Clinical and Laboratory Standards Institute (CLSI)

Consensus Standards to Support Operational Excellence and Regulatory Compliance

CLIAC Meeting

Barb Jones, PhD | April 10, 2024

CLIA and CLSI Standards Clarification

(2) ***Establishment of performance specifications.*** Each laboratory that modifies an FDA-cleared or approved test system, or introduces a test system not subject to FDA clearance or approval (including methods developed in-house and standardized methods such as text book procedures), or uses a test system in which performance specifications are not provided by the manufacturer must, before reporting patient test results, establish for each test system the performance specifications for the following performance characteristics, as applicable:

(i) Accuracy.

(ii) Precision.

(iii) Analytical sensitivity.

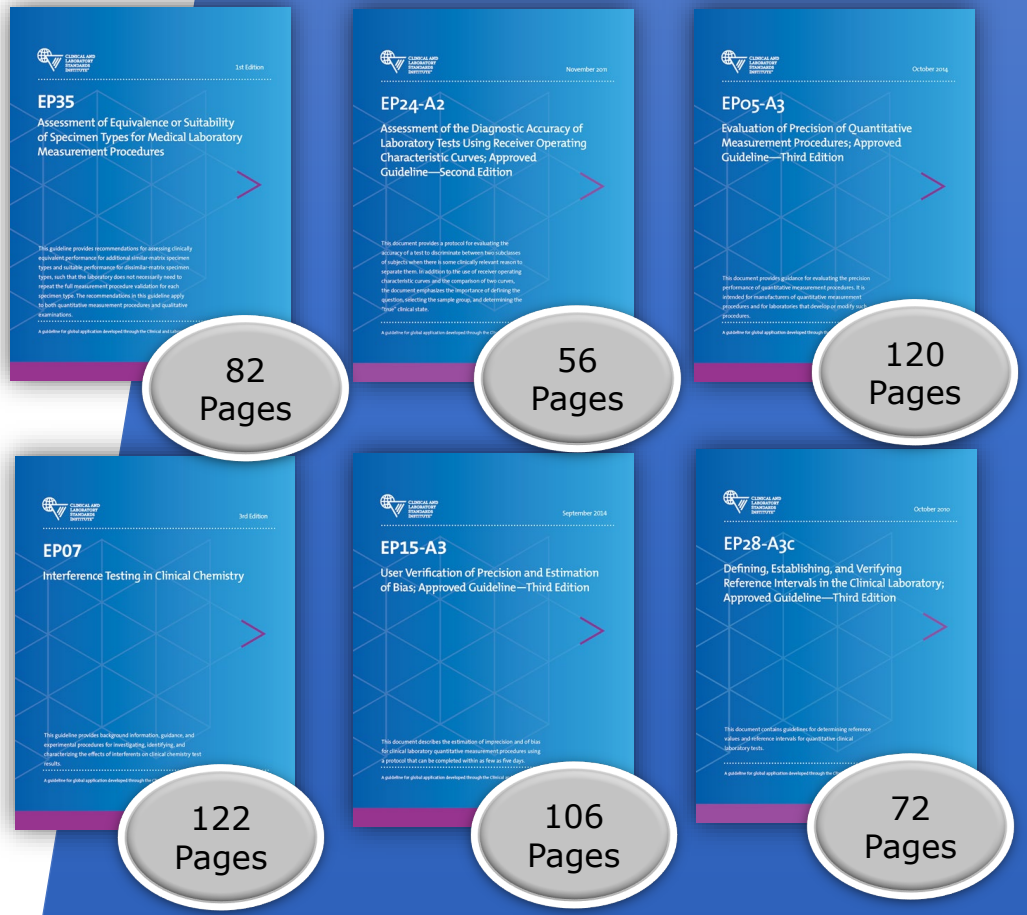
(iv) Analytical specificity to include interfering substances.

(v) Reportable range of test results for the test system.

(vi) Reference intervals (normal values).

CLIA LDT Standard

Some Relevant CLSI Standards



CLSI Organization and Process

Accredited Standards Development Organization

Who Is CLSI?

The Global Leader in Setting Clinical Laboratory Standards

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit organization that develops laboratory standards worldwide.

CLSI Role in the Diagnostics Ecosystem

- Founded in 1967 as NCCLS
  - 2 months before CLIA enacted
  - 20+ years before Amendments
- Created by members of 36 organizations
  - Department of Health Services (now CDC)
  - the College of American Pathologists (CAP)
  - the National Research Council (NRC)
  - the American Chemical Society (ACS)
  - the American Academy of Microbiology (now ASM)
  - National Bureau of Standards (now NIST)
- Accredited since 1977 by American National Standards Institute (ANSI) as a standards development organization (SDO)

"…advisory group for the improvement of standards in clinical laboratories and serve as a mechanism to achieve con-census on standards."

Requirements for SDO Accreditation

- Openness
- Lack of Dominance
- Balance
- Coordination and Harmonization
- Notification of Standards Development
- Consideration of Views and Objectives
- Consensus Vote
- Appeals
- Procedures
- Compliance with Normative ANSI Policies and Procedures

CLSI At-a-Glance

Globally recognized accredited not-for-profit standards development organization

Made up of 24,000+ individuals with membership access and 1,600+ active subject matter experts

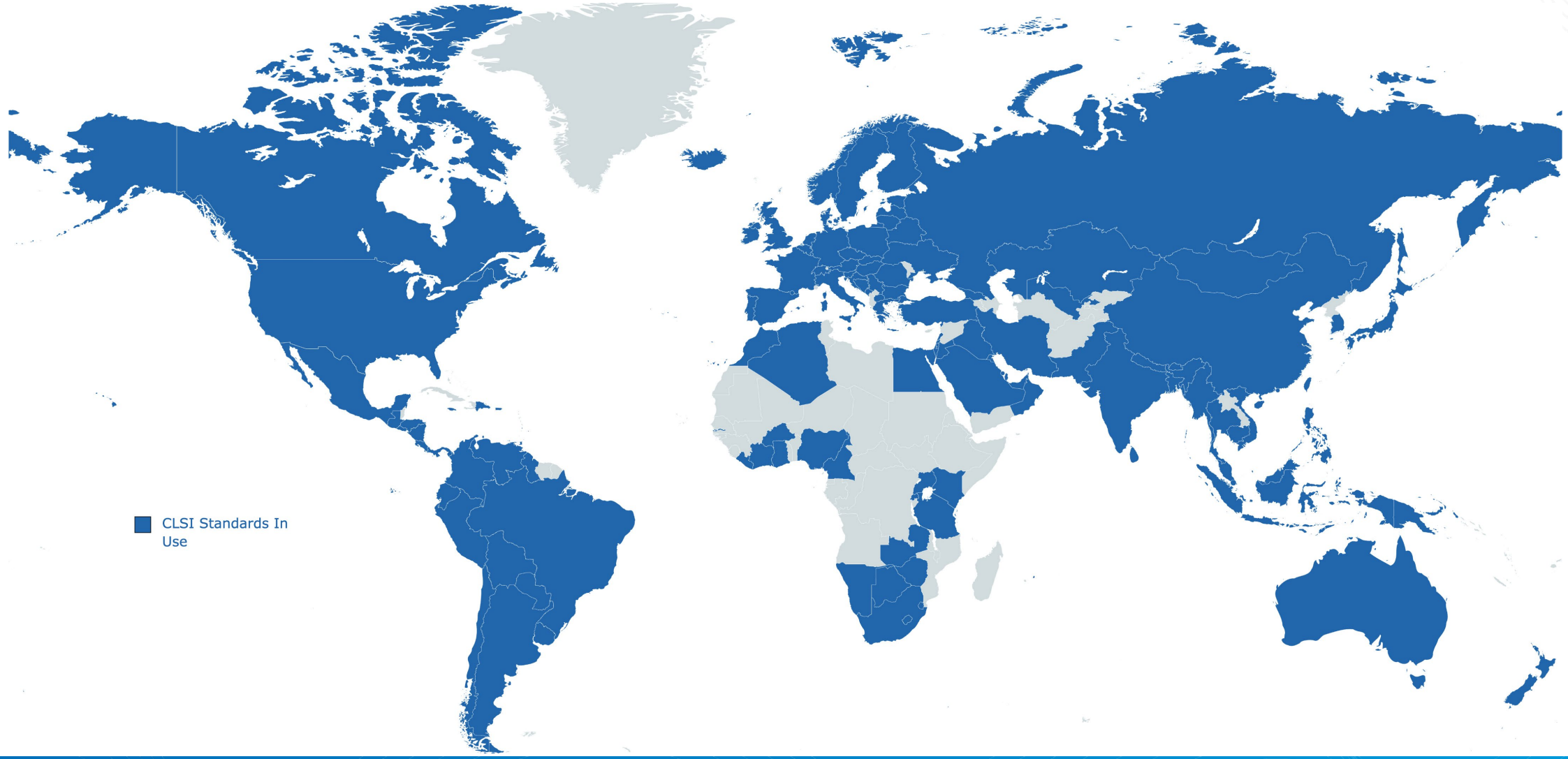
300 products:

standards, guidelines, educational resources, and more

Recognized by labs, accreditors, and government agencies as the best way to improve medical lab testing

Our products help improve testing outcomes, maintain accreditation, bring products to market faster, and navigate regulatory hurdles

CLSI Standards in Use Around the Globe



GLOBAL CONSENSUS-BASED STANDARDS

Bringing constituencies together through balanced, inclusive, and participatory processes

Professions

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

Government

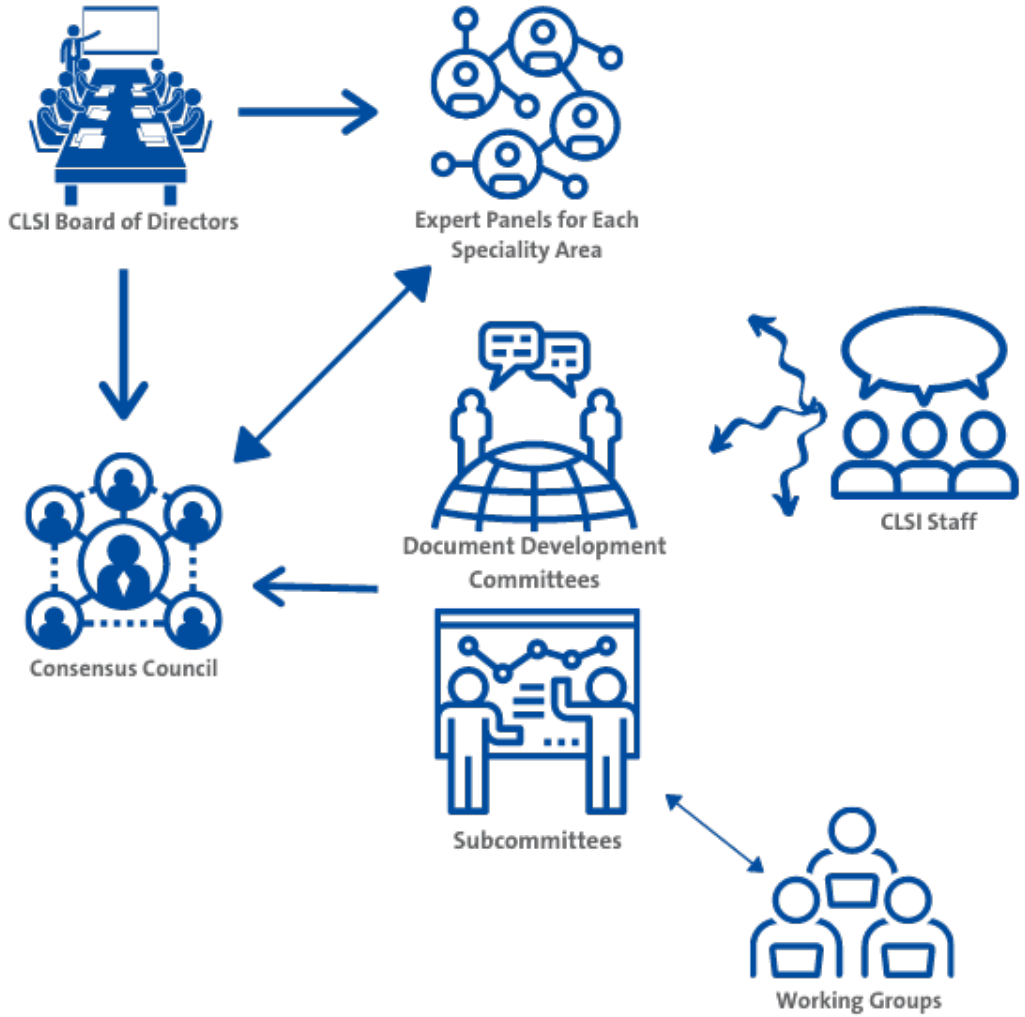
- Public Health Agencies
- Public Health Ministries
- Regulatory Bodies
- Accreditors

Industry

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

Members & Subject Matter Experts

How We Work



THE CLSI CONSENSUS PROCESS

11 Expert Panels

Automation and Informatics

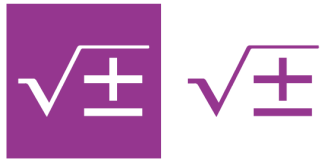
Clinical Chemistry and Toxicology

General Laboratory

Preexamination

Hematology

Immunology and Ligand Assay



Method Evaluation

Microbiology

Molecular Methods

Newborn Screening

Point-of-Care Testing

Quality Management Systems

Veterinary Medicine

More than 300 Clinical and Laboratory Standards

Automation and Informatics	18
Clinical Chemistry and Toxicology	57
IVD Development (Industry)	132
Emergency Response	5
Evaluation Protocols	62
General Laboratory & Lab Safety	36
Hematology and Immunology	36
Medical Office Practices	28
Microbiology	89
Molecular Diagnostics	28
Newborn Screening	42
Point-of-Care Testing	21
Preexamination Processes	9
Quality Management Systems	38
Specimen Collection & Handling	57
Veterinary Medicine	8

CLSI's Support of CLIA

Accreditation Crosswalks

190+ Documents provide guidance for accreditation requirements (CAP, JC)

Quality System Essentials

24 Documents and over **2800 pages** of guidance directly applied to CLIA quality regulations

CLIA Regulation (What must be done)	CLSI Quality System Essentials (How to do it)
Sub-part J: 493.1100-493.1101	Facilities and Safety Management
Sub-part K: 493.1200-.1239 / 493.1242-.1249 / 493.1282 / 493.1289 / 493.1299	Organization and Leadership
Sub-part M: 493.1351-.1495	Personnel Management
Sub-part K: 493.1252-.1255	Equipment Management
Sub-part K: 493.1252	Supplier and Inventory Management
Sub-part K: 493.1232 / 493.1240-.1242 / 493.1250-.1251 / 493.1256-.1282 / 493.1290	Process Management
Sub-part K: 493.1231 / 493.1291	Information Management
Sub-part J: 493.1101e / 493.1105 / Sub-part K: 493.1283	Documents and Records Management
Sub-part K: 493.1233-.1234 / 493.1291e / Sub-part M: 493.1407 / 493.1419	Customer Focus
Sub-part H: 493.801-.807 / Sub-part K: 493.1239 / 493.1249 / 493.1253-.1254 / 493.1289 / 493.1299	Assessments
Sub-part K: 493.1233-.1234 / 493.1282	Nonconforming Event Management
Sub-part K: 493.1236-.1239 / 493.1249 / 493.1289 / 493.1299	Continual Improvement

Federal Agency Use of Consensus Standards

Consensus Standard Use Requirements

- **National Technology Transfer and Advancement Act (NTTAA) (1996)**
  - Mandates that all federal agencies use technical standards developed and adopted by voluntary consensus standards bodies

- **Office of Management and Budget (OMB) Circular A-119,** *Federal Participation in the Development and Use of Voluntary Consensus Standards and in Conformity Assessment Activities*
  - Definition of "Standard" or "Technical Standard" including:
    - Guidelines or characteristics for products or related processes and production methods
    - related management systems practices
    - the definition of terms
    - test methods and sampling procedures
  - Considerations for standards selection, including:
    - the **costs and benefits** to the Federal government and the regulated public of the agency developing its own standard;
    - the **ongoing use of the standard by other agencies** for the same or a similar requirement, [to] increase consistency across the Federal government

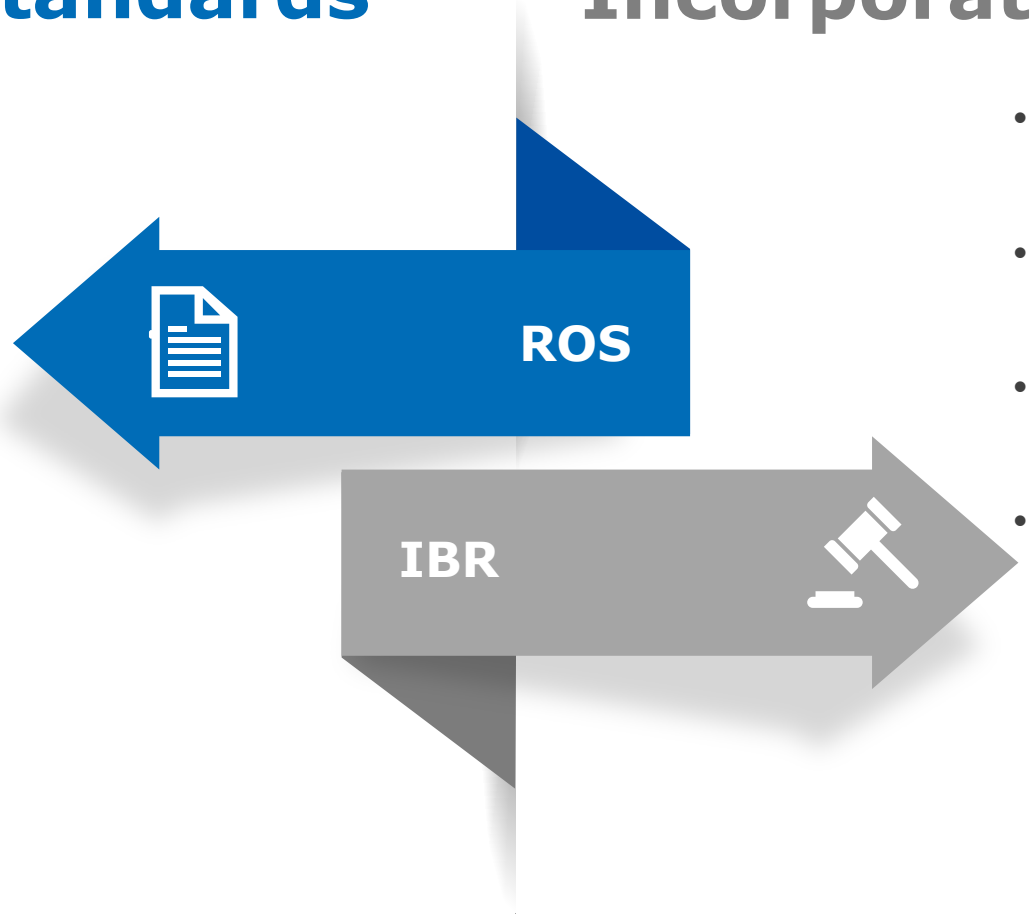
"[A]ll Federal agencies and departments shall use technical standards that are developed or adopted by voluntary consensus standards bodies, using such technical standards as a means to carry out policy objectives or activities determined by the agencies and departments."

-OMB Circular A-119

Federal Agency Vehicles for Consensus Standards

Recognition of Standards

- Use of standards is voluntary
- Agency has discretion to define process, procedure, requirements
- Can be partially recognized
- Not legally enforceable
- Revocation of recognition does not require lengthy rule change
- Can be easily modified as standards are revised



Incorporation by Reference

- Entire standard becomes part of rule (1 CFR part 51)
- Has the force and effect of law
- Rule change process must be followed to remove reference
- Example: FDA IBR of ISO 13485:2016 *Medical devices - Quality management systems - Requirements for regulatory purposes*

FDA Recognized Standards Program

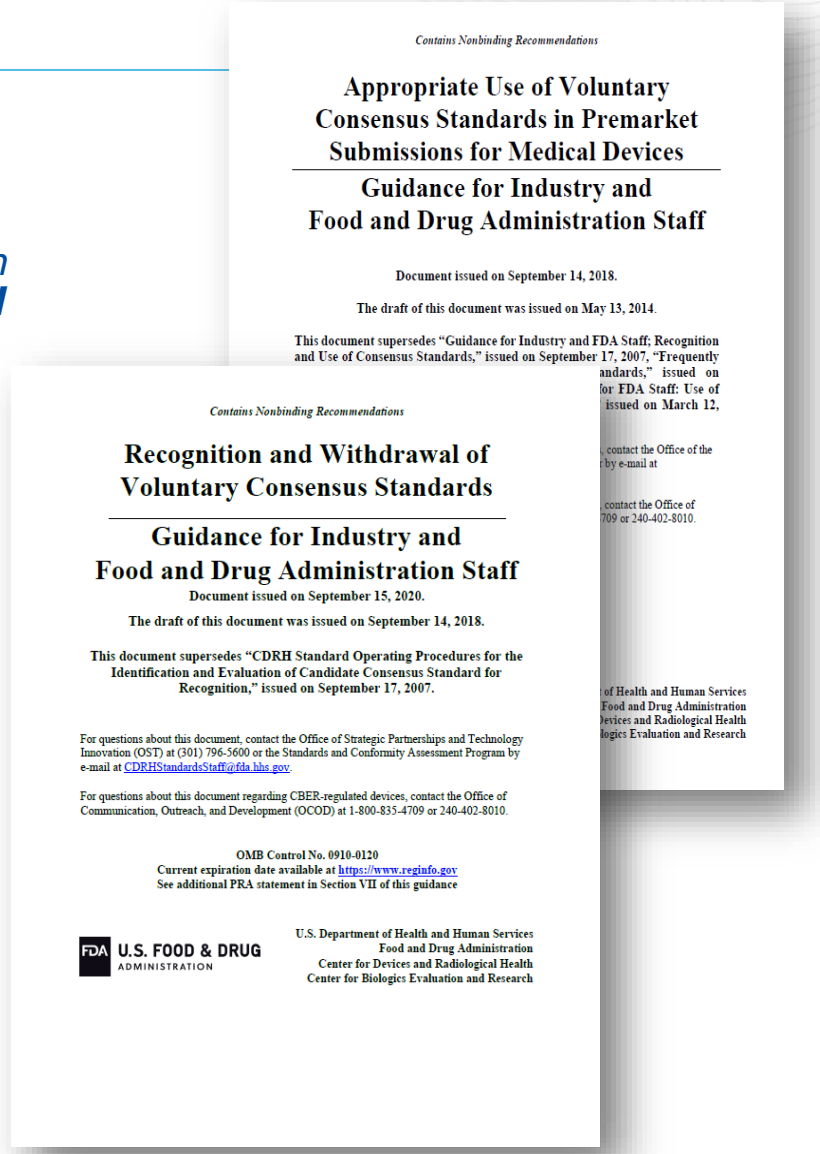
- FDA recognition is in FD&C Act

  *514(c)(1)(A) In addition to establishing a performance standard under this section, the Secretary shall, by publication in the Federal Register, recognize all or part of an appropriate standard **established by a nationally or internationally recognized standard development organization*** for which a person may submit a declaration of conformity in order to meet a premarket submission requirement or other requirement under this Act to which such standard is applicable.*

- FDA recognizes over 1400 standards from 32 SDOs

- Full or partial recognition of 132 CLSI Standards

- Clear process for recognition, withdrawal, and external request for recognition



* Emphasis added

Recommendation for CLIAC

Recommendations for CLIAC Regarding Standards

1. CMS can and should provide CLIA certified labs with further guidance regarding “How to” meet regulation
2. CMS can and should develop a Recognized Standards Program (RSP)
3. FDA’s RSP can serve as a model for development
4. CMS has the discretion to develop a RSP without legislative authorization and should take steps towards implementation
5. CMS can compel accreditors to refer laboratories to recognized standards when applicable
6. CMS, FDA, and CDC can provide communication to CLIA certified laboratories about the RSP

Thank You

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