How to really understand and improve the system of internal quality control and external quality assessment in the accreditation process of the medical laboratory?

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ABSTRACT

Internal quality control (IQC) regarding process to monitor analytical stability has a long tradition in laboratory medicine. The satisfactory results with different quality specifications of the IQC ensure the acceptability of the examination results. Although the statistical IQC is satisfactory some problems exist, resulting in unreliable patients' results due several reasons (non-commutable control materials, lot to lot difference of reagents, false interpreting test results regarding autovalidation or autoverification, different analytical and clinical specifications or goals etc.). Therefore, the results and findings of IQC have to be connected with external quality assessment (EQA) in order to provide the system of measurement of uncertainty (MU) with correct interpretation of laboratory result and detection relevant and significant shifts and drifts in medical laboratory.

INTRODUCTION

IQC is an important tool within the laboratory testing to assure the quality of results produced in medical laboratories. It is one of the cornerstones of the accreditation process of medical laboratories, primarily used in routine practice to monitor system performance under stable conditions and to allow analytical failures that affect performance to be detected [1,2]. The reliable tests depend on both IQC and EQA being performed. Commutability of reference and control materials in IQC and EQA is key to ensuring the quality of measurements in laboratory medicine. The International Vocabulary of Metrology (VIM) defines the commutability of a reference material (RM) as the property demonstrated by the closeness of agreement between the relation among the measurement results for a stated quantity in the material (employed as a calibrator), obtained according to two given measurement procedures, and the relation obtained among the measurement results for patient samples. In a simple way, the commutability is the ability of an RM or control material to show inter-assay properties comparable to those of human samples [3,4]. How to assess commutability has been covered in the Clinical and Laboratory Standards Institute (CLSI) guidelines and through the recommendations of the International Federation of Clinical Chemistry (IFCC) Working Group on Commutability (WG-C) [5-9].

IQC PROGRAMS

There is considerable variation in laboratory practices with regard to the review of IQC, and the literature is not exhaustive on the subject of own control limits and its interpretation. This is the main difference regarding IQC from other scientific disciplines in comparison with laboratory medicine where some questions have recently been raised about understanding of IQC [10]. Many efforts was made to stress the routine interpretation and challenges related to own results for IQC management including for the selected tumor markers and hormones which proved that the quality specifications based on biological variation best fit the analytical and clinical purpose of laboratory tests. We must be aware that the manufacturer's method specifications and control ranges should be used carefully comparing with our results on field and our own analytical goals. While the average results in IQC tended to get closer to the manufacturer value by increasing the number of measurements, the analytical coefficient of variation (CV_A) tended to increase. Most parameters showed significant differences between initial and cumulative CV_A, which were lower than the manufacturer's specifications [11].

EQA PROGRAMS

The EQA programs are optimal tools for evaluating the reliability of commercial measuring systems and the clinical suitability of measurements provided by clinical laboratories. However, EQAs must be appropriately structured. Efforts by EQA providers should be made to meet criteria allowing the evaluation of the performance of participating laboratories in terms of traceability of their measurements. This requires assigning values (and uncertainty) to control materials with reference measurement procedures, defining and applying clinically allowable performance specifications for judging the quality of results and using materials of proved commutability. Only materials with proved commutability are relevant for directly transferring of laboratory testing to the measurement of patient samples [12].

UNCERTAINTY

By quantifying the measurement uncertainty (MU) or the previously used total allowable error

(TAE), both the clinical laboratory and the physician can have an objective estimate of the results' quality. ISO 15189 declare that "laboratory shall consider MU when interpreting measured quantity values. Upon request, the laboratory shall make its estimates of MU available to laboratory users" [1]. In our opinion MU should be available with interpretation on laboratory report without any request from users.

Different approaches and formulas have been proposed how to determine the MU in medical laboratory with imprecision and bias of the methods considered as components of the MU (Nordtest, Eurolab, Cofrac etc.). The bias could be obtained from certified reference calibrators (CRC), proficiency tests (PT), and inter-laboratory internal quality control scheme (IQCS) programs. The bias uncertainty, the combined and the expanded uncertainty could be estimated using the different mentioned models or approaches. In our study the bias was highest using PT, followed by CRC and IQC data, which were similar. The Cofrac approach showed the highest uncertainties and the Eurolab approach requires additional measurements to obtain uncertainty data. In summary, the Nordtest approach using IQC data was therefore found to be the most practical formula [13-15].

COMMUTABILITY

IQC and EQA materials are frequently not assessed for commutability because of technical and economic concerns. The use of single-donor samples, which is preferable to overcome commutability problems, may however limit the achievement of adequate volumes of samples needed for preparing sufficient amount of control materials [16,17]. On the other hand, pooled samples have the potential limitation that interactions of components such as proteins may cause modification of the matrix.The European Federation of Laboratory Medicine

(EFLM) has recently stressed the need that the especially EQA material matrix and its commutability should be specified by providers, because the interpretation of differences between results in an EQA program is strongly dependent on the nature of the employed material [18]. Based on the results of some projects of analytical performance in general clinical chemistry using commutable samples targeted with reference measurement procedures it's obvious that the use of commutable samples especially in EQA is mandatory to change conventional EQA using non-commutable materials and consensus 'peer' group assessment with the EQA programme based on clinically oriented analytical performance specifications that meet metrological criteria and traceability [19-21]. The commutability also matters for IQC materials that should be used by clinical laboratories to derive the random component of the uncertainty of measured results. The material evaluating the random uncertainty must be different from the control material used for checking the alignment of the measuring systems and should be commutable, closely resembling to patient sample, to provide accurate information about the imprecision performance of the assay [22-23].

DISCUSSION

We provided a brief overview of the practical importance of IQC in connection with EQA programs using commutable materials in laboratory medicine. They have to be employed either as common calibrators for implementing metrological traceability or as control materials in EQA and IQC programs within the total testing pathway. The use of non-commutable RMs may introduce a significant bias in the calibrated procedures producing incorrect results for patient samples. The non-commutable materials in EQA programs prevents the transferability of participating laboratory performance

to the measurement of patient samples. Only commutable control materials may provide the proper information for the imprecision, bias and estimation of measurement uncertainty. Providers of reference and control materials should assess the commutability of those materials before their use.

The importance of commutability has essential role in standardization and accreditation process, consistent clinical decisions and improving patient outcomes with additional use and rarely implemented of patient's test results for laboratory QC monitoring. The only exception is haematology testing where Bull's patient based real-time QC algorithm which was accepted and implemented in routine QC practices [24]. In the last two decades we have faced progress with the improved laboratory total automation, information technology and standardization/harmonization of laboratory methods, so there are no more obstacles and limitations for such algorithms and use of "big data" in laboratory QC monitoring processes.

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