

**Early
Detection
Research
Network**



CLIA/CAP Standardization from the Ground Up

EDRN-FDA-NIST Workshop on
Standards in Molecular Diagnostics

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Clinical Laboratory Improvement Act (CLIA)

1988 - Congress passed the Clinical Laboratory Improvement Act in response to public furor over deaths attributed to false-negative Pap smear readings.

Congressional definition of “laboratory” is all-inclusive:

“facility for the biological, microbiological, serological, chemical, immuno-hematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of human beings.”

CLIA's Do's and Don't's

CLIA requires:

- certification and re-certification
- frequent proficiency testing
- a quality control program
- employment of properly accredited personnel
- submission to on-site inspections
- procedure manuals, and extensive documentation

(Tests must be certified by Center for Medicaid and Medicare Services - CMS).

CLIA does NOT address: clinical utility, test sensitivity, result interpretation, nor are there any specific regulations for genetic testing.

College of American Pathologists (CAP)

CAP Mission Statement:

“The College of American Pathologists ... serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.”

The goal of the CAP Laboratory Accreditation Program (LAP) is to improve patient safety by advancing the quality of pathology and laboratory services through education, standard setting, and ensuring laboratories meet or exceed regulatory requirements.

LAP is based on rigorous accreditation standards that are translated into detailed and focused checklist requirements, and unlike CLIA, CAP does require information on test sensitivity, etc.

Summary of CAP Timeline

- 1947 – CAP is established**
- 1949 - First chemistry survey conducted**
- 1951 - First standard solutions offered**
- 1952 - Liaison committee established with Joint Commission on Accreditation of Hospitals later known as JCAHO**
- 1965 - First laboratory accreditation checklist compiled**
- 1984 - Performance Improvement Program in Diagnostic Surgical Pathology and Cytopathology (PIP) established**
- 1992 - Forensic identity and parentage testing survey initiated**
- 2003 - Laboratory Accreditation Program (LAP) offers inspection checklists customized for individual labs**
- 2005 - LAP announces new initiatives including mandatory inspector training and unannounced inspections**

CAP Accreditation Programs

Laboratory Accreditation:

the only one of its kind that utilizes teams of practicing laboratory professionals as inspectors.

Biorepository Accreditation:

- 3-yr, peer-based program to adoption of standards through consistent application of best practices and evidence-based standards
- further strengthen the quality of patient care and ensure consistent, verifiable quality of biospecimens and biorepositories lacking in the current environment

Reproductive Accreditation Program

Forensic/Drug Testing Accreditation Program

Why do we need CLIA and CAP?

Laboratory Developed Test (LDT): is a test used in patient management that has the following characteristics:

- The test is performed by the clinical laboratory in which the test was developed;
- The test is neither FDA-cleared nor FDA-approved, or is an FDA-cleared/approved test **modified** by the laboratory. These modification include type of collection devices, etc.
- The test was first used for clinical testing after April 2003

FDA approved: PSA – Prostate CA; ALK gene rearrangements Lung CA

LDT non-FDA approved: gene rearrangements in hematopoietic malignancies

Characteristics of a CAP Inspection

- **Use of the same version of checklists for all sites**
- **Criteria to ensure inspection is conducted by a similar system**
- **A pre-inspection visit by a CAP specialist – necessary to understand the size and scope of laboratory**
- **An on-site CAP specialist during the inspection**
- **A post-inspection summation conference and a final report to provide system-level feedback**

On-Site Inspections Evaluate the following:

- Standard operating procedures (SOP) and laboratory records
- Quality control procedures/quality assurance programs
- Initial qualifications and periodic training of directors/staff
- Certification and maintenance of all laboratory equipment
- Evaluation of infrastructure and appropriateness of facilities
- Safety monitoring program
- Overall laboratory management

SOP/Lab Records: Written Documentation

Test Results:

- Calculations for Quantitative Tests
- Analytic Interpretation Guidelines
- Intended Use of Assay and Turnaround Time
- Validation Studies - LDTs or Modified FDA-Approved/Cleared Tests – record of specimen selection; specimen types
- Reference/Reportable Range
- Clinical Performance Characteristics
- Physician Notification
- Post testing reporting

Specimen Handling:

- Requisition information
- Specimen ID (proof on possession)
- Storage/Preservation
- Specimen Rejection Criteria (including disposal)

SOP/Lab Records: Written Documentation

Processing of Specimens:

- Aliquots including storage and retention data
- Preparation, i.e., nucleic acid extraction
- Quality and quantity evaluation

Reagents: Q/C for probes/primers, buffers, etc

Assays:

- Quantitative and Qualitative Controls - tolerance limits, Q/C verification
- Corrective actions
- Q/C statistics and review of results
- Specialized regulations for amplification and sequencing (next gen) assays
- (including interpretation guidelines and criteria for positive/negative results)
- Specialized regulations regarding ISH, FISH and paternity/foresnics

Bioinformatics: documentation of the process used to support the analysis, interpretation, and reporting of results (sequencing)

SOP/Lab Records: Written Documentation

Equipment:

- Checklist of calibration thresholds/tolerance, etc.
- Plan/schedule for maintenance and recalibration
- Comparability of Instrument/Methods
- Analytical measurement range validation
- Troubleshooting guides

Included:

Freezers/refrigerators, water baths/heating blocks, incubators, centrifuges, spectrophotometers, thermocyclers, hybridization, and sequencing equipment, photography, gels, pipettors, automated extractors, balances, ddH₂O, power supplies, etc.

SOP/Lab Records: Written Documentation

Personnel:

- qualifications of director and bench testing personnel
- training and schedule for annual/regular re-training

Safety Records:

- Inspection/maintenance of chemical and safety cabinets, biohazard and biological hoods
- MSDS - Materials Safety and Data Sheets
- radiation safety: including policies/procedures; storage and waste and bench surveys