Measuring Analytical Quality

Total Analytical Error Versus Measurement Uncertainty

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KEYWORDS

• Total analytical error (TAE) • Allowable total error (ATE)
• Measurement uncertainty (MU) • Accuracy • Bias

KEY POINTS

- The accuracy of a laboratory test depends on both the trueness (bias) and imprecision (SD) of the examination procedure because only a single measurement is made to produce a reportable test result in a medical laboratory.
- Total analytical error (TAE) has been the common way of estimating a 95% limit of the error expected from the combined effects of random and systematic errors when a single measurement is reported as a test result.
- Trends in global practice (International Organization of Standards [ISO]15189) recommend the determination of measurement uncertainty (MU) to characterize the accuracy of medical laboratory tests and discourage the use of allowable total error (ATE).
- Bias is not included in an estimate of MU but rather should be eliminated, corrected, or ignored. If bias were truly eliminated, the TAE and MU models would reduce to a common form and provide consistent estimates of analytical quality.
- The concept of TAE and the definition of quality goals in the form of ATE are critical for a quantitative quality management system (QMS) that provides guidance on acceptability of methods, design of statistical quality control (SQC) procedures, development of risk-based quality control (QC) plans, and external assessment of comparability of results.

INTRODUCTION

Quality continues to be an issue in medical laboratories, both how good laboratory tests are today (precision, trueness or bias, accuracy, total analytical error, and MU) and how good they need to be (goals, allowable errors, and target specifications).

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Quality is generally defined as conformance to requirements; thus, there is a need to compare the measured performance to a requirement for intended use. In analytical and metrological laboratories, the separate characteristics of precision (random error) and bias (systematic error) are evaluated when multiple measurements are made on each sample. In medical laboratories where only a single measurement is made on each sample, common practice is to estimate the combined effect of precision and accuracy, or TAE, to characterize an upper limit (often 95%) of the size of error expected in a medical test result. More recently, the ISO has recommended that MU be determined for all measurement procedures.

As shown in **Box 1**, accuracy is defined by ISO as the "closeness of agreement between a test result and the accepted reference values; note: The term *accuracy*, when applied to a set of test results, involves a combination of random components (imprecision) and a common systematic error or bias component (ISO 5725-1)." The estimation of TAE in medical laboratories conforms to this definition of accuracy because

Box 1
Definitions of important performance characteristics

Accuracy – closeness of agreement between a test result and the accepted reference value (ISO 5725–1); note: the term *accuracy,* when applied to a set of test results, involves a combination of random components (imprecision) and a common systematic error or bias component (ISO 5725-1).

Precision (measurement) – closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions (JCGM200:2012); note 1: measurement precision is usually expressed numerically by measures of imprecision, such as SD, variance, or CV under the specified conditions of measurement (JCGM 200:2012).

Trueness (measurement) – closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value (JCGM 200:2012); note 1: trueness is expressed numerically using the observed bias.

Bias (of measurement) – difference between the expectation of the test result or measurement results and a true value (ISO 3534-2); note 1: bias is an estimate of the systematic measurement error (JCGM 200:2012).

Traceability – (metrological) property of a measurement results where the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the MU (JCGM 200:2012).

Uncertainty of measurement – parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand.

TAE – in the context of this guideline, TAE defines the interval that contains a specified proportion (usually 95% or 99%) of the distribution of analytical measurement differences between a measurement procedure operating in its stable in-control state and a comparative measurement procedure that is either a definitive reference method or one that is traceable to one. (Note: also called Total Error [TE])

ATE – an analytical quality requirement that sets a limit for both the imprecision (random error) and bias (systematic error) that are tolerable in a single measurement or single test result; note: also called total error allowable (TEa).

Total error – includes all random and systematic errors that can occur during the total testing process and also includes the combined effect of all precision and bias errors that can affect the accuracy of an analytical result; note: total error incorporates error sources from the preanalytical, analytical, and postanalytical phases of a measurement procedure.