample identification, preparation and transportation
- 4) laboratory testing
- 5) reporting the results of testing, and
- 6) interpretation of laboratory results and decision making,

within which it is possible to define the laboratory quality indicators.

Health care is a sector with relatively high risk, and, for instance, according to certain data, the total error rate in the health care system of the United States is estimated to be 31–69% (7). The error rate is often estimated by applying the Sigma concept, defined by the number of standard deviations found between the mean value of the process and the determined limits. Application of this measure reveals that health care is found at the 1–2 Sigma level, which is very low in relation to e.g. luggage handling in air traffic that is around 4 Sigma (7).

The analytical phase in laboratory medicine is by all means the field with the least amount of errors in health care, whose feasibility is close to 5 Sigma (0.002%) (7, 8). However, the number of errors in the two extra-analytical phases is 4–5 times higher than in the analytical phase, with most of the detected errors appearing in the pre-analytical phase (9–12).

The pre-analytical phase includes a series of procedures that are hard to define since they take place at different locations and at different times. Generally speaking, the pre-analytical phase includes all proce-

dures from the moment when a clinician has formulated his request to the point when the sample is ready for analysis.

The main procedures within the pre-analytical phase that should be considered are: test selection, patient preparation, the collection, transportation, handling and storage of samples and interferences. Knowledge of the characteristics of each individual patient and biological variations also belong to this phase. As has been said, the number of laboratory errors in the analytical phase is significantly reduced by technological development; however, the frequency of errors in the pre-analytical phase is up to 70% of the total number of laboratory errors, which is very important since information coming from the laboratory affects 60–70% of clinical decisions. This is why laboratories should pay special attention to the pre-analytical phase of their work.

The quality control system is well known to ensure quality in the analytical phase, and in most cases laboratory workers dedicate themselves fully to this phase; however, one should keep in mind that the sources of error are found in the pre-analytical phase. This is precisely why the ISO 9001 (13) and ISO 15189 (14) Standards require careful definition of all

the laboratory processes, including the pre-analytical phase, with the requirement for establishing quality indicators for each phase.

For this reason the IOM article from 1999 *To Err Is Human* (15) points to the necessity of ensuring patient safety at the national and international level, and to the constant need to reduce errors in all the segments of health care, considering the fact that in the USA some 98,000 people die each year due to medical errors. After this document by the IOM, two new documents followed, entitled *Crossing the Quality Chasm: A New Health Care System for the 21st Century* (16) and *To Err is Human – To Delay is Deadly* with the subtitle *Ten years later, a million lives lost, billions of dollars wasted* (17), suggesting that little has been done within the USA health system to improve quality, and that errors occur in all segments of treatment, including the diagnostic sector where errors may also appear that cause patient jeopardy.

In the past decades laboratory workers worldwide have therefore dedicated their full attention to this problem, striving to reduce the number of errors in the total testing process (TTP) (12, 18). The American Society of Clinical Pathologists (ASCP), now the College of American Pathologists (CAP), pointed to the

**Table I** Quality indicators of the pre-analytical phase.

a) Test ordering	
QI-1	Percentage of »Number of requests with clinical question from general practitioners/Total number of requests from general practitioners«
QI-2	Percentage of »Number of appropriate requests, with respect to clinical question from general practitioners/Number of requests that report clinical question from general practitioners«
b) Formulation and input of request	
QI-3	Percentage of »Number of requests without physician identification/Total number of requests«
QI-4	Percentage of »Number of unintelligible requests/Total number of requests«
QI-5	Percentage of »Number of requests with errors concerning patient identification/Total number of requests«
QI-6	Percentage of »Number of requests with errors concerning physician identification/Total number of requests«
QI-7a	Percentage of »Number of requests with errors concerning input of tests (missing)/Total number of requests«
QI-7b	Percentage of »Number of requests with errors concerning input of tests (added)/Total number of requests«
QI-7c	Percentage of »Number of requests with errors concerning input of tests (misinterpreted)/Total number of requests«
c) Identification, collection, handling and transportation of samples	
QI-8	Percentage of »Number of samples lost–not received/Total number of samples«
QI-9	Percentage of »Number of samples collected in inappropriate containers/Total number of samples«
QI-10a	Percentage of »Number of samples hemolyzed (hematology)/Total number of samples«
QI-10b	Percentage of »Number of samples hemolyzed (chemistry)/Total number of samples«
QI-11a	Percentage of »Number of samples clotted (hematology)/Total number of samples with anticoagulant«
QI-11b	Percentage of »Number of samples clotted (chemistry)/Total number of samples with anticoagulant«
QI-12	Percentage of »Number of samples with insufficient sample volume/Total number of samples«
QI-13	Percentage of »Number of samples with inadequate sample–anticoagulant/Total number of samples with anticoagulant«
QI-14	Percentage of »Number of samples damaged in transport/Total number of samples«
QI-15	Percentage of »Number of samples improperly labeled/Total number of samples«
QI-16	Percentage of »Number of samples improperly stored/Total number of samples«

**Table II** Quality indicators of the analytical phase.

QI-17	Percentage of »Number of unacceptable performances in EQAS/PT per year/Total number of performances in EQAS/PT«
QI-18	Percentage of »Number of unacceptable performances in EQAS/PT occurring as a result of a case previously corrected, per year/Total number of unacceptable performances«
QI-19	Percentage of »Number of tests with CV% higher than selected target, per year/Total number of tests«
QI-20	Percentage of »Number of reports delivered outside the specified time for instrument failures, per year/Total number of reports«

**Table III** Quality indicators of the post-analytical phase.

QI-21	Percentage of »Number of reports delivered outside the specified time/Total number of reports«
QI-22	Percentage of »Number of critical values communicated/Total number of critical values to communicate«
QI-23	Average time to communicate critical values
QI-24	Percentage of »Number of interpretative comments provided in medical reports that impacted positively on the patient's outcome/Total number of interpretative comments provided in the medical report«
QI-25	Number of guidelines issued in co-operation with clinicians, per year

need for analytic quality control 80 years ago (19), and devised a series of programs for the control of the laboratory process and as tools for discovering errors (20, 21). Significant advances in the control of the total testing process and the identification and reduction of the number of errors as the next step were made owing to the application of ISO 15189 Standard for the accreditation of medical laboratories (14).

In the year 2008 the IFCC formed within its Education and Management Division (EMD) a task force called *Laboratory Errors and Patient Safety (WG-LEPS)* with the aim of promoting the investigation of errors in laboratory data, collecting data and developing a strategy to improve patient safety (22). This task force came up with the Model of Quality Indicators (MQI) for the total testing process (TTP) including the pre-, intra- and post-analytical phases of work (12, 22, 23).

Tables I–III show quality indicators determined by the IFCC task force within the project *Laboratory Errors and Patient Safety* for all three phases of laboratory work (22). According to the most recent data from the work of Plebani (12), the frequency of errors by phases of laboratory work is as follows:

Pre-pre-analytical (46–68%): inappropriate request to the laboratory, erroneous identification of patient/sample, sample taken at the infusion site, collection of unsuitable specimens (hemolysis, coagulation, insufficient volume, etc.), inappropriate containers for collection, handling, storage and transport;

Pre-analytical (3–5%): improper sorting, aliquoting, pipetting and labeling (signing), centrifugation (time and/or speed);

Analytical (7–13%): broken equipment, mixed samples, interferences (endogenous or exogenous), not detecting errors during quality control;

Post-analytical (13–20%): wrong validation of results, errors in reporting and delivering reports, prolonged turn-around time, lack of or delayed reporting on critical values;

Post-post-analytical (24–46%): late or delayed reaction to laboratory reporting, incorrect interpretation, absence of proper consultations.

Identification of quality indicators is necessary in order to avoid potential errors in the listed phases.

### Quality Indicators in the Preanalytical Phase

In the pre-analytical phase major sources of pre-analytical variability can be found during patient preparation (i.e. biological variability, environmental conditions (e.g., climate, pollution), postural changes); sample collection (patient identification and sample labeling, type of disposal for blood collection (e.g., straight needle, butterfly, cannula), caliber (gauge) of the needle, tourniquet time, container (e.g., primary tube), order of draw, phlebotomy procedure, contamination, tube/s mixing); sample transportation (length and environmental conditions, pneumatic tube systems); sample preparation for analysis (length, speed and temperature of centrifugation, preparing aliquots); sample storage (length, temperature, freezing & thawing) (25).

Errors that may occur in this process often become obvious in the analytical and post-analytical phase as well. So, for example, the effects of interferences may be discovered during analysis or the clinical interpretation of results. For this reason current recommendations suggest that a laboratory error should be defined as a defect that occurs at any point in the

cycle, from the formulation of a request till the interpretation of results by the clinician. For these reasons identification of quality indicators is necessary in order to avoid potential errors in the listed steps of the pre-analytical phase.

#### Test ordering

The most frequent deviations occur during patient identification in the doctor's office or a clinical unit, therefore this phase requires special quality control. The ISO 15189 Standard dictates which information a report form should include, regardless of whether it is in electronic or paper form, and these are:

- a. unique patient identification
- b. name or other signature mark of the medical professional or legally authorized person
- c. type of primary sample
- d. required laboratory parameters
- e. relevant clinical information about the patient necessary for interpretation; minimally, the sex and year of birth
- f. date and time of primary sample collection.

Two quality indicators may be defined related to the laboratory referral, namely if it is appropriate or inappropriate.

The lack of patient identification or patient misidentification have serious consequences for reaching the final conclusion and clinical decision, as well as for patient safety, thus this is one of the key indicators in the process. Errors in patient identification may also occur during the procedures of sample preparation.

Ordering inappropriate tests is another pre-analytical variable with a negative impact on patient safety. It is the cause of unnecessary test repetitions (up to 30%, according to some data) (24), demands for multiplying other tests, seeking out new investigation methods that would be more efficient, which is also the result of the clinician's insufficient knowledge of the tests, etc.

The application of laboratory diagnostics may be promoted by the development and introduction of profiles of laboratory analyses that would be specific for certain pathologies, stemming from recommendations based on practice and the principles of evidence-based medicine, and on the consensus reached between the clinicians and laboratory experts. Despite the efforts made in the last years, implementation of such protocols is still insufficient. It is also necessary for the laboratory to keep providing clinicians with enough information about the diagnostic usefulness of laboratory tests, and to eliminate outdated tests that have lost diagnostic value.

The next very important factor are all the additional information that a clinician must provide to a laboratory within the laboratory investigation request form, related to the *individual characteristics of the patient*, such as age, sex, race, physiological state (pregnancy or menopause), dietary habits, physical exercise, use of medications and suspected diagnosis. Such data are necessary to provide the right reference values and avoid unneeded repetitions if the result is impossible to interpret due to lack of information.

Laboratory experts should acquaint the clinician with the importance of biological variations, potentially significant in the pre-analytical process (test selection) but also in the post-analytical process (interpretation of test results). It is necessary for the clinician to understand the concept of biological variations that include intra-individual biological variations (deviation of results in relation to the person's homeostasis) and inter-individual biological variations (variations between different persons in relation to the established homeostatic value). On the basis of such knowledge it is possible to select between two tests the best one with the highest diagnostic value.

#### Preparation of the patient for sample collection

The ISO 15189 Standard (14) instructs laboratories to prepare a manual for the pre-analytical procedure that will give clear instructions provided to the patient before the collection of biological samples. Among other things, and depending on the type of analysis, patients would be instructed to control their diet, physical activities, stress, use of medications, etc. This problem is most easily solved by the application of computerized referrals, where all the necessary data are obtained from the patient; however, the problem is much bigger when samples are collected at sites dislocated from the laboratory. This is why the

1. IMPORTANT: In order for this test to be carried out, you need to be awake 2 hours before the blood is taken, but you must not do any exercise or exert yourself during this time.
2. The day before the test you should avoid food which is rich in proteins.
3. The day before the test you should avoid any breast stimulation.
4. You must not eat or drink anything during the 8 to 10 hours before you have the sample taken. You may drink water.
5. Go to the location where you are to have a blood sample taken, at the time started.
6. If you are taking any medication, please tell the person who is taking the sample.

**Figure 2** An example of prepared instructions for patient preparation for serum prolactin measurements (26).

laboratory must standardize its forms by preparing a check-list and training its staff to use it.

#### *Sample collection*

It should be known that there may be significant differences in the quality of a sample depending on whether it is collected by trained staff or by the patient himself. ISO 15189 also states that standardized procedures for the collection of samples should be made available at the site of sample collection. Manuals for collecting primary samples should include the following information:

- patient identification, that will provide traceability between the patient, request and primary sample
- procedures for taking primary samples with a description of used containers, necessary additives, type and volume of the primary sample, location of sample collection and time of vein occlusion during sample collection of venous blood
- identification of the person collecting the primary sample, the date and hour of sample collection
- safe disposal of the material used during sample collection.

Improperly identified primary samples cannot be processed in a laboratory. Errors in patient or sample identification have serious consequences for clinical decision making and patient safety, which is why this procedure is considered a key quality indicator in the process.

Most of the pre-analytical errors arise during the sampling of biological materials, even up to 60% (25). The most frequent errors in the pre-analytical phase are »sample not received«, »hemolyzed sample«, etc. This means that the laboratory must control the samples and reject all hemolyzed samples, since they would lead to inaccurate results. Also, the necessary volume of a sample should be kept in mind, and should be defined by the laboratory in relation to the needs of analyzing, application on analyzers, repetition and storage for repeated determinations (26).

#### *Sample transportation*

To provide the stability of a sample, special attention should be paid to the transport of a sample from the collection site to the clinical laboratory. The ISO 15189 Standard suggests that a laboratory should control the transportation of samples to the laboratory so that they reach it in time, at an appropriate temperature and in a way that will be safe for all the staff involved in the transport, all in accordance with the national and international regulations. The 2009 ADR European Norms for Highway Transport define the means of packing biological samples for transport that are considered infectious materials (Category B) (available at <http://www.unece.org/trans/danger/publi/adr/adr2009/09ContentsE.html>).

The National Committee for Clinical Laboratory Standards (NCCLS) H5-A3 1994 has recommended a maximum of 2 hours for transporting blood samples at a temperature of 10–22 °C. A directive in the 2009 GP16-A3 NCCLS recommends transporting urine samples during maximally 2 hours at a temperature of 2–8 °C (27, 28).

It is advised to take notice of the fact that during transport a sample may be exposed to shaking, light, change in temperature, prolonged transport, etc. For the reasons mentioned here it is the duty of the laboratory to prepare instructions for sample transportation, and control them when receiving the samples. The minimal quality indicators in this domain could be: control of temperature during transport, type of package and time from sample collection till delivery to the laboratory. It is hard, however, to control if the sample had been exposed to light or had been shaken, etc. The data on the application of pneumatic pipes for sample delivery are controversial, saying that there are no significant changes in the analytical results, but also that during this type of transport the samples are most susceptible to hemolysis (29).

#### *Reception, handling and storage of samples in the laboratory*

In the case of reception, handling and storage of samples in the laboratory, guidelines for this section of the pre-analytical phase should also be respected, described within the ISO 15189 Standard, with regard to the following:

- the received specimens of samples should be registered in the laboratory protocol or information system if it is being applied,
- the date and time of reception as well as the identity of the person that brought the sample should be recorded,
- the criteria for reception or rejection of a primary sample should be clearly defined; in case a compromised sample was received, the report must state the nature and problem that may affect sample interpretation,
- samples that are received must always be examined,
- laboratory should have a documented procedure for receiving and labeling samples,
- sample aliquots should be traceable to the original primary sample,
- samples should be stored until the determined period under conditions that provide stability of the sample for the purpose of necessary examinations and repeated analyses, and also potential additional investigations.

One of the key quality indicators in this segment of the pre-analytical phase is the error rate during the reception of samples, such as, for instance, sample

**Table IV** CLSI Recommendations and Guidelines related with the pre-analytical phase.

<b>H3-A6:</b> Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard – Sixth Edition. October 2007
<b>M29-A3:</b> Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline – Third Edition (Vol. 25, No. 10) March 2005
<b>H04-A6:</b> Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard – Sixth Edition (Vol. 28, No. 25) September 2008
<b>C49-A:</b> Analysis of Body Fluids in Clinical Chemistry; Approved Guideline (Vol. 26, No. 14) April 2007
<b>H56-A:</b> Body Fluid Analysis for Cellular Composition; Approved Guideline (Vol. 26, No. 26) June 2006
<b>H18-A4:</b> Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline – Fourth Edition (Vol. 30, No. 10) May 2010
<b>GP16-A3:</b> Urinalysis; Approved Guideline – Third Edition (Vol. 29, No. 4) February 2009
<b>H21-A5:</b> Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Homeostasis Assays; Approved Guideline – Fifth Edition (Vol. 28, No. 5) January 2008

not sent, sample clotted, hemolyzed sample, insufficient sample, etc. For this reason it is also necessary to standardize this phase by applying a series of recommendations related to the above-mentioned potential errors (25). During further manipulation of the samples: centrifuging, aliquoting, freezing, etc, errors may also arise, especially during the distribution and manual identification of each aliquot. ISO 15189 again suggests that each aliquot should be traceable to the primary sample, so manual labeling of samples should be specially standardized. The error rate is reduced by the automation of the pre-analytical process (30–33).

Further on in the procedure, if they are not used straight away, the primary samples should be protected from the influence of light or temperature. It should be known for how long the samples may be kept, and how stable they are, meaning that a laboratory should clearly define these conditions and control them during the time of keeping. In view of this, there is a series of recommendations given primarily by the CLSI (*Table IV*).

#### *Detection of interferences in the samples*

As known, interferences may be recorded in the pre-analytical phase (visual detection of hemolysis, lipemia, bilirubins), analytical (quantification of the detected interferences) and post-analytical phase (unexpected results during validation). This is why it would be advised to prepare a procedure on the basis of which interferences in a sample would be identified depending on their type, a list of analytic tests prone to interferences, the established concentrations of ingredients above which the possibility of interference arises, etc. (34).

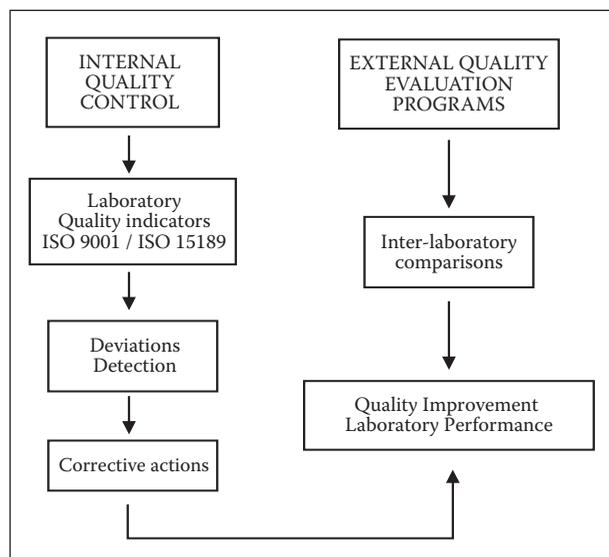
#### **Quality Assurance in the Pre-analytical Phase**

Quality control of the analytical phase of work was introduced back in the 1950s, while the control of the pre-analytical phase became a subject of thought during the nineties. International consensus accepted in 1999 has significantly promoted the quality control of the analytical process (35). The consensus established a hierarchy of the models of specifications for analytical quality that include the following:

- estimation of the effect of analytical feasibility on the clinical outcome
- estimation of the effects of analytical feasibility on clinical assessment in general
- publishing of expert guidelines
- establishing the aims of feasibility
- goals based on contemporary findings.

For the purpose of ensuring total quality of the laboratory work, it is also necessary to implement a system of internal control for the pre-analytical phase of work, and the laboratories should be involved in schemes of the external quality control of this work process.

Internal quality control in the fields of pre-analytical phase should include relevant quality indicators for each segment of the pre-analytical phase. Quality indicators should allow early detection of deviations from the normally anticipated process and its permanent improvement. Having in mind that quality indicators are made up of data or a collection of data that help the objective estimation of a process or activity, quality indicators in this field should also provide objective assessment of the possibility of error. Such quality indicators should be constantly improved (26, 36).



**Figure 3.** Quality assurance in the pre-analytical phase (26).

In accordance with the above, all laboratories should establish quality indicators for the processes whose application they can control and monitor. It is also necessary to define *detailed descriptions of quality* or the *limits of acceptance for each indicator*. If the results are outside these limits, corrective actions should be undertaken.

With regard to the indicators of the pre-analytical phase, there is still no international consensus on the limits of acceptance for certain quality indicators. Should this be the case, results published in literature, obtained in similar laboratories, or previous results in the same laboratory may be used.

The most frequent errors in the pre-analytical phase are: missing sample and/or test request, wrong/missing identification, *in vitro* hemolysis, undue clotting, wrong container, contamination from infusion route, insufficient sample, inappropriate blood to anticoagulant ratio, insufficient mixing of the sample, inappropriate transport and storage conditions, inappropriate centrifugation conditions, etc.

Here we present some examples for calculating the frequency of errors depending on the quality indi-

cator. According to literature, there are different data for certain indicators, e.g. incorrect number of samples with a frequency of 2.3% (37–39), sample not received 2.9%, hemolyzed sample 0.8%, clotted sample 0.55% (25).

External programs for the control of the pre-analytical process may be implemented as inter-laboratory comparisons, where each laboratory is assessed in relation to another one included in the control program. Statistical analysis is used to evaluate the data delivered by the laboratories participating in the control program, in relation to the number of errors that occur in the pre-analytical phase. In this way each laboratory may assess its position and take necessary corrective measures. This type of quality indicator control is still not widely used.

## Conclusion

In conclusion it may be said that proper organization, standardization and computerization of the laboratory and hospital process may largely improve the testing process as a whole, while reducing the error rate and ensuring patient safety (38–41). Patient misidentification can thus be resolved by process automation, errors in laboratory requests through computerized processing, remainder of a large quantity of samples by listing the precise number of requested analyses, errors in sample identification through automatic labeling of samples, incorrect sampling through applying quality materials, informing and training the staff. The accreditation of medical laboratories according to the ISO 15189 Standard has allowed the control of all the phases of laboratory work with regard to the management of the quality and competence system.

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## Conflict of Interest Statement

The authors stated that there are no conflicts of interest regarding the publication of this article.

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