Module 1 - Background

October 26, 2021

AACC
Better health through laboratory medicine.

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

AMP
Association for Molecular Pathology

Association of Pathology Chairs
APC
Established 1967

CLIA oversight of clinical molecular testing in 1980s

- 5 methods-based CPT codes
  - Nucleic Acid (NA) isolation, enzymatic digestion, gel, probe, report
- Few tests
  - T and B cell gene rearrangements
  - BCR/ABL
  - Linkage analysis for genetics
  - Qualitative detection of some microbes
- Few methods
  - Southern blots, Sanger sequencing, Restriction endonucleases, Dot blots….
  - NO KITS!
  - All done by Laboratory-Developed Testing Procedures (LDT/LDP)
    - Note different uses of terms that are synonymous

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LDTs/LDPs generally precede development of kits

- LDTs/LDPs help demonstrate the clinical value of assays
  - T and B cell gene rearrangements
  - HSV PCR for encephalitis
  - CMV in transplant patients, perinatal CMV
  - Fragile X, Huntington Disease
- LDTs/LDPs can more quickly/readily fill a need
  - KRAS mutation testing in 2007
  - BRAF in thyroid, melanoma, brain tumors….don’t need separate assays
- Kits can make it easier to offer a test broadly

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LDTs/LDPs are not marketed for use in other labs

- LDT/LDP is an optimized laboratory procedure, not a kit
- Developed and optimized in a single lab
- Quality controlled according to CLIA
  - CLIA is the Clinical Laboratories Improvement Amendments: Federal regulations regarding oversight of clinical laboratory testing, originally published in 1967 and revised in 1988.
- Consensus guidelines for assay performance written by CLSI, others
- Performance compared to that of other labs via ongoing proficiency testing to ensure quality, under CLIA

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Clinical Laboratory Improvement Amendments (CLIA)

Get Online Payment Info (PDF)

The Centers for Medicare & Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments (CLIA). In total, CLIA covers approximately 260,000 laboratory entities. The Division of Clinical Laboratory Improvement & Quality, within the Quality, Safety & Oversight Group, under the Center for Clinical Standards and Quality (CCSQ) has the responsibility for implementing the CLIA Program.

The objective of the CLIA program is to ensure quality laboratory testing. Although all clinical laboratories must be properly certified to receive Medicare or Medicaid payments, CLIA has no direct Medicare or Medicaid program responsibilities.

For the following information, refer to the downloads/links listed below:

Extensive control of process and results under CLIA

- Most testing is not molecular; requires highly trained staff, specialized equipment and materials
- Most molecular laboratory testing does not use a kit
  - Kit not available
  - Kit does not encompass full testing process
- Significant pre- and post-analytic steps must be monitored
- CLIA covers the whole process
  - Pre- and post-analytical issues
  - Personnel competency and training]
  - Validation
  - Reporting
- CLIA oversight of FDA-approved kits is still needed

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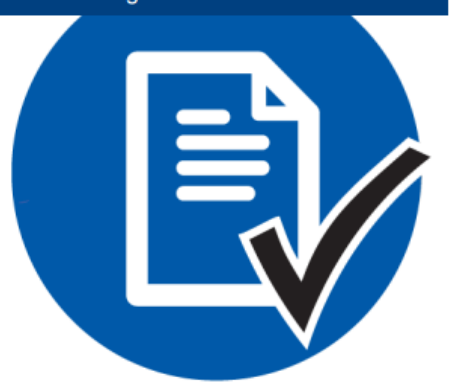
COLLEGE of AMERICAN PATHOLOGISTS

Master

CLIA oversight of most clinical labs is College of American Pathologists

Molecular Pathology Checklist

CAP Accreditation Program



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Molecular Pathology Checklist

TABLE OF CONTENTS

Validation of assays delineated in detail

- Labs carefully validate assays and define:
  - Sensitivity
  - Specificity
  - Limit of detection
  - Accuracy
  - Reproducibility
  - Interfering substances
- Pre- and post-analytical processes also validated
- Quality and accuracy of end result is the goal for LDTs/LDPs and CLIA

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Current Regulatory Pathways for Laboratory Tests

CMS under CLIA

- Laboratory Developed Testing Procedures (LDTs/LDPs)
- Tests that are developed and performed within single laboratory
- Addresses full and ongoing procedure performance

FDA

- In Vitro Diagnostic Tests (IVDs)
- Testing kits that are boxed, sold and shipped over state lines
- “Black boxes” for lab
- Addresses kit performance only

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Corporate development of kit based on potential market

- Cost of FDA approval process, clinical trials and more must be recovered by manufacturer
- Kits generally target large market assays (Chlamydia, HPV, etc.)
- New FDA approvals rarely sought as new clinical needs arise for an assay already marketed
- Changes in panels difficult to incorporate

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