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MINI REVIEW

The Importance of Expertly Evaluated Tests Underlined by COVID-19 Pandemic: A Mini Review

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ABSTRACT

Background: The joint interest of clinicians and the laboratory test industry during the recent pandemic of the Coronavirus Disease 2019 (COVID-19) resulted in an explosion of accessible assays for COVID-19 serological testing.

Content: The need of properly evaluated laboratory tests is more apparent today than ever before. Clinical application of the assay, analytical specifications, and performance convenience are the key criteria that must be followed while selecting an analytical method. An analytical evaluation is always performed before deciding to apply a procedure in the laboratory routine practice.

Summary: Only after the evaluation, data collection, and analysis of the results in accordance with the established eligibility criteria can be concluded that the new assay is suitable for laboratory use.

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INTRODUCTION

The joint interest of clinicians and the laboratory test industry during the recent pandemic of the Coronavirus Disease 2019 (COVID-19), which was caused by the novel severe acute respiratory syndrome coronavirus 2, resulted in an explosion of accessible assays for COVID-19 serological testing [1-3]. Today, more than ever, the importance of properly evaluated tests cannot be overstated.

In the medical laboratory, selecting an analytical assay is almost a daily task. The abundance of novel analytical methods, as well as the rapid introduction of new biomarkers, make selection more difficult. When it comes to selecting a routine assay, budget is often a crucial factor. The necessity of expertly evaluated diagnostics became obvious during the COVID-19 pandemic [4], as evidenced by our previous published findings [5,6].

AIM

This paper provides an overview and reminder of the assay selection criteria, basic concepts of analytical evaluation, and eligibility requirements that should be met before an assay is being used routinely.

Selection of the assay and procedure

Prior to making any decisions, it is critical to consider the biomarker's clinical usefulness, disclosed analytical specifications, and robustness. The procedure principle, recommended sample types, time of analysis, appropriate pre-analytical requirements, and test stability are all used to determine robustness and feasibility.

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If the instrumentation is required for the assay to perform, the equipment's capacity, device dimensions, ability to interface to the laboratory information system, and service availability should all be reviewed. In routine laboratory practice, all these criteria will be important. Environmental considerations such as the amount of waste produced and the options for disposal in line with local regulations, as well as sensitivity to constant temperature conditions, are also important [7].

The method's analytical evaluation

The decision to apply a method in the medical laboratory is always preceded by an analytical evaluation, the scope of which varies depending on the method's type and applicability. Reagents that have already been examined and are intended for in vitro diagnostics can usually be evaluated in a reduced method verification process. The method verification procedure verifies and confirms the analytical assessment claims made by the manufacturers. If a laboratory develops a new method or changes validated methods, it is required to conduct a more extensive analytical evaluation of the procedure [7,8]. The Clinical and Laboratory Standards Institute (CLSI) recommends protocols for evaluating analytical methods based on expert guidance.

Precision

Even though the majority of new automated analytical systems are precise and reliable, the method's precision must be assessed and monitored. It is defined by the analytical system's stability. Repeatability (or prior precision in a series of measurements) and reproducibility are two precision components (or previous precision between a series of measurements) [8,9].

Trueness

The analytical method's trueness is defined as the ability to agree on the average value of multiple measurements and the true value. True value, which represents the amount of pure material measured by the reference method, is accessible for many analytes, especially in serological testing, in very few circumstances. As samples that are closest to the definition of reference material accessible in the laboratory, the laboratory most usually uses a calibrator/standard or, alternatively, an external quality control sample [8,10]. The absence of standardization is the primary reason of discrepancies between methods.

Linearity

In laboratory practice, the term linearity is frequently employed. A more proper term would be a measuring range that incorporates several mathematical models of the calibration curve. Linearity testing is useful for calibration

curves with no more than three points; however, if the calibration curve is confirmed with six or more points or is not linear, the linearity test is no longer necessary. It is also crucial to distinguish between the limit of detection (a number that can be consistently separated from zero) and the limit of quantification from an analytical standpoint (a value that can be determined with acceptable precision and bias). Simple models are provided for calculating both [7].

Specificity

In serological testing, the analysis of analytical specificity is of particular interest. In immunochemistry, cross-reactivity is one of the three different forms of interference. Heterophilic antibodies, an analyte metabolite, or other compounds with a similar and/or the same epitope might cause cross-reactivity [7]. Clinical specificity is the likelihood that a test will be negative in the absence of the evaluated clinical variables when the true value is below the decision limit. The clinical relevance of an assay is determined by comparing the results to a gold standard method, which could be a reference method or other clinical data. In the absence of a gold standard, it is only possible to compare the two tests, not to estimate which is more accurate [8].

A comparison of methods

Any analytical evaluation should include a comparison of the results obtained by two methods. When preparing a technique comparison experiment, it is crucial to determine how many samples will be evaluated, how concentrations will be distributed, and who will be involved. Various CLSI standards recommend protocols for comparing procedures. It is important to highlight that when comparing a routine procedure to a reference method, only random error can be expected; however, when comparing two routine methods, predicted bias caused by calibration and likely sample non-specificity can also be expected. While nonspecificity can be seen in each situation or sample, calibration bias can be shown in any measurement [11].

Traceability

The term was introduced to ensure that there was an acceptable difference between the two measurements. A continuous chain of comparison measures leading to reference material is defined as traceability. Traceability is measured by measurement uncertainty. It is a result parameter that describes the range of values that can be assigned to the analyte, which can be considered of as data for the end-user (clinician). In today's laboratory medicine, there are still a lot of questions concerning how to calculate measurement uncertainty and how to apply it. Can the bias be disregarded, and if so, when? Is the measurement uncertainty affected by the concentration of the analyte? [12].

Eligibility requirements

The results of the evaluation procedure should be assessed using the established eligibility criteria. Manufacturer specifications (for in vitro diagnostic tests), biological variation data, and professional guidelines are the most utilized criteria [13]. Biological variation database of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) was recently updated and evaluated (using the BIVAC–Biological Variation Data Critical Appraisal Checklist rating system) and is now available on their website [14].

CONCLUSION

Finally, today's health-care system is under pressure to meet a variety of clinical and analytical issues. In terms of analytical problems, prior to implementing any new assay/method in routine work, an evaluation process, data collection, and analysis of the results based on the established eligibility criteria should be carried out.

IMPACT STATEMENT

The need of correctly evaluated laboratory tests is more apparent today than ever before. The joint interest of clinicians and the laboratory test industry during the recent pandemic of the Coronavirus Disease 2019 (COVID-19) resulted in an explosion of accessible assays for COVID-19 serological testing.

The aim of this paper is to emphasize the need of conducting an analytical evaluation of a method before using it in a medical laboratory, as well as to remind medical professionals on the fundamental concepts in laboratory test selection.

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