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To characterize analytical quality of a laboratory test, common practice is to estimate Total Analytical Error (TAE) which includes both imprecision and trueness (bias). The metrologic approach is to determine Measurement Uncertainty (MU), which assumes bias can be eliminated, corrected, or ignored. Resolving the differences in these concepts and approaches is currently a global issue.	
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Laboratory medicine decreases diagnostic uncertainty, but is influenced by factors causing uncertainties. Error and uncertainty methods are commonly seen as incompatible in laboratory medicine. New versions of the Guide to the Expression of Uncertainty in Measurement and International Vocabulary of Metrology will incorporate both uncertainty and error methods, which will assist collaboration between metrology and laboratories. Law of propagation of uncertainty and bayesian statistics are theoretically preferable to frequentist statistical methods in diagnostic medicine. However, frequentist statistics are better known and more widely practiced. Error and uncertainty methods should both be recognized as legitimate for calculating diagnostic uncertainty.	
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The scientific debate on goals, measurement uncertainty, and individualized quality control plans has diverged significantly from the reality of laboratory operation. Academic articles promoting certain approaches are being ignored; laboratories may be in compliance with new regulations, mandates, and calculations, but most of them still adhere to traditional quality management practices. Despite a considerable effort to enforce measurement uncertainty and eliminate or discredit allowable total error, laboratories continue to use these older, more practical approaches for quality management.	

Biologic Variation Approach to Daily Laboratory

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Carmen Ricós, Virtudes Álvarez, Joana Minchinela, Pilar Fernández-Calle, Carmen Perich, Beatriz Boned, Elisabet González, Margarita Simón, Jorge Díaz-Garzón, José Vicente García-Lario, Fernando Cava, Pilar Fernández-Fernández, Zoraida Corte, and Carmen Biosca

Biological variation gives valuable information about how the living organism regulates its constituents within and between subjects; this information on the behavior of body components allows us to derive consequences concerning reference populations and intervals. With a more pragmatic approach biological variation has three uses: setting the appropriate analytical performance specification for each analyte to limit the amount of error that laboratory could introduce in its measurements, to help distinguish health from disease, and to implement internal quality control with the automatic verification of results.

Understanding the Use of Sigma Metrics in Hemoglobin A1c Analysis

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Erna Lenters-Westra and Emma English

This study uses three unique data sets to show the state of the art of hemoglobin A1c (HbA1c) analyzers in a range of settings and compares their performance against the international guidance set by the International Federation of Clinical Chemistry and Laboratory Medicine task force for HbA1c standardization. The data are used to show the effect of tightening those criteria, and the study serves as a guide to the practical implementation of the sigma-metrics approach in a range of clinical settings.

State-of-the-art Approach to Goal Setting

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Angel Salas, Carmen Ricós, Enrique Prada, Francisco Ramón, Jorge Morancho, Josep M. Jou, and Raquel Blazquez

Four external quality assurance programs combined their data to calculate the minimum acceptable quality specifications for laboratory testing. Other sources of quality specifications may be too stringent for the current market, or too lenient given the clinical demands on the test result, but these state-of-the-art goals may be practical and useful. Two main approaches were used: (1) defining the 95% percentile and comparing with other quality specifications, and (2) using an iterative approach to increase the quality specification until 90% of laboratories could achieve 75% of their results within the specification. 72 out of 82 analytes followed procedure 2.

Six Sigma Quality Management System and Design of Risk-based Statistical Quality Control

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James O. Westgard and Sten A. Westgard

Six sigma concepts provide a quality management system (QMS) with many useful tools for managing quality in medical laboratories. This Six Sigma QMS is driven by the quality required for the intended use of a test. The most useful form for this quality requirement is the allowable total error. Calculation of a sigma-metric provides the best predictor of risk for an analytical examination process, as well as a design parameter for selecting the statistical quality control (SQC) procedure necessary to detect

medically important errors. Simple point estimates of sigma at medical decision concentrations are sufficient for laboratory applications.

Sigma Metrics Across the Total Testing Process 97

Navapun Charuruks

Laboratory quality control has been developed for several decades to ensure patients' safety, from a statistical quality control focus on the analytical phase to total laboratory processes. The sigma concept provides a convenient way to quantify the number of errors in extra-analytical and analytical phases through the defect per million and sigma metric equation. Participation in a sigma verification program can be a convenient way to monitor analytical performance continuous quality improvement. Improvement of sigma-scale performance has been shown from our data. New tools and techniques for integration are needed.

Metrological Traceability of Assays and Comparability of Patient Test Results 119

David Armbruster

At the start of the twenty-first century, a dramatic change occurred in the clinical laboratory community. Concepts from Metrology, the science of measurement, began to be formally applied to clinical laboratory field methods, resulting in a new appreciation of metrological calibrator traceability. It is a change because clinical laboratories test complex patient samples, for example, whole blood, serum, plasma, urine, and so forth, using commercial assay systems, not reference methods, and patient samples are tested once, not in replicate. Analytical harmonization is necessary for optimal patient care but is challenging to achieve.

A Total Quality-Control Plan with Right-Sized Statistical Quality-Control 137

James O. Westgard

A new Clinical Laboratory Improvement Amendments option for risk-based quality-control (QC) plans became effective in January, 2016. Called an Individualized QC Plan, this option requires the laboratory to perform a risk assessment, develop a QC plan, and implement a QC program to monitor ongoing performance of the QC plan. Difficulties in performing a risk assessment may limit validity of an Individualized QC Plan. A better alternative is to develop a Total QC Plan including a right-sized statistical QC procedure to detect medically important errors. Westgard Sigma Rules provides a simple way to select the right control rules and the right number of control measurements.

Accreditation of Individualized Quality Control Plans by the College of American Pathologists 151

Gerald A. Hoeltge

The Laboratory Accreditation Program of the College of American Pathologists (CAP) began in 2015 to allow accredited laboratories to devise their own strategies for quality control of laboratory testing. Participants now have the option to implement individualized quality control plans (IQCPs). Only nonwaived testing that features an internal control (built-in, electronic, or procedural) is eligible for IQCP accreditation. The accreditation

checklists that detail the requirements have been peer-reviewed by content experts on CAP's scientific resource committees and by a panel of accreditation participants. Training and communication have been key to the successful introduction of the new IQCP requirements.

Sunway Medical Laboratory Quality Control Plans Based on Six Sigma, Risk Management and Uncertainty

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Jamuna Jairaman, Zarinah Sakiman, and Lee Suan Li

Sunway Medical Centre (SunMed) implemented Six Sigma, measurement uncertainty, and risk management after the CLSI EP23 Individualized Quality Control Plan approach. Despite the differences in all three approaches, each implementation was beneficial to the laboratory, and none was in conflict with another approach. A synthesis of these approaches, built on a solid foundation of quality control planning, can help build a strong quality management system for the entire laboratory.

Applying Sigma Metrics to Reduce Outliers

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Joseph Litten

Sigma metrics can be used to predict assay quality, allowing easy comparison of instrument quality and predicting which tests will require minimal quality control (QC) rules to monitor the performance of the method. A Six Sigma QC program can result in fewer controls and fewer QC failures for methods with a sigma metric of 5 or better. The higher the number of methods with a sigma metric of 5 or better, the lower the costs for reagents, supplies, and control material required to monitor the performance of the methods.

Quality Indicators for the Total Testing Process

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Mario Plebani, Laura Sciacovelli, and Ada Aita

ISO 15189:2012 requires the use of quality indicators (QIs) to monitor and evaluate all steps of the total testing process, but several difficulties dissuade laboratories from effective and continuous use of QIs in routine practice. An International Federation of Clinical Chemistry and Laboratory Medicine working group addressed this problem and implemented a project to develop a model of QIs to be used in clinical laboratories worldwide to monitor and evaluate all steps of the total testing process, and decrease error rates and improve patient services in laboratory testing. All laboratories are invited, at no cost, to enroll in the project and contribute to harmonized management at the international level.

Using Sigma Quality Control to Verify and Monitor Performance in a Multi-Instrument, Multisite Integrated Health Care Network

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Harold H. Harrison and Jay B. Jones

The authors developed a system-wide integrated network of instrumentation and Sigma-based quality control for fundamental chemistry, coagulation, and hematology analysis. The authors have based selection of Westgard rules for run management on a straightforward, Sigma-driven selection process. The network includes multiple hospitals and large

regional clinic laboratories. Most hospitals have multiple instruments; overall there are at least four distinct instrument models active from each manufacturer. The authors have measured and monitored Sigma values in this network for more than five years, to verify and validate performance and to provide ongoing justification for rules selection and rules changes when necessary.