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Expression of Measurement Uncertainty in Laboratory Medicine; Approved Guideline

This guideline describes a practical approach to assist clinical laboratories in developing and calculating useful estimates of measurement uncertainty, and illustrates their application in maintaining and improving the quality of measured values used in patient care.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Expression of Measurement Uncertainty in Laboratory Medicine; Approved Guideline

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Abstract

Clinical and Laboratory Standards Institute document EP29-A—*Expression of Measurement Uncertainty in Laboratory Medicine; Approved Guideline* describes the principles of estimating measurement uncertainty and provides guidance to clinical laboratories and *in vitro* diagnostic device manufacturers on the specific issues to be considered for implementation of the concept in laboratory medicine. This document illustrates the assessment of measurement uncertainty with both bottom-up and top-down approaches. The bottom-up approach suggests that all possible sources of uncertainty are identified and quantified in an uncertainty budget. A combined uncertainty is calculated using statistical propagation rules. The top-down approach directly estimates the measurement uncertainty results produced by a measuring system. Methods to estimate the imprecision and bias are presented theoretically and in worked examples.

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Foreword

When measurements are repeated, some variation of the results will be observed due to random variation of the measurement conditions. The differences will be noticeable if the sensitivity and resolution of the measuring system is sufficient. Therefore, for measurement results to be useful, such result variability (uncertainty) needs to be quantified so that those performing measurements and those receiving results have an objective estimate of the quality (reliability) of the results produced. Quantification of the variability of measurement results also allows a result to be meaningfully compared with the results of other similar measurements that may have been made at different times using the same measurement system. The concept of measurement uncertainty provides a theoretical and practical framework for objectively estimating the reliability of results produced by any given measurement system.

Knowledge of the sources of uncertainty and their relative magnitude may also provide opportunities for modifying a measurement system to improve the quality of results. Uncertainty estimates at various analyte concentrations also contribute to determining uncertainty profiles, which can be important in defining the measuring interval of measurement systems to ensure that the quality of results issued meets clinical requirements.

This document describes the principles of estimating measurement uncertainty and gives guidance on the specific issues to be considered for implementation of the concept in laboratory medicine. The concept of measurement uncertainty and its use in measuring quantities in laboratory medicine is provided for clinical laboratories and *in vitro* diagnostic device manufacturers.

Key Words

Bias, bottom-up, measurement uncertainty, precision, top-down, trueness

Expression of Measurement Uncertainty in Laboratory Medicine; Approved Guideline

1 Scope

This guideline explains the concept, estimation, and application of measurement uncertainty in the field of clinical laboratory medicine. The recommendations provided are consistent with the *Guide to the expression of uncertainty in measurement* (GUM)[1] and with the International Organization for Standardization (ISO) standards concerned with laboratory accreditation.[2,3]

This guideline briefly discusses, but does not fully address, the following nonmeasurement sources of uncertainty of a measurement result:

- Biological variation of the measurand
- Pre- and postmeasurement processes

The guideline discusses the definition of what is intended to be measured, lists sources of measurement uncertainty, describes the generation of statistical estimates of uncertainties and their combination, and discusses the use of uncertainty estimates. The guideline applies only to quantitative measurements. In measurement procedures that are reported in qualitative terms based on a quantitative measurement, the uncertainty at the threshold(s) for a qualitative interpretation should be considered when making the qualitative assessment.

This guideline is intended for clinical laboratories and *in vitro* diagnostic (IVD) device manufacturers.

2 Introduction

Regardless of method, repeated measurements produce different results due to inherent variations within a sufficiently sensitive measurement procedure. Some knowledge of the result variability expected from a given measurement system is required if results are to be meaningfully compared with previous results from the same patient or important clinical decision limits. In addition, evaluation and elimination of bias in a measuring system relative to the relevant reference material or reference procedure is essential if results from different laboratories using the same or different measuring systems are to be compared for the same patient.

Characterization of the variability of repeated measurement results and identification of the factors that contributed to that variability can provide useful insights into the reliability of results and potential means for improvement. Existing quality control (QC) and method verification data can be used to define the performance characteristics of routine measuring systems. This document provides guidance on how measurement uncertainty can be estimated and used in the field of laboratory medicine. The principles for expression of measurement uncertainty provided in this document illustrate how the components of measurement uncertainty can be combined to help estimate the performance characteristics that can be reliably achieved by the measuring system.

The objectives of this document are to:

- Familiarize the reader with the concept of measurement uncertainty.

- Describe the processes of implementing the concept of measurement uncertainty in laboratory medicine.