CLSI Update

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AMDM IVD Focus Meeting| October 19, 2023

OVERVIEW OF TODAY'S WEBINAR

CLSI Overview and History

Consensus Standards Development Process

Participation

CLSI Method Evaluation Resources

Q&A

About CLSI

Clinical and Laboratory Standards Institute (CLSI)

CLSI MISSION

Develop clinical and laboratory practices and promote their use worldwide

OFFERING

1. Global consensus-based standards development
2. Lab training and implementation guidance
3. Public education and advocacy

55 YEARS OF LABORATORY LEADERSHIP

Cultivating best practices and fostering innovation through standards and training


from the Laboratory Program

ESTABLISHMENT OF A PROVISIONAL NATIONAL COMMITTEE ON CLINICAL LABORATORY STANDARDS

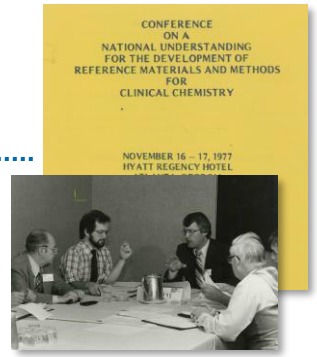
1967
Founding of the National Committee on Clinical Laboratory Standards (NCCLS)


PATHOLOGIST

THE ROLE OF PROFESSIONAL ORGANIZATIONS IN THE ESTABLISHMENT OF STANDARDS AND THE EVOLUTION OF THE NCCLS

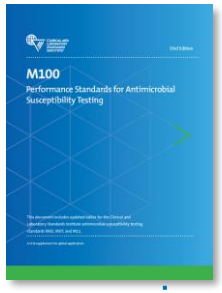
1969
First standard published: *Preparation of Manuals for Installation, Operation, and Repair of Laboratory Instruments*

1985
Designated WHO Collaborating Center for Clinical Laboratory Standards.


CONFERENCE ON A NATIONAL UNDERSTANDING FOR THE DEVELOPMENT OF REFERENCE MATERIALS AND METHODS FOR CLINICAL CHEMISTRY

NOVEMBER 16 – 17, 1977
HYATT REGENCY HOTEL

1977
Accredited by American National Standards Institute (ANSI) as voluntary consensus standards organization


M100
Performance Standards for Antimicrobial Susceptibility Testing

1986
First edition of M100—*Performance Standards for Antimicrobial Susceptibility Testing*

1997
Interational Organization for Standardization (ISO) Technical Committee 212 (ISO/TC 212) established with NCCLS as the Secretariat

2005
NCCLS becomes Clinical and Laboratory Standards Institute (CLSI) and launches Global Health Partnerships.


EXECUTIVE DIRECTORS QUALITY SYSTEMS MANAGEMENT TRAINING - MOROGORO
FACILITATED BY CLSI 11SEPT 2011

Today
More than 250 standards, 25000 members and standards in practice in more than xxx countries

FACILITATING INNOVATION, IMPROVING CARE

Bettering diagnostic tools & methods to improve health and prevent the spread of disease

GLOBAL CONSENSUS-BASED STANDARDS

Bringing constituencies together through balanced, inclusive, and participatory processes

Professions

- Hospital & Clinical Laboratories
- Research & Reference Laboratories
- Colleges & Universities
- Pharmacies

Government

- Public Health Agencies
- Public Health Ministries
- Regulatory Bodies
- Accreditors

Industry

- *In Vitro* Device Manufacturers
- Pharmaceutical Manufacturing
- Commercial & Clinical Trial Laboratories
- Testing Companies

Consensus Document Development Process and Participation in CLSI

THE CLSI CONSENSUS PROCESS

11 SPECIALTY AREAS, 250+ STANDARDS & PRODUCTS

Automation and Informatics

Clinical Chemistry and Toxicology

General Laboratory

Preexamination

Hematology

Immunology and Ligand Assay

Method Evaluation

Microbiology

Molecular Methods

Newborn Screening

Point-of-Care Testing

Quality Management Systems

Veterinary Medicine

EXPERTISE RECOGNIZED AROUND THE GLOBE

Collaborating with and supporting regulatory and public health agencies worldwide

Recognized CLSI Standards

FDA U.S. FOOD & DRUG ADMINISTRATION

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SEARCH

Home | Food | Drugs | Medical Devices | Radiation-Emitting Products | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Tobacco Products

Recognized Consensus Standards: Medical Devices

FDA Home › Medical Devices › Databases

1 to 59 of 59 Results

Standards Designation Number: *EP*

Results per Page 100

New Search | Export To Excel | StandardsSearchAssistance

Date of Entry	Specialty Task Group Area	Recognition Number	Extent of Recognition	Standards Developing Organization	Standard Designation Number and Date	Title of Standard
05/29/2023	InVitro Diagnostics	7-315	Complete	CLSI	EP12 3rd Edition	Evaluation of Qualitative, Binary Output Examination Performance
12/19/2022	InVitro Diagnostics	7-313	Complete	CLSI	EP27 2nd Edition	Constructing and Interpreting an Error Grid for Quantitative Measurement Procedures
12/20/2021	InVitro Diagnostics	7-311	Complete	CLSI	EP39, 1st Edition	A Hierarchical Approach to Selecting Surrogate Samples for the Evaluation of In Vitro Medical Laboratory Tests
06/07/2021	InVitro Diagnostics	7-306	Complete	CLSI	EP06 2nd Edition	Evaluation of the Linearity of Quantitative Measurement Procedures
12/21/2020	Dental/ ENT	4-270	Complete	ANSI ADA	Technical Report No. 146-2018	CAD/CAM Abutments in Dentistry
07/06/2020	InVitro Diagnostics	7-296	Partial	CLSI	EP09c 3rd Edition	Measurement Procedure Comparison and Bias Estimation Using Patient Samples

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/search.cfm

CLSI ALSO SERVES AS ISO SECRETARIAT

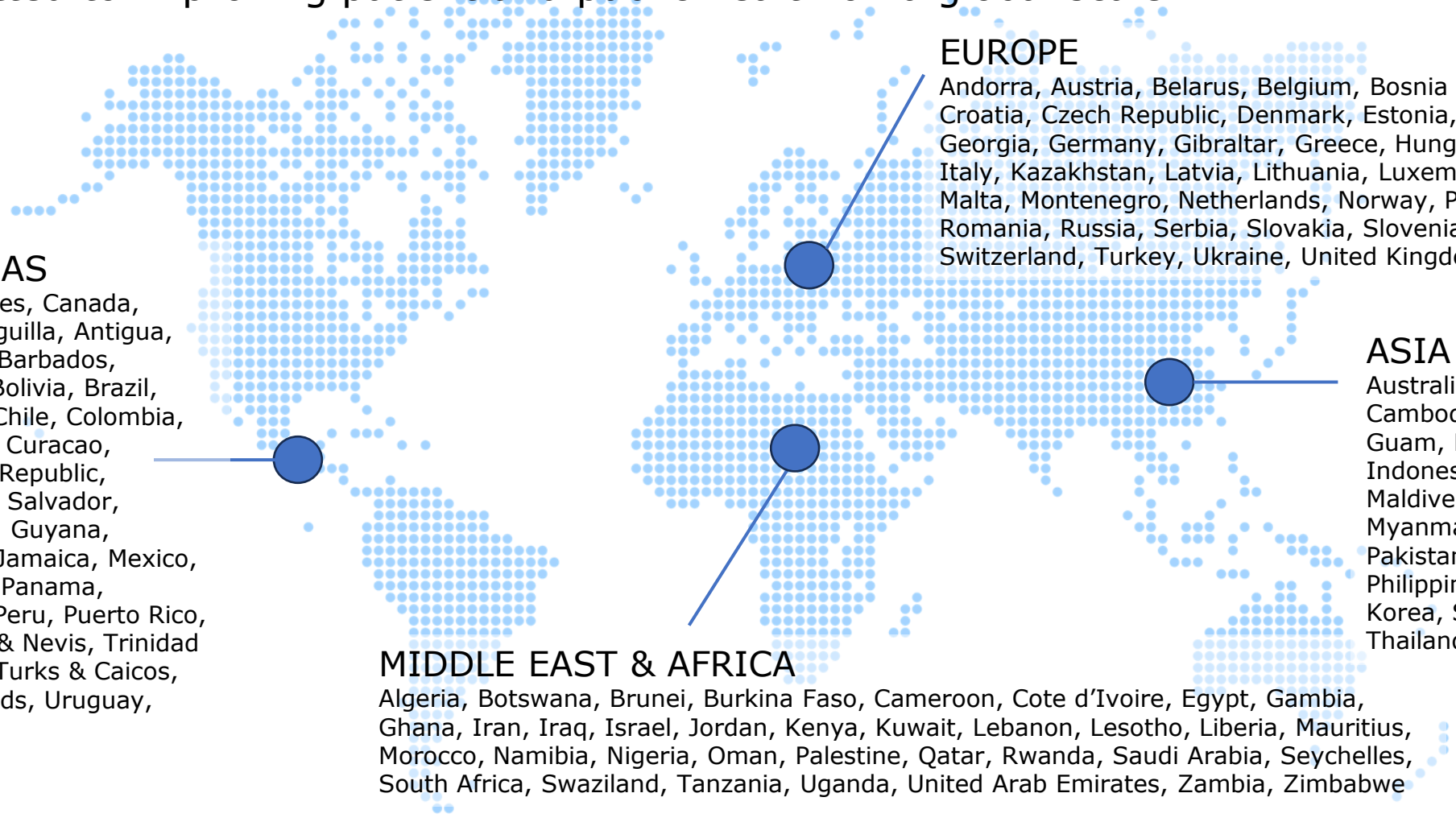
Providing guidance for *how* to implement regulatory requirements

Secretariat for ISO Technical Committee 212 (Clinical Laboratory Testing and *In Vitro* Diagnostic Test Systems)

Working Group 1: Quality and competence in the medical laboratory
Working Group 2: Reference systems
Working Group 3: *In vitro* diagnostic products
Working Group 4: Microbiology and molecular diagnostics
Working Group 5: Laboratory biorisk management

SUPPORTING USERS IN 140 COUNTRIES

Committed to improving patient and public health on a global scale



EUROPE

Andorra, Austria, Belarus, Belgium, Bosnia & Herzegovina, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Gibraltar, Greece, Hungary, Iceland, Ireland, Italy, Kazakhstan, Latvia, Lithuania, Luxembourg, Macedonia, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine, United Kingdom, Uzbekistan

AMERICAS

United States, Canada, Mexico, Anguilla, Antigua, Argentina, Barbados, Bermuda, Bolivia, Brazil, Caymans, Chile, Colombia, Costa Rica, Curacao, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Saint Kitts & Nevis, Trinidad & Tobago, Turks & Caicos, Virgin Islands, Uruguay, Venezuela

ASIA PACIFIC

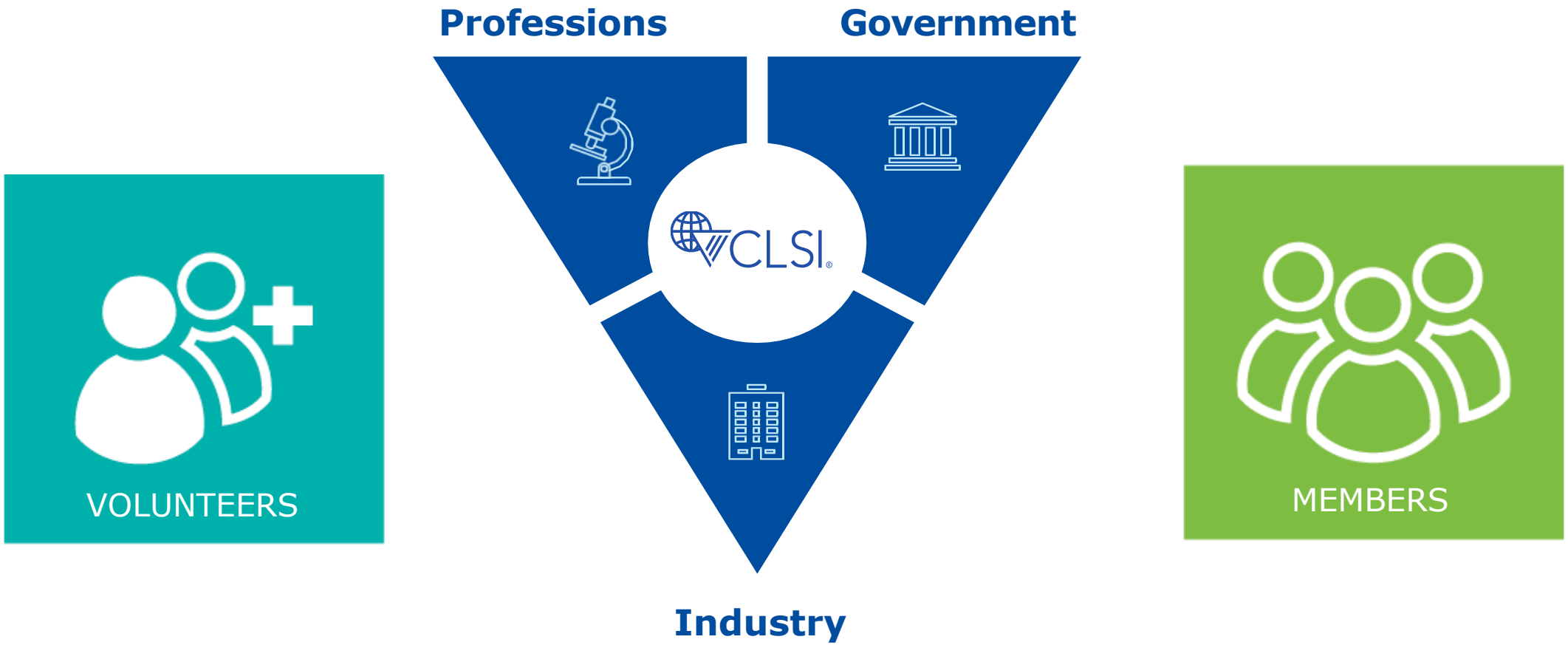
Australia, Bangladesh, Bhutan, Cambodia, China, East Timor, Guam, Hong Kong, India, Indonesia, Japan, Malaysia, Maldives, Micronesia, Mongolia, Myanmar, Nepal, New Zealand, Pakistan, Papua New Guinea, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, Vietnam

MIDDLE EAST & AFRICA

Algeria, Botswana, Brunei, Burkina Faso, Cameroon, Cote d'Ivoire, Egypt, Gambia, Ghana, Iran, Iraq, Israel, Jordan, Kenya, Kuwait, Lebanon, Lesotho, Liberia, Mauritius, Morocco, Namibia, Nigeria, Oman, Palestine, Qatar, Rwanda, Saudi Arabia, Seychelles, South Africa, Swaziland, Tanzania, Uganda, United Arab Emirates, Zambia, Zimbabwe

2200 ACTIVE VOLUNTEERS & 25K MEMBERS

Active and engaged constituency participating and benefitting as well as networking



CLSI MEMBERSHIP – Why join?

- ✓ Stay current and informed
- ✓ Network with other leaders
- ✓ Grow and learn with CLSI training
- ✓ Participate in standards development
- ✓ Contribute your expertise
- ✓ Influence the evolution of laboratory medicine!

CLSI VOLUNTEER OPPORTUNITIES

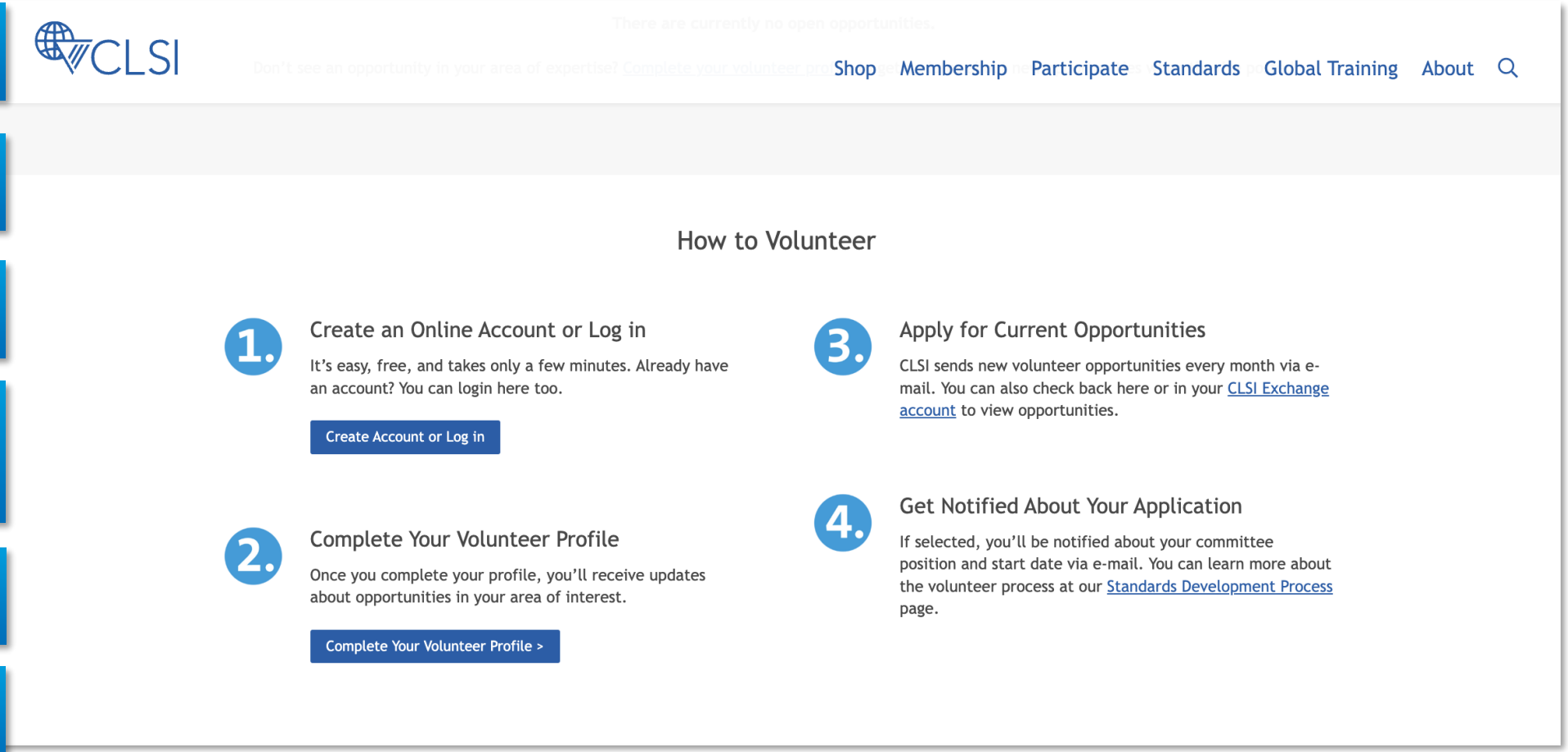
Why Participate?

- ✓ Assist with new documents & document revisions
- ✓ Participate on expert panel or governance committee
- ✓ Collaborate with industry leaders to shape standards and ensure guidance is designed for optimal implementation
- ✓ Advance career and receive recognition as a thought leader

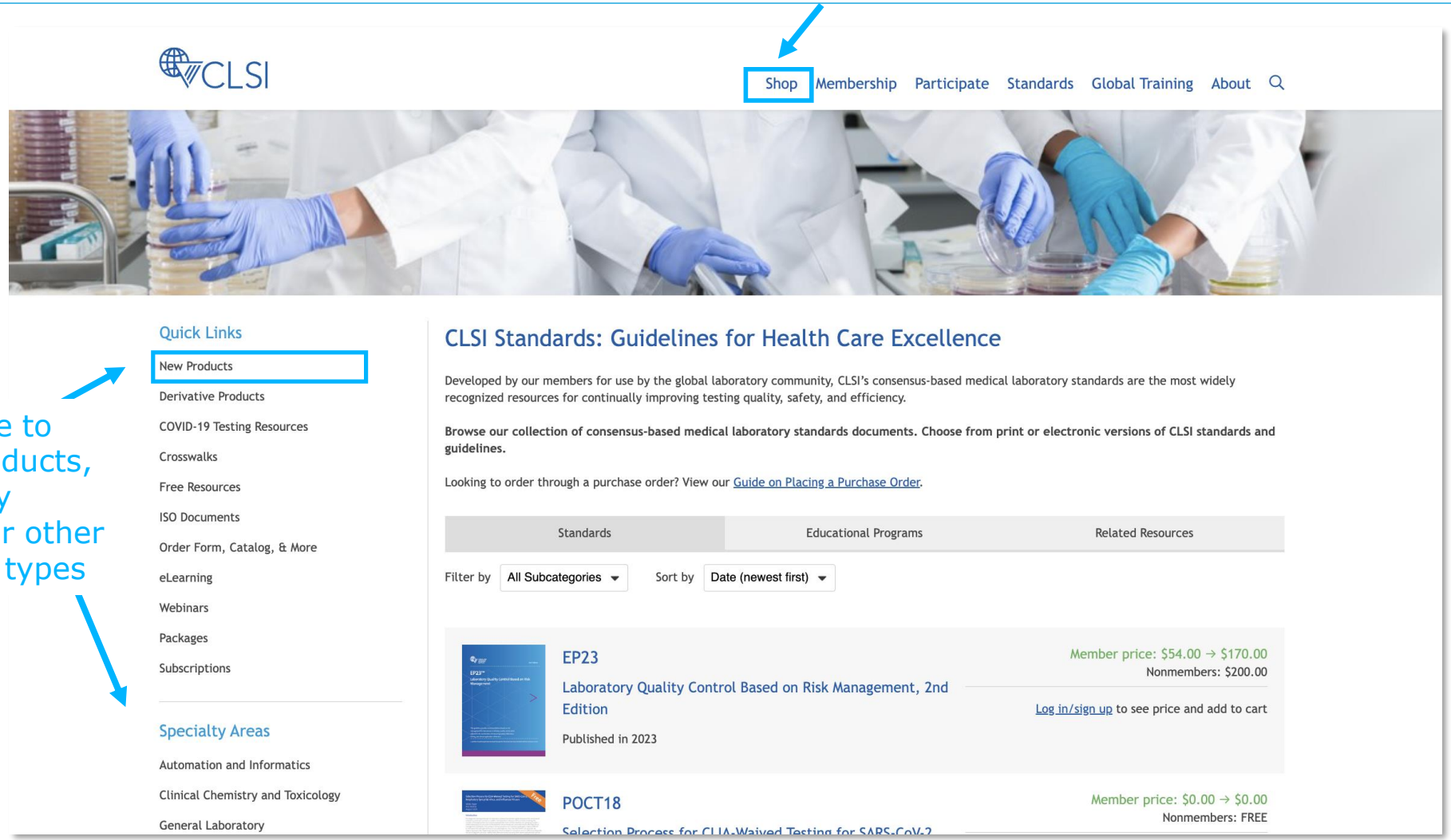
HOW TO GET INVOLVED?

More than 2200 subject matter experts contribute their expertise in many capacities

- Board of Directors
- Consensus Council
- Expert Panels
- Document Development Committees
- Subcommittees
- Working Groups



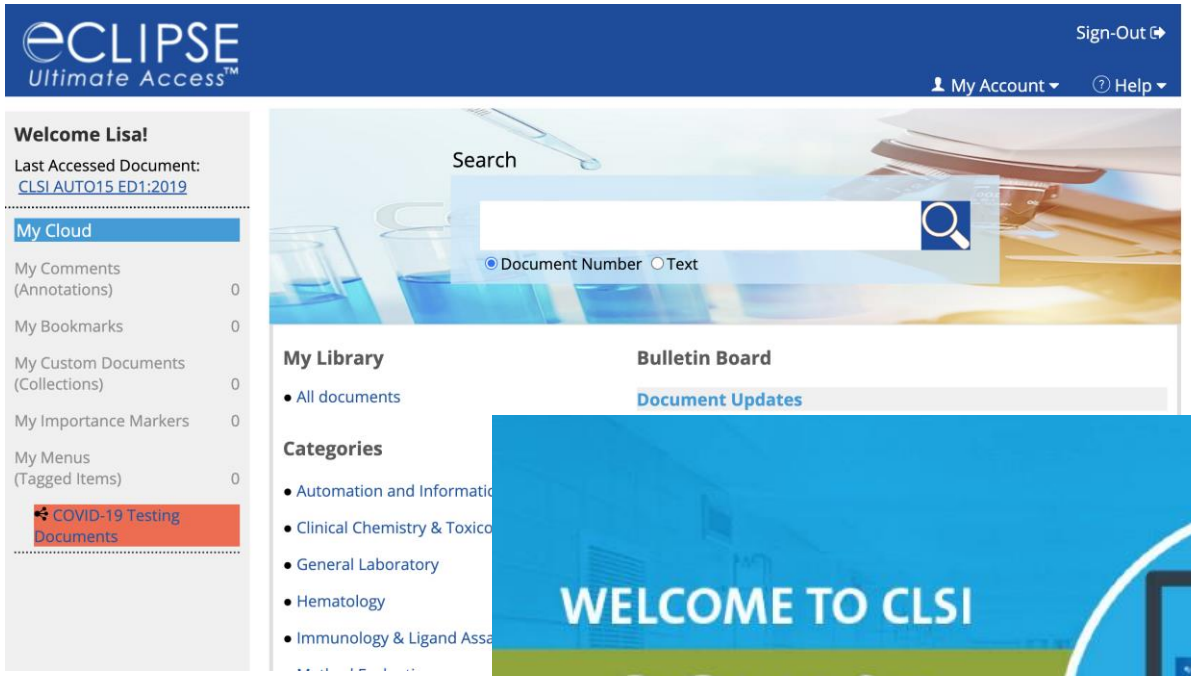
CLSI STANDARDS – How to Access?



Navigate to new products, specialty areas, or other product types

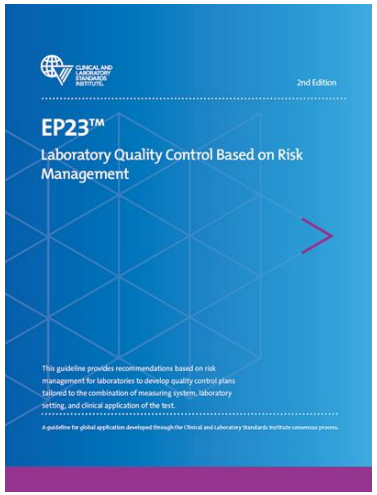
CLSI ECLIPSE – Digital Library Access

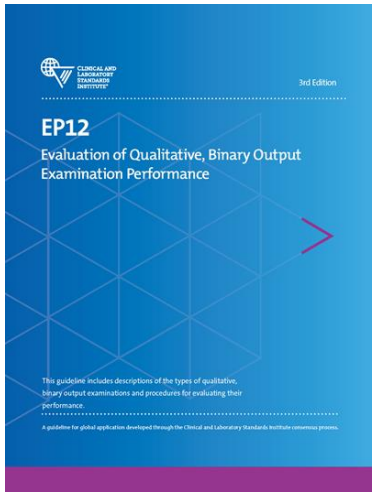
- Unlimited 24/7 access
- Full library of current standards
- Easily search and find related content
- Bookmarks and annotate
- Create custom collections and share with colleagues
- Advanced printing options

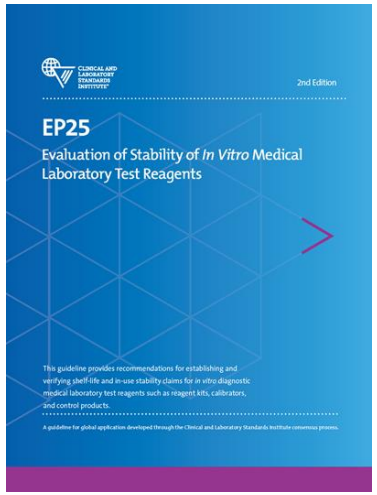


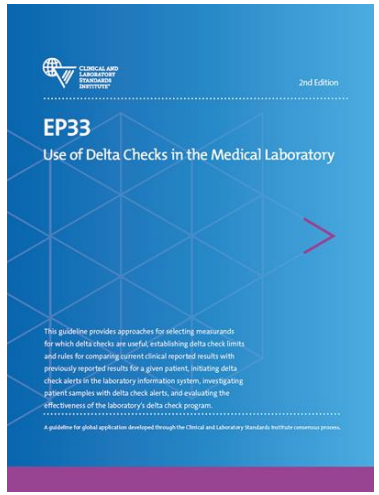
CLSI Method Evaluation Resources

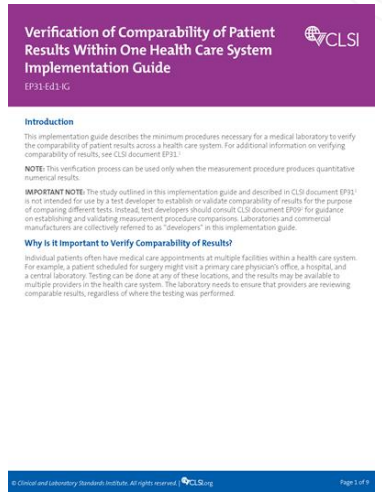
THE BEST OF CLSI'S EP TOOLS

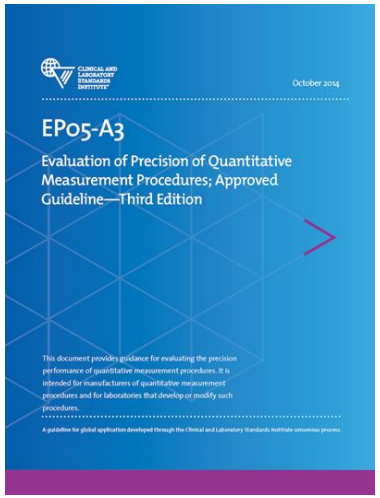


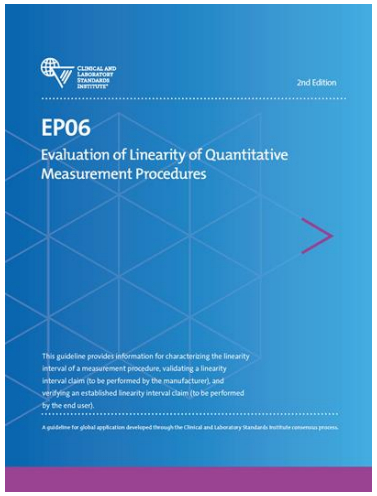


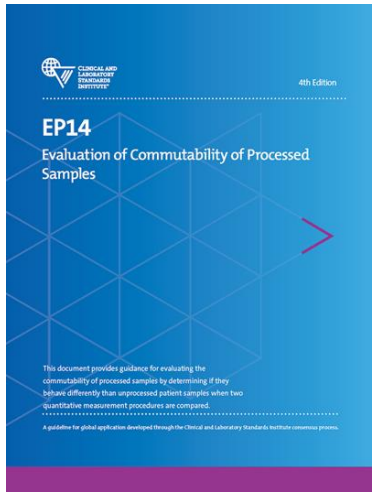


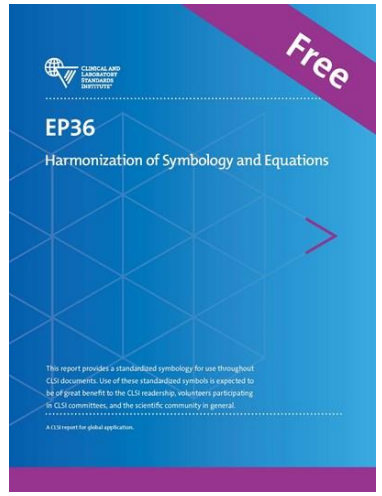


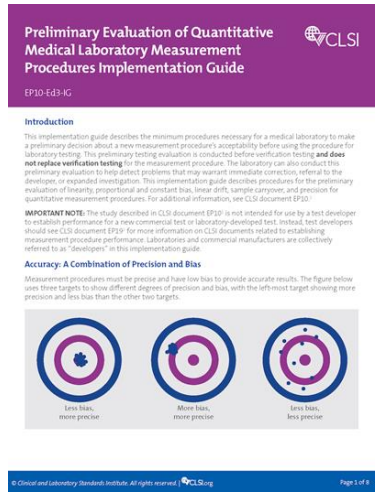








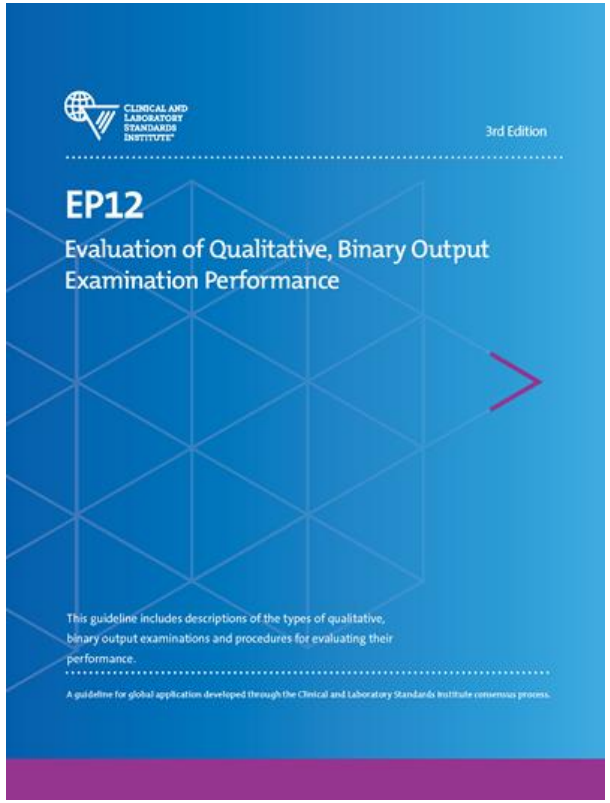




Key changes & updates

KEY DOCUMENT CHANGES & UPDATES

CLSI EP12 – Ed3



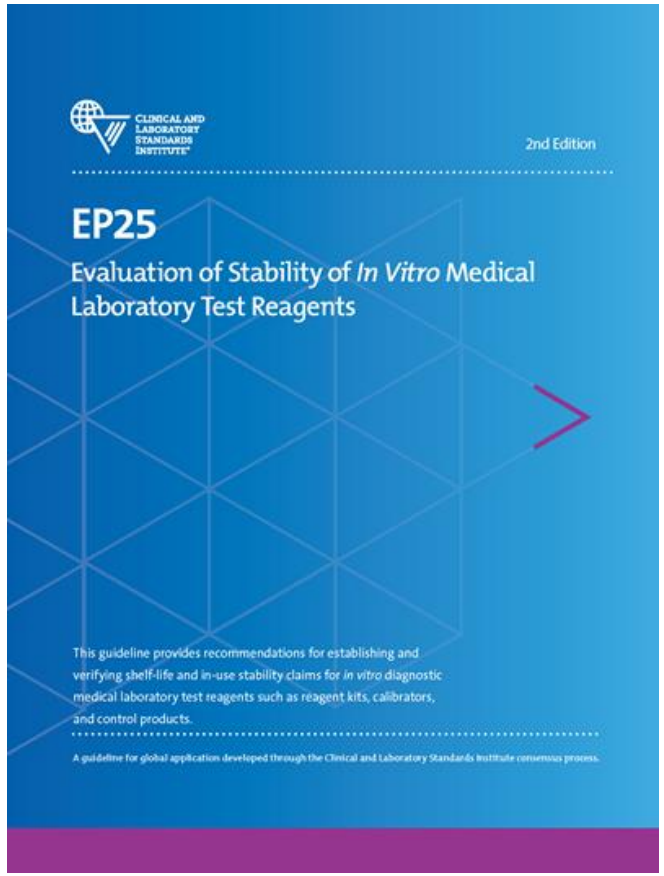
This guideline describes the categories of qualitative, binary output examinations and covers their performance evaluations for imprecision, clinical performance (sensitivity and specificity), and stability and interferences.

Several changes were made including:

- Expanding the types of procedures covered to reflect ongoing advances in laboratory medicine
- Adding protocols to be used by developers during examination procedure design as well as for validation and verification
- Adding topics such as stability and interferences to the existing coverage of the assessment of precision and clinical performance (or examination agreement)

KEY DOCUMENT CHANGES & UPDATES

CLSI EP25 – Ed2



This guideline provides recommendations for establishing and verifying shelf-life and in-use stability claims for *in vitro* diagnostic medical laboratory test reagents such as reagent kits, calibrators, and control products.

Several changes were made including:

- Revising the approach to statistical power analysis for planning studies to assume there will be some drift in reagent performance
- Eliminating the custom of using the t-test of regression slope results ($P > 0.05$) as a rationale for passing a stability assessment
- Eliminating the requirement for a confidence interval within the acceptance criteria as a basis for stating claims
- Expanding the practices for transport simulation stability testing
- Expanding the use and practices for accelerated stability testing

KEY DOCUMENT CHANGES & UPDATES

CLSI EP23 – Ed2

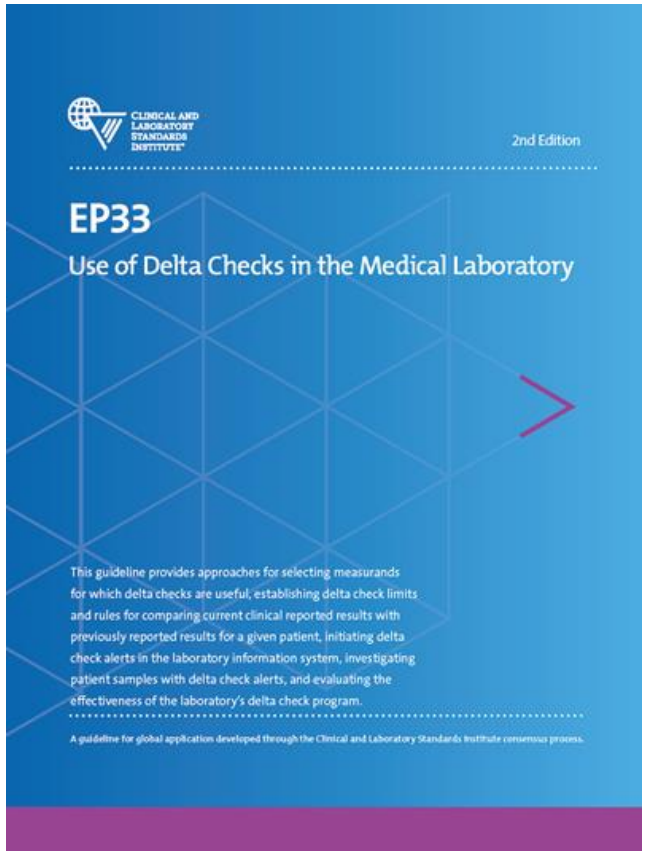
This guideline provides recommendations based on risk management for laboratories to develop quality control plans tailored to the combination of measuring system, laboratory setting, and clinical application of the test. CLSI EP23 aligns with the application of risk management requirements of ISO 22367 (medical laboratories) and ISO 14971 (medical devices).

Several changes were made including:

- Incorporating detectability in the risk assessment
- Adding real-world examples of QC plans for a
  - Noninstrumented single-use device
  - Instrumented single-use device, and
  - Exempt microbiological media

KEY DOCUMENT CHANGES & UPDATES

CLSI EP33 – Ed2



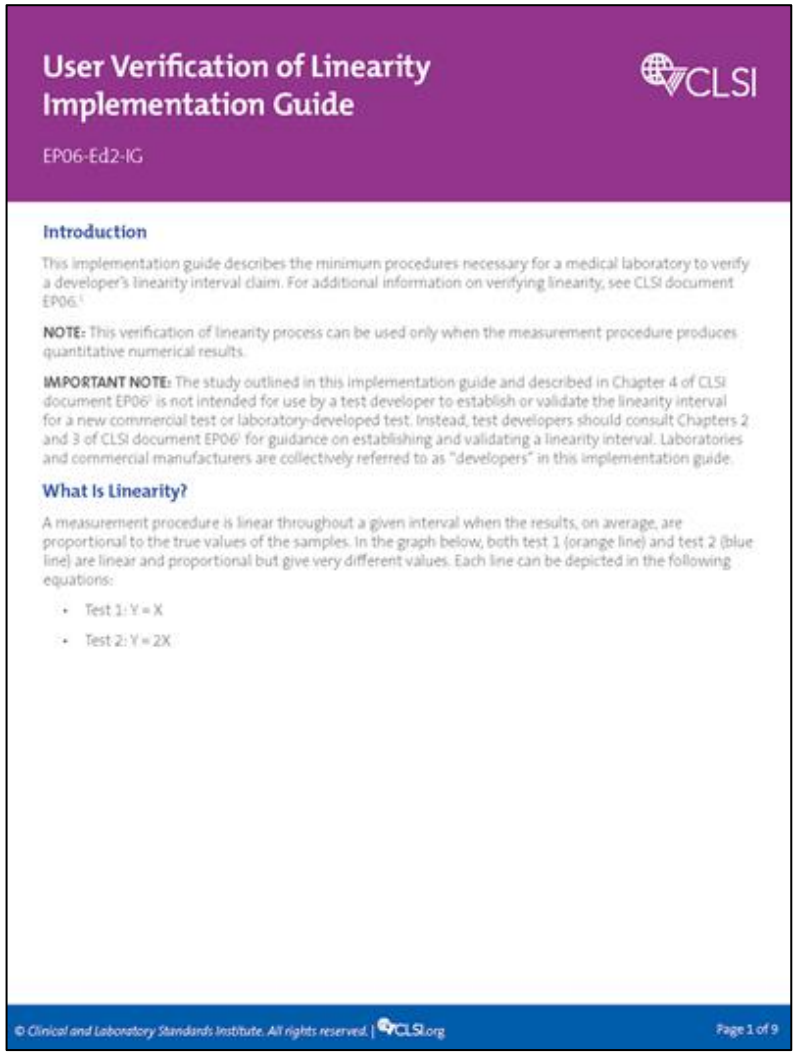
This guideline provides approaches for selecting measurands for which delta checks are useful, establishing delta check limits and rules for comparing current clinical reported results with previously reported results for a given patient, initiating delta check alerts in the laboratory information system, investigating patient samples with delta check alerts, and evaluating the effectiveness of the laboratory's delta check program.

Several changes were made including:

- Emphasizing validation of the methods and published results for estimates of biological variation, which are important in setting limits for EP33
- Aligning this guideline with recommendations of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM),3 which uses a strict methodology to assess the validity of published biological variation estimates

What's New?

Implementation Guides and Workbooks



User Verification of Linearity Implementation Guide

EP06-Ed2-IG

CLSI

Introduction

This implementation guide describes the minimum procedures necessary for a medical laboratory to verify a developer's linearity interval claim. For additional information on verifying linearity, see CLSI document EP06.[1]

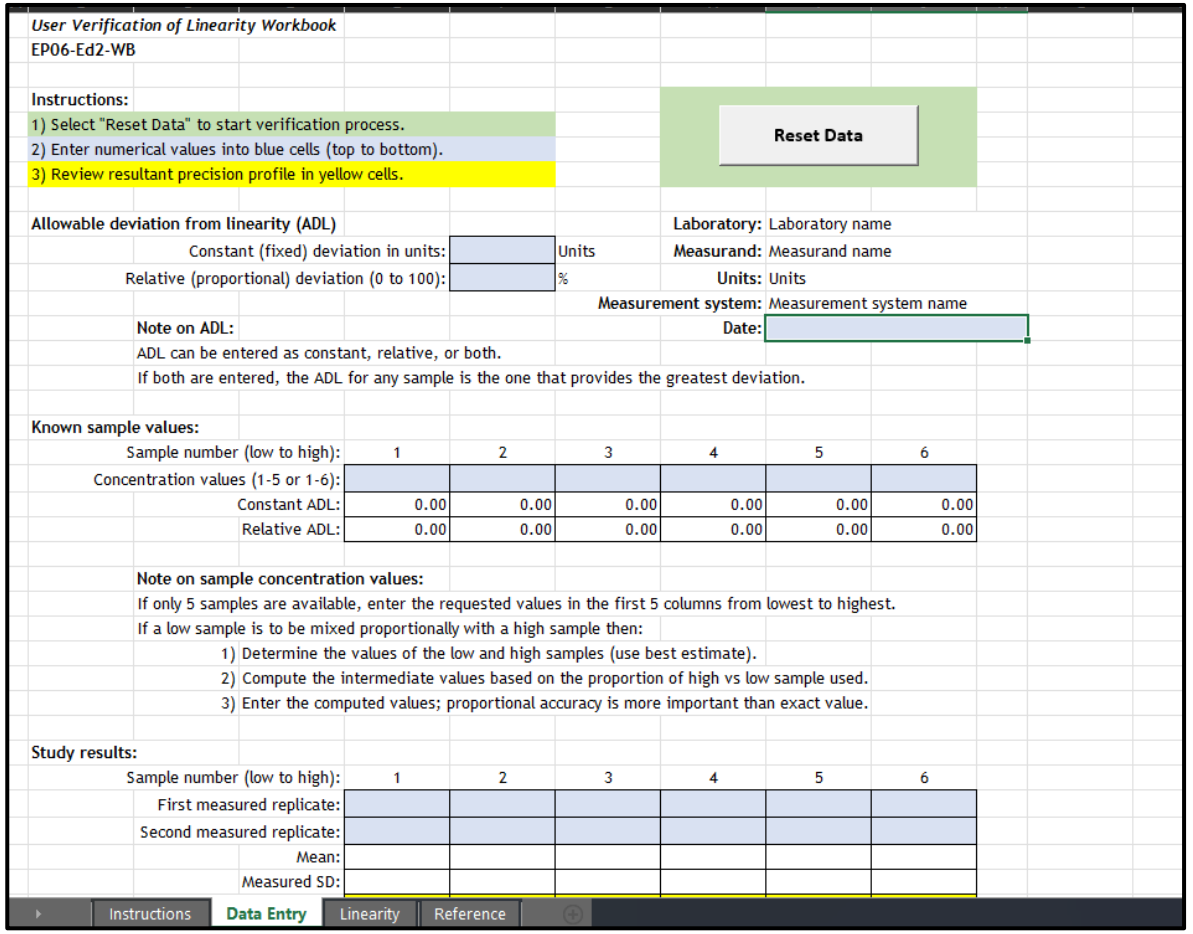
NOTE: This verification of linearity process can be used only when the measurement procedure produces quantitative numerical results.

IMPORTANT NOTE: The study outlined in this implementation guide and described in Chapter 4 of CLSI document EP06[1] is not intended for use by a test developer to establish or validate the linearity interval for a new commercial test or laboratory-developed test. Instead, test developers should consult Chapters 2 and 3 of CLSI document EP06[1] for guidance on establishing and validating a linearity interval. Laboratories and commercial manufacturers are collectively referred to as "developers" in this implementation guide.

What Is Linearity?

A measurement procedure is linear throughout a given interval when the results, on average, are proportional to the true values of the samples. In the graph below, both test 1 (orange line) and test 2 (blue line) are linear and proportional but give very different values. Each line can be depicted in the following equations:

- Test 1: Y = X
- Test 2: Y = 2X



User Verification of Linearity Workbook
EP06-Ed2-WB

Instructions:
1) Select "Reset Data" to start verification process.
2) Enter numerical values into blue cells (top to bottom).
3) Review resultant precision profile in yellow cells.

Reset Data

Allowable deviation from linearity (ADL)
Constant (fixed) deviation in units: Units
Relative (proportional) deviation (0 to 100): %

Laboratory: Laboratory name
Measurand: Measurand name
Units: Units
Measurement system: Measurement system name
Date:

Note on ADL:
ADL can be entered as constant, relative, or both.
If both are entered, the ADL for any sample is the one that provides the greatest deviation.

Known sample values:

Sample number (low to high):	1	2	3	4	5	6
Concentration values (1-5 or 1-6):						
Constant ADL:	0.00	0.00	0.00	0.00	0.00	0.00
Relative ADL:	0.00	0.00	0.00	0.00	0.00	0.00

Note on sample concentration values:
If only 5 samples are available, enter the requested values in the first 5 columns from lowest to highest.
If a low sample is to be mixed proportionally with a high sample then:
1) Determine the values of the low and high samples (use best estimate).
2) Compute the intermediate values based on the proportion of high vs low sample used.
3) Enter the computed values; proportional accuracy is more important than exact value.

Study results:

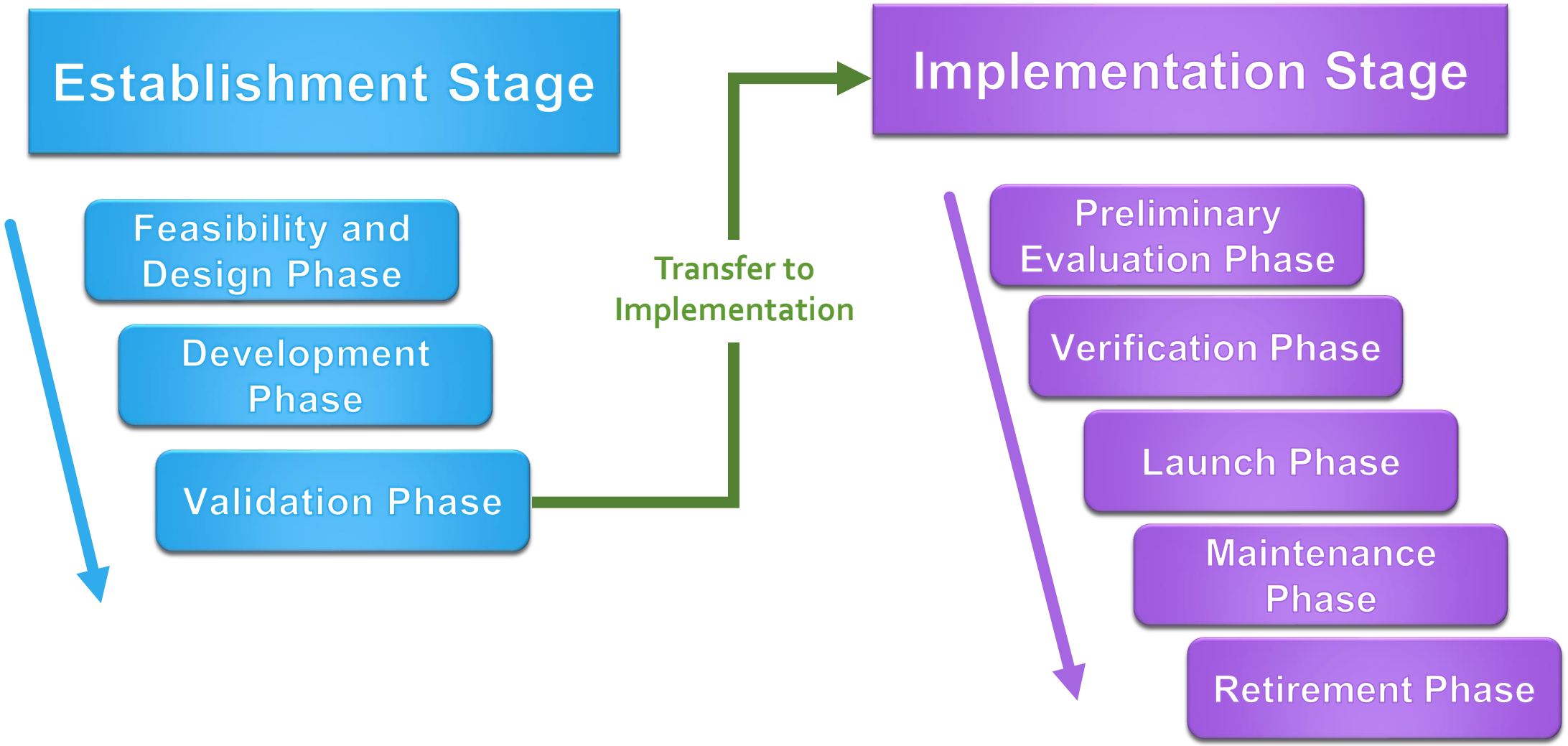
Sample number (low to high):	1	2	3	4	5	6
First measured replicate:						
Second measured replicate:						
Mean:						
Measured SD:						

Instructions | Data Entry | Linearity | Reference

Method Navigator

- NEW electronic subscription product from CLSI
- Helps you meet applicable regulatory and accreditation requirements
- For establishing and implementing LDTs or implementing an FDA-cleared test method
- Helps provide guidance on the necessary documents and records

Test Life Phases Model



Why Use Method Navigator?

- Reproducible outline for any new test method
- Easily create needed documents and records as you develop
- Helps your laboratory meet requirements
- Contributes to good quality laboratory results and improves patient safety

Projects in Progress & Recent Publications

PROJECTS IN PROGRESS – 2023 – early 2024

Projects below are in final stages of development, however, timing may be subject to change

CLSI QMS02	Quality Management System: Development & Management of Laboratory Documents, Ed7
CLSI PRE01	Preexamination Processes for Identification, Collection, Transport & Handling of Medical Laboratory Specimens
CLSI M100	Performance Standards for Antimicrobial Susceptibility Testing, Ed34
CLSI QMS29	Conducting Effective Management Reviews
CLSI M02	Performance Standards for Antimicrobial Susceptibility Tests, Ed14
CLSI M07	Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically
CLSI QMS27	Decontamination of Laboratory Instrumentation
CLSI POCT16	Emergency and Disaster Point-of-Care Testing

Visit **clsi.org/standards** for latest

NEW

Recently Published Documents

CLSI PRE04, Procedures for Handling, Transport, and Processing of Blood Specimens for Common Laboratory Tests, 1st Ed

CLSI AUTO17, Semantic Interoperability for In Vitro Diagnostic Systems, 1st Ed

CLSI EP33, Use of Delta Checks in the Medical Laboratory, 2nd Ed

CLSI M23, Development of *In Vitro* Susceptibility Test Methods, Breakpoints, and Quality Control Parameters, 6th Ed

CLSI MM01, Molecular Testing for Heritable Genetics and Specimen Identification, 4th Ed

CLSI QMS18, Process Management, 2nd Ed

CLSI M53, Criteria for Laboratory Testing. Diagnosis of Human Immunodeficiency Virus Infection, Ed2

CLSI QMS17, External Assessments, Audits, and Inspections of the Laboratory

QUESTIONS?

A COMMON GOAL: QUALITY HEALTH CARE








Thank you

Jennifer K. Adams | jadams@clsi.org

