REVIEW

QUALITY ASSURANCE AND CONTROL IN THE LABORATORY OF MEDICAL ANALYSIS

Daniela Tiță, Irina Zaharia

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CONTENTS

INTRODUCTION

The Medical Analysis Laboratory has an increasingly important place in medical practice. Close cooperation between the clinician and the laboratory specialists often results in diagnosis. The informative power of paraclinical examinations is variable, often laboratory data is the basic information on which the diagnosis is based.

The quality of data obtained by laboratory specialists and provided to the clinician should inspire confidence in both. The intensification of the supervision of the work in the medical analysis laboratory led to the definition of the complex concept of quality control and to the specification of the systems through which the action translates into fact. For this it is necessary to define the following terms: 1. quality; 2. quality assurance; 3. internal control; 4. external control [11,12].

1. QUALITY CONTROL

According to ISO 8402/1995, quality is: "The set of characteristics of an entity that gives it the ability to meet the known and potential needs of the user." By the notion of "user" - laboratory services, we understand the family doctor / specialist doctor and directly the client (patient).

"Known needs" actually occurring: usual analyzes by common techniques of classical biological products (blood, urine, etc.) and implicitly correct results, allowing a correct diagnosis, by "potential needs" we understand: - new analyzes by modern techniques from other products than classical (eg hair); - interpretation of laboratory data; - the possibility of identifying interferences and their quantification[12].

Quality assurance is the set of measures taken to ensure the correctness of the laboratory investigations so that the final results reflect as accurately as possible the state of the investigated sample, from the preanalytical, analytical and post-analytical stage [6].

Internal quality control is a set of procedures performed by laboratory personnel for ongoing control of operations and measurement results to determine whether the results are reliable enough to be released[3].

The internal quality control strategy involves: 1. control planning: - choice of control materials - their number and matrix - placing them within the analytical series 2. statistical analysis of results -

automatic plotting / plotting of Levey Jennings diagrams - setting limits and rules Westgard control - interpretation of the results according to established rules [1,4,10].

The role of internal quality control is to detect in a very short time any measurement error and alert the specialist if there are problems that may affect the medical utility of the results[11]. Also, internal control should provide a clear view of the timing of all error factors that would affect the measurement performance of the method (precision and measurement accuracy) [3,5].

The external quality control service is carried out by the medical analysis laboratories in Romania according to the national legislation in force (OMS 1301/2007 and OMS 2071/2008) to check the performance of the medical analysis laboratories in order to provide the patients with the right results as closely as possible of their real value, coming to the direct help of the patient, the direct beneficiary of the medical act / service provided by the medical analysis laboratory [25,26].

According to SR EN ISO 15189: 2013, ch.1.4.6; 4.14.7, Risk Management "The laboratory must establish quality indicators to monitor and evaluate performance over all critical aspects of pre-screening, examination and post-processing processes" The responsibility of each laboratory consists of eliminating errors likely to occur during pre- and post-processing processes [24].

2. MEASUREMENT ACCURACY / INACCURACY

Measurement accuracy / inaccuracy is the degree of consistency between the result of a measurement and the actual measurement value. It is expressed by the Bias Trueness of measurement, the degree of approximation between the average that could be obtained from an infinite number of quantitative values obtained under specified conditions and the true value of the measure [5].

Measurement precision / inaccuracy, degree of approximation between the results of repeated measurements of an analyte under specified conditions. It is a measure of the dispersion of measured value values[5,27]. It is expressed by statistical formulas: mean arithmetic, standard deviation (DS) and coefficient of variation (CV). The standard deviation (mean square deviation, DS) is the measure of the dispersion of a measurement value around the average of the measurement values, and the coefficient of variation is given by the ratio between the standard deviation and the arithmetic mean of the determinations and expressed in percent [4].

According to ISO 5725-1, measurement accuracy is defined by the two terms: accuracy and precision (ISO 5725-1, Accuracy and accuracy of measurement methods and results)[3].

In medical analysis labs, analytical procedures are subject to measurement errors that represent the difference between the result of a measurement and the true value of the measurement. These errors can be cached into: random errors affecting the accuracy of the test (causes: voltage variations, sample contamination, pipette air bubbles, control material placed in a position other than specified, etc.) and systematic errors affecting the accuracy of the test (causes: calibration - reconstitution with uncalibrated pipettes, inappropriate reaction temperature, damage to the light source, etc.) [2,9,13].

The Total Admitted Error (Tea) is a quality requirement that sets the tolerances of inaccuracy and inaccuracy for a single measurement or a single test result. The total admitted error signifies a magnitude of the measurement error which, if exceeded, would cause unacceptable results and which besides random errors and systematic errors also encompass the preanalytical variables and the intra-individual biological variation[14].

Analytical series (analytical run) is a timeframe where the accuracy and measurement accuracy of a measurement system are stable. No more than 24 hours [11].

3. WESTGARD RULES

James Westgard applied the concepts and techniques of quality management for medical laboratories and is known for the 6 rules of acceptance and rejection of controls, now known as the "Westgard Rules" [18]. These rules are decision criteria, established on a control map, Levey Jennings, for accepting / rejecting the results of internal quality control and running or not of the biological patient measurement process.

a) the control materials are chosen according to:

- the number of controls used for a series (one, two or three)
- type of levels - normal, low or elevated - low, high-);
- stability
- price, etc.

b) Select the number of control measurements to be used for a series,

c) Analyze these materials to characterize the performance of the method by

collecting at least 20 measurements from at least the last 10 days,

d) Calculate the mean and standard deviation of these data.

e) Select the control rules to be applied!

Rule 1 / 2s

• The series is accepted if the results of both controls are within a

2 DS from the average of values; is the most used rule; has a particular value of attention. Rule 1: 2s is the rule that gives the highest level of false rejections and false alarms!

Rule 1 / 3s

• 13s The series is considered out of control if only one of the control results exceeds the limit of ± 3 DS;

Rule 2 / 2s

• 2 2s The series is rejected when two successive checks exceed the mean value +2 DS or the -2DS average limits;

R / 4s RULE

• R 4s The series is rejected when a control in a group of controls exceeds the average + 2DS limit and one exceeds -2DS or when the range of a control group exceeds 4DS;

Rule 4 / 1s

• 41s The series is rejected when the results of 4 consecutive checks exceeds the same average + 1DS or media -1DS;

Rule 10 / x

• 10-x Series is rejected when the results of 10 consecutive checks are on the same side of the average [18].

The quality of internal quality control is expressed by: the probability of false rejection (Pfr) and the probability of error detection (Ped). The probability of false rejection is a performance feature that shows how often an analytical series is rejected when no measurement errors occur, except for the inherent inaccuracy of the measurement method. Theoretically 0%, acceptable 5% [5,19].

Probability of error detection is a performance feature that describes how often an analytical series is excluded when internal control results show errors that include inherent inaccuracy of the method. Theoretically 100%, acceptable 90%. Ped and Pfr have opposite effects depending on the setting of control limits [5,19].

Laboratories can establish their own combination of Westgard rules according to their performance parameters: two rules for random errors and - at least two rules for systematic errors [11,15]. A common practice in our country is to use the values in the insert to set control limits. This practice leads to too large the values reflecting the variation observed in the laboratories used by the control material manufacturer.

According to the regulations in force the control limits must be set against the average of the measured values and the standard deviation of the mean so as to reflect the behavior of the measuring procedure in its own laboratory [19]. The values of the control materials provided by the manufacturer should only be used as a guide for setting the initial control limits or for new control materials.

The average of the laboratory must be within the range set by the manufacturer on the analyzed material. Control limits should be set by their own mean and standard deviation. Just at the beginning of a new control batch. the target value and the standard deviation of the control materials from the inserts (provided by the manufacturer) are used as a guide [10].

The choice of the control procedure for each test is the responsibility of each laboratory and it must establish the number, type, frequency of the control materials used and their position within the analytical series [24].

Control procedures should immediately detect errors occurring due to the failure of the measurement system, environmental conditions and / or operator performance (accuracy and measurement accuracy) [20]. The control procedure alerts promptly on the errors, but the lab monitors how they can influence their accuracy and accuracy over time.

4. QUALITY MANAGEMENT IN THE PRE-ANALYTICAL PHASE

A successful medical act depends to a large extent on the accuracy of the results provided by the medical analysis laboratories. Getting the right lab results as quickly as possible also involves the clinician knowing the principles behind the laboratory investigations. In the clinical laboratory practice, these investigations consist of three phases: 1. preanalytical phase (extra and intra-laboratory); 2. analytical phase; 3. the post-analytical phase.

If the latter two are more in the attention of clinical laboratory staff, the preanalytic phase is almost entirely patient, nurse and clinician [7].

5. PRE-ANALYTICAL PHASE (EXTRA AND LABORATORY)

With the increasing automation of laboratory work and the widespread application of quality management policies, the source of most errors has become the pre-analytical phase. Specialty studies have shown that the proportion of errors in the pre-analytical phase reaches up to 80% [10].

The pre-analytical phase is the result of a step-by-step phase that can be done outside the lab or in-house, such as: requiring analyzes, sampling, laboratory samples, evidence recording, evidence storage, sample centrifugation [13].

5.1. Request analysis

The main causes of errors are:

- a non-legible, filled-in claim form without all patient identification data,

- Inaccuracies or omissions when transcribed from the application form into the computer system of the laboratory (eg the name of the physician requesting the tests or the test priority status are the most common mistakes at this stage, representing about 2% of the total of the required tests).

The main causes of these mistakes are the high volume of required tests, verbal requests or the lack of policies or quality assurance procedures.

Requesting the tests directly by the clinician with the help of the computer reduces the errors

associated with the wrong transcription of applications, reduces costs and improves their use [2,16].

5.2. Sampling

To reduce the influence of intra and inter-individual variation on laboratory results, it is necessary to standardize the harvesting conditions:
a. a standard 12 hour post (minimum 4 hours);
b. a period of 12 hours of reduced physical effort;
c. 30 minutes of physical rest before harvesting;
d. the same position of the patient at harvest;
e. the same harvest time, 7-9 am;
f. the same duration of application of the garment (max. 1 min);
g. avoiding repeated closing and opening of the fist;
h. During infusions or transfusions harvesting will be done from the other arm, in no case near the site of administration;
i. if it is necessary to repeat the phlebotomy, the harvesting will be done from the other arm;
j. if harvesting is done through the catheter, the cannula should be washed with a volume of isotonic saline equal to the catheter volume.

The medication form must be specified on the application form: by what, how long, how long. Between the start of the stool for the collection of blood samples on the anticoagulants and the time of homogenisation of the blood with the anticoagulants should not be longer than 2 minutes.
Blood collection for: blood gases, pH, free (ionic) calcium must be anaerobic [2,22].

• Harvesting capillary blood

a. the place of picking is chosen;
b. purify the skin with an aqueous solution of 70% isopropanol;
c. Wipe the puncture area with a sterile buffer;
d. Puncture with appropriate lancets at the site of the puncture and the required amount of blood (preferably semi-automatic lancets);
e. the first drop is wiped with the sterile buffer (it is contaminated with tissue fluids);
f. harvested in tubes without eating or milling;
g. the tubes are tightly closed, the additives are homogenized by overturning;
h. Light tubes approx. 10 times; the harvest quality is checked;
i. place the puncture site with a sterile swab to stop the bleeding;
j. in children it is not advisable to apply bandage because the adhesive can cause irritation, the bandage can detach and be swallowed by the child;
k. the lances are placed in a special container [2,23].

• The amount of blood needed in the laboratory

In laboratories equipped with automatic analyzers, for adults it is necessary:
- clinical serum chemistry, 4-5 ml blood, plasma, 3-4 ml blood; for gas dosing in the blood: capillary - 50µl; arterial blood or venous blood -1 ml heparin blood;
- immuno-enzymatic tests: 1 ml blood / 3-4 tests;
- hematology: 2-3 ml of blood;
- haemostasis: 2-3 ml blood;
- VSH: 2-3 ml blood.

Sampling should be done in special tubes for each type of test, on the specific anticoagulant, respecting the required sample volume.

The recommended anticoagulant for clinical chemistry dosages is lithium heparinate (12-30 IU / ml). But not for lithium and calcium dosing and for immunological methods [2,23].

• Harvesting other samples

The results of the laboratory tests may be influenced by: the conditions in which samples are taken (ex. Body position), the materials (eg expired vacuum) and the procedures used for sampling[3].

These errors can be easily detected, for example: hemolysis, insufficient volume or inadequate sampling container[22].

Other causes may be: unsuccessful phlebotomy procedure, coagulation of the sample, lack of label on the sample tube and loss of sample. Some studies show that 0.35% of the samples sent for clinical cloning tests are rejected due to hemolysis and about 0.45% of the samples sent for haematological tests are rejected due to coagulation and clotting in the samples. The quality of coagulation tests largely depends on a good sampling technique [12].

• Urine collection

- Random urine: for qualitative chemical determinations.
- First morning urine - Make a standard for urine urine urine summary; can also be used for qualitative chemical determinations.
- Second morning urine (7-10 am): for quantitative chemical determinations relative to creatinine.
- Urine in 24 hours: for quantitative chemical determinations [12].

5.3. Transport of samples in the laboratory

- After sampling the samples are brought to the laboratory as soon as possible.

- It is recommended that urine, other than 24 hours, is analyzed within one hour of harvesting [12].

5.4. Sample registration

All primary samples received must be recorded in an entry register (workbook, computer, etc.) along with the date and time of receipt of the samples and identifying the recipient.
Acceptance or rejection of primary evidence is based on clear and documented criteria. If compromised primary samples are accepted, the final report must indicate the nature of the problem and, if possible, interpreting precautions [2].

5.5. Criteria for rejecting biological samples

a.unidentified sample;
b. unproductive biological product of analysis request;
c. Inadvertence between request and specimen;
d. insufficient amount of biological product;
e. a coagulated sample harvested in an anticoagulant device;
f. Inappropriate container;
g. expired harvesting device;
h. request for unprivileged, incorrectly completed analysis [16].

5.6. Preservation of evidence

When possible, primary blood samples are checked to see if they are hemolysed; if found to be hemolyzed, a new primary sample is required if this is necessary and possible[9].

In order to make it possible to repeat the examination after reporting the result or for additional examinations, the primary samples must be kept for a period of time during which the stability of the sample properties is ensured [13].

5.7. Identification of samples

Primary samples lacking a correct identification must neither be accepted nor processed by the laboratory. When there is uncertainty in identifying primary evidence, but the primary sample can not be replaced or critical, the laboratory will not release the results until the physician who made the analysis request or the person responsible for harvesting and collecting the primary sample assumes responsibility for identifying and accepting the sample and / or providing the correct information. In these cases, the application form must have the signature of the person responsible for the identification of the sample [11].

5.8. Sample centrifugation

- For serum, the total blood after clot emergence is centrifuged at 1200-1500g for 10-15 minutes.
- For plasma, the blood harvested on heparin is centrifuged at 2000-3000g for 10-15 minutes.
- The blood harvested on the separating gel is centrifuged at 1200-1500g for 10-15 minutes; do not refresh!
- Horizontal, non-angular centrifuges are recommended [12].

5.9. Other factors that influence the quality of the results

For good interpretation of laboratory analyzes, account should also be taken of the biological variations that may influence the results of the analyzes. Classification of biological variation factors is difficult, therefore it was proposed to classify them in intra- and inter-individual variations, in genetic and acquired variations, in variations due to the environment, in variations due to exogenous and endogenous factors [17].

Among the most important factors that can influence the results of the analyzes, we distinguish: race, age, sex of particular physiological states (pregnancy, menopause, menstruation), nutrition, physical effort, stress, altitude, absence of gravity, orthostatism, circadian rhythms, body weight, tobacco, drugs [8,21].

CONCLUSIONS

Internal control must be performed in accordance with applicable legislation and / or standards.

Each specialist needs to know and apply the Westgard rules and each laboratory must have an Internal Control Procedure.

Laboratory specialists assume full responsibility for evaluation the accuracy of the analysis system and the absence of errors in each series of measurements.

The internal control and the results obtained allow the laboratory staff to continuously pursue the precision and in the alternative the accuracy of the measurements made.

Existence and observance of clear procedures, known by all the involved medical staff, lead to the development of final results that reflect the state of the investigated sample as accurately as possible.

Quality control rules must be the same for all medical analysis laboratories to ensure the medical utility of the results obtained.

Internal quality control in the pre-analytical phase prevents knowledge of all sources of error of the obtained results and their elimination.

ABSTRACT

The quality of data obtained by laboratory specialists and provided to the clinician should inspire confidence in both. The intensification of the supervision of the work in the medical analysis laboratory led to the definition of the complex concept of quality control and to the specification of the systems through which the action translates into fact. A successful medical act depends to a large extent on the accuracy of the results provided by the medical analysis laboratories. In the clinical laboratory practice, these investigations consist of three phases: 1. preanalytical phase (extra and intra-laboratory); 2. analytical phase; 3. the post-analytical phase. Specialty studies have shown that the proportion of errors in the pre-analytical phase reaches up to 80% [2].

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AUTHORS' ADDRESS

TIȚĂ DANIELA, ZAHARIA IRINA - County Emergency Hospital Bacau St. Spiru Haret no.2-4, Bacau, Romania, e-mail:
danielatita2007@yahoo.com;
irina_fartade@yahoo.com