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IMPORTANCE OF IMPLEMENTING AN OUTSOURCED INTERNAL CONTROL SYSTEM IN THE QUALITY OF BIOCHEMICAL RESULTS

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Abstract

Outsourced internal control (OIC) is a statistical process used to control and evaluate the analytical process that produces patient results. It is a quality control performed by several laboratories on the same batch of control samples compared to each other by periodic averaging. It allows an inter-laboratory comparison and an estimation of the accuracy and precision. The use of external internal controls is recommended for the good functioning of a laboratory. In our laboratory, the OIC covers and evaluates the analytical performance of serum and urine chemistry, immunoassay and cardiac markers. The OIC is performed regularly, three times a week in our biochemistry laboratory of Mohammed VI University Hospital of Oujda, and sent to an external organization for statistical processing. In an anonymous way, the external organization compares our data with those of other laboratories. Any discrepancy concerning fidelity or accuracy is a sign of a dysfunction specific to the laboratory, the cause of which must be identified and corrected, and its traceability and archiving ensured. The central laboratory of the Mohammed VI University Hospital of Oujda is committed to a quality policy that includes a method verification, and an accreditation process. Our work will constitute a solid basis for the implementation of an accreditation procedure for the tests used in our laboratory.

Keywords: OIC, control, quality

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1. Introduction

Medical biology is a regulated profession which must guarantee the quality and reliability of examinations for clinicians and patients [1], for this, the medical biology laboratory must participate in quality programs, as well as, the implementation of controls, which are of essential interest for the improvement of the quality of laboratory services [2]. They constitute a formal recognition of the competence of the laboratory and therefore an undeniable asset for its accreditation, based on harmonized standards: the ISO 15189 standard [3, 4].

As a result, the laboratory may use externalized internal quality controls (EIC), the results being statistically processed by the supplier, allowing inter-laboratory comparison and an estimation of accuracy and fidelity [5].

Our objective is to show the interest of the outsourced internal control **(**OIC) in the identification and detection of analytical errors, and the validation of analysis series, thanks to control preparations, whose concentrations are known.

2. Materials and methods

In our biochemical analysis laboratory, within the Mohammed VI University Hospital in Oujda, the outsourced internal control (OIC) covers and evaluates the analytical performance of serum and urinary chemistry, immuno-analysis and cardiac markers.

The OIC is performed regularly, three times a week in our biochemistry laboratory.

The results obtained are sent to an external body for statistical processing. This 100% online system manages daily results, international inter-laboratory comparison and document monitoring.

Internal quality control (IQC) results are analyzed in real time as soon as they are received. Anonymously, the software compares our data with those of other laboratories that use the same machines and IQC.

3. Results

The Lablink xL quality assurance program is 100% online software. It allows you to exploit your results on a daily basis but also to put them in perspective with those of your peers (average, bias, coefficient of variation (CV), Standard Deviation Index (SDI), ..).

Finally, this tool offers smooth and intuitive online navigation. Configuration, data transfer and updates are automatic and secure. No physical intervention is required.

Concerning the stability and quality of the samples; they are all liquid and ready to use. They come in several concentration levels, all made from human matrix, and are suitable for most automata. Presented in multiparametric vials, they are economical and reduce handling and dead volumes. They are packaged in refrigeration packs to maintain their temperature. The stability of the vials is also guaranteed up to 30 days after opening at 2-8 °C, and 3 to 5 years before opening with storage between [-15 and -25 °C].

The results are analyzed in real time as soon as they are received.

Their main asset is undoubtedly to concentrate in a single bottle many parameters (liver, kidney, lipid assessment, martial balance, cholesterol and uric acid levels ...). The analytical performance and reproducibility are pretty good. It may have happened that there were small "batch effects" on the reactants and that we noticed a slight discrepancy in our control values, but these few anomalies and measurement uncertainties remained manageable.
It also allowed for a broad use of data and input into practical decisions and reporting.

4. Discussion

Quality control is the part of management focusing on quality requirements. In the medical biology laboratory, it is a question of examining the control equipment of known nature, together with the samples, to check the accuracy and accuracy of the analytical process as a whole, and which constitutes a requirement for accreditation [6].
Quality control consists of two components: internal quality control, which makes it possible to verify mainly fidelity and accuracy, and in the alternative, accuracy; and external quality control or external quality assessment, which is used to verify the accuracy of analyses and facilitates comparison with other methods.
Outsourced internal control is an internal quality control, carried out by several laboratories on the same batch of control samples; the results of the different laboratories can be compared with each other by establishing the averages, it allows an estimate of the accuracy and fidelity, (figure 1) [5, 7].

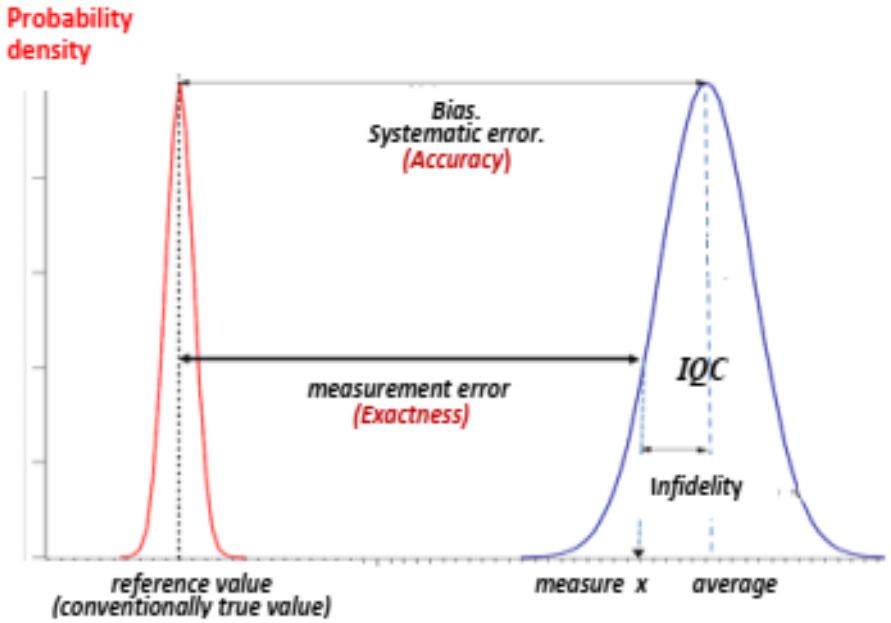

Figure 1: Representation of measurement error, bias and infidelity [8].
Probability density curve of a series of measured values:
about 95% of the values are located in the range m ± 2s.

Accuracy:

- Narrowness of the agreement between the average **m** of a high number of repeated measured values and a reference value **v** [8].
- Quantified by the bias expressed in % (systematic error) which represents the difference between the mathematical expectation of the results and the reference value.
- The reference value **v** can be obtained by outsourcing the results, or by using a certified control material.

$$\textbf{Bias}\ (\%) = \frac{(\mathbf{m} - \mathbf{v}).\mathbf{100}}{\mathbf{v}}$$

Fidelity:

Estimated by the Coefficient of Variation Ratio (CVR) ; which can be evaluated by calculating the ratio of the laboratory CV to the CV of the comparison group.

$$\mathbf{CVR} = \frac{\mathbf{CV\ lab}}{\mathbf{CV\ group}}$$

If the accuracy error is greater than the recommendations, the cause of the anomaly should be investigated, if necessary with the help of the inspection body, and the necessary corrective action taken [6]. There are two main categories of errors: random errors and analytical errors. They differ in their origins and their consequences on the interpretation of the data and on the corrective actions to be taken.

Random errors:

This is usually a deviation from the internal quality control (IQC) result for no apparent reason. It is often due to one-off handling errors, sample or result reversal, or a change in reagent batch or IQC sample. This type of error does not reflect a defect in the scanning system, and therefore is not expected to repeat itself. Test results should be rejected for any IQC result outside the alarm threshold.

Systematic errors

These errors are constant and repeat until the cause has been eliminated. They are not acceptable because they indicate a defect in the analysis system and must be corrected. These errors can be induced by poor calibration, degradation of reagents, variation in the incubation temperature of the device, systematic error in the analysis procedure or a change in method.

Westgard Control Rules [9, 10].

Westgard's rules (Figure 2) are a means of technically validating a series by examining the statistical distribution of values obtained on control samples. They constitute a decision criterion for judging whether an analytical series is under control or out of control.

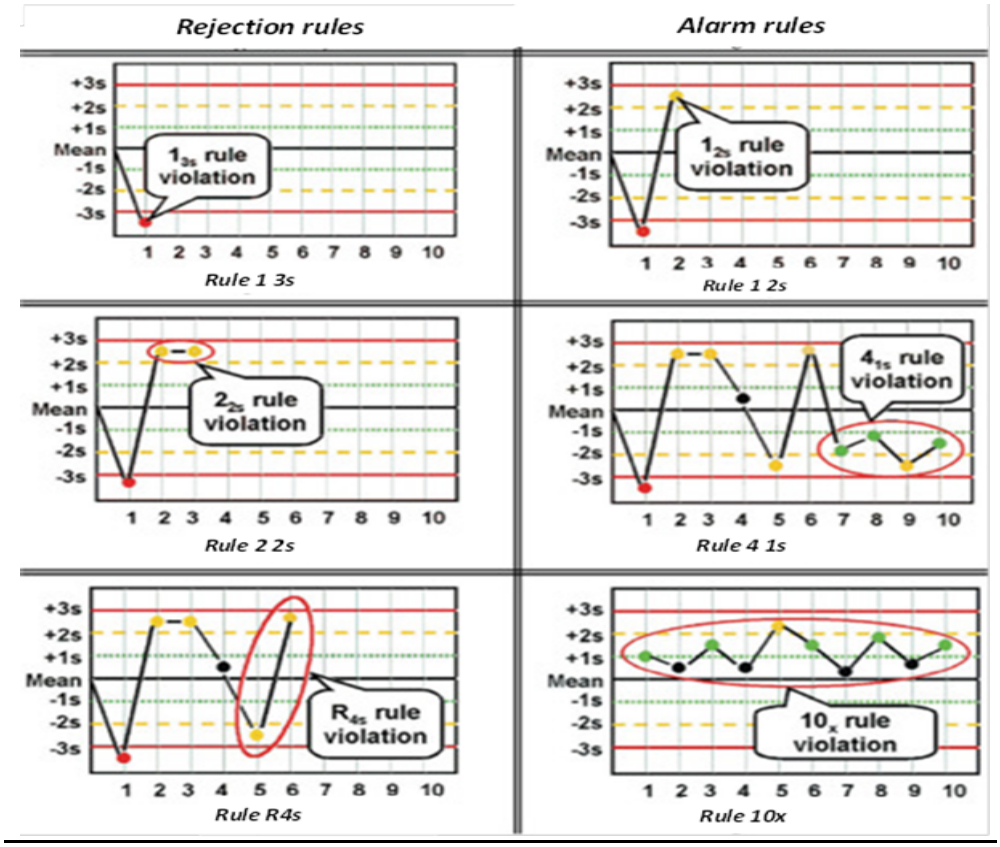

Figure 2: Westgard Control Rules [11]

Rule 1 2s: 1 measure between ± 2s and ± 3s. This rule is considered a warning and not a criterion for rejecting a series. It is violated when a IQC result is between the warning threshold and the alarm threshold [11,12].

Action: The results of patient samples can be used. Continue the series by monitoring the progress of the control which must be repeated if necessary.

Rule 2 2s: 2 consecutive measurements between ± 2s and ± 3s. This rule only detects systematic errors. It is violated when two consecutive IQC results are between the warning threshold and the alarm threshold, on the same side of the target.

Action : IQC results are non-compliant and patient sample results are to be rejected. It is necessary to search for and correct the source of error and repeat the entire series of measurements.

Rule 1 3s: 1 measure > ± 3s.

This rule detects random errors. It is violated when a single IQC result is outside the limits of the alarm threshold.

Action: The result of IQC is non-compliant, the results of patient samples are to be rejected. It is necessary to search for and correct the source of error and repeat the entire series of measurements.

Rule R4s: 2 consecutive measurements spaced > 4s.

This rule detects too large random errors. It is violated when two consecutive IQC results are spaced more than 4s apart. The two successive IQC results are therefore on either side of the target value.

Action: The results of IQC are non-compliant, the results of patient samples are to be rejected. It is necessary to search for and correct the source of error and repeat the entire series of measurements

Rule 4 1s: 4 consecutive measures > ± 1s.

This rule detects systematic errors, even of small importance. It is violated when four consecutive IQC results are above +1s or below -1s.

Action: It is necessary to search for and correct the source of errors (often calibration problem).

Rule 10 x̃: 10 consecutive measurements on the same side of the target. This rule detects systematic errors, even of very small importance, and requires precise validation of the target value. It is violated when ten consecutive IQC results are located on the same side of the target.

Action: The source of error (often calibration problem) must be investigated and corrected.

If the controls are rejected when using Westgard's multi-rule system, an investigation must be conducted to find the cause of the problem [12].

First, verify that the guidelines and procedures have been followed, and then consider other sources of error:

- Degradation of the reagent;
- Degradation of control equipment;
- Operator error procedure manual not updated;
- Failure to follow the manufacturer's instructions;
- Equipment failure;
- Calibration error.

When choosing, the laboratory favours the outsourced internal control (OIC) integrating reagent suppliers from different origins in order to ensure the relevance of this estimate [5]. The supplier of an inter-laboratory comparison program (ILC) must be critical and meet laboratory specifications, established on the basis of the requirements of the NF EN ISO 15189 standard and regulatory texts (SH REF 02 document). The laboratory shall check with the supplier [7]:

- The type of program,
- Levels of control,
- The choice of the number of participants and the size of the comparison groups,
- Types of samples,
- The method of statistical processing of data,
- The frequencies of inter- comparisons,
- The method of calculating acceptable limits and discharge limits, ...

The laboratory will choose the comparison group (peers or any methods) according to the parameter or method (e.g. immuno-analysis), the size of the comparison groups and the interpretation of the result. When there are national or international recommendations (High Authority of Health, World Health Organisation), the result is interpreted independently of the

assay methods (e.g. HbA1c, cholesterol, glucose, ...); the laboratory will compare its results to the overall results (general average for example for accuracy) [5].

The purpose of this inter-laboratory comparison is to harmonize the different laboratories, the idea being that if the same patient sample is analyzed simultaneously in several laboratories, the differences between the results obtained should in no way lead to contradictory medical interpretations or decisions [13].

This type of program is interesting because it makes it possible to determine the accuracy of our methods, to control their intermediate fidelity, while the external quality assessment (EQEs) only makes it possible to assess the accuracy of the results. It also has the advantage of being inexpensive for the laboratory: no additional dosage is necessary since the daily data of the internal quality control are exploited. In addition, the estimation of measurement uncertainty from outsourced IQC data is much more relevant than with external quality assessments (EQEs), since accuracy and fidelity are determined with the same control equipment, at the same concentration level [14, 15].

The OIC is not considered as an EQEs within the meaning of HS REF 02 since the laboratory knows the theoretical values of the IQC known sample. The OIC is considered complementary to the EQEs [4, 5] and cannot replace them.

5. Conclusion

Continuous quality improvement in the medical biology laboratory can only be considered if tools for evaluating its quality management system are in place and regularly used. The outsourced internal control is an innovative method in biochemistry for a quality assurance program. It is an additional level of verification, exceeding those specific to the laboratory playing a key role in the identification of the anomalies observed and the implementation of appropriate and effective curative and corrective measures. Any discrepancy concerning fidelity or accuracy reflects a malfunction specific to the laboratory whose cause of error must be identified, corrected and ensured traceability and archiving.

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