IVD Roundtable
510(k) Workshop
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Update 2003: FDA and CLIA

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Surviving CLIA

- **CLIA Overview**
  --Something OLD
  --Something NEW
- **Key Features**
- **Who are the players**
- **FDA and CLIA**
- **CLIA regulations**
- **What is categorization**
- **What requires categorization**
- **What is not regulated under CLIA**

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Surviving CLIA

- How FDA categorizes tests
  -CDRH
  -CBER
- "Automatic" categorizations
- Specific requests for categorizations
- Categorization letter; CLIA website
- Where do you go for help

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What is CLIA?

- Clinical Laboratory Improvement Amendments of 1988 (CLIA)
- Enacted as result of reports of inaccurate test results from Pap smears
- Questions were raised about how labs functioned and what quality control procedures existed

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CLIA ‘88

- CLIA’88 - President Reagan- 10/31/1988
- Social Security Act
- Labs receiving Medicare funds must be CLIA-certified.
- All clinical labs must be CLIA-certified to test human specimens
- Notice Proposed Rule 1990/60,000 comments
- Final Rule 2/28/1992
- Final QC Rule 1/24/03

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Highlights Final QC Rule

- Removes FDA’s review of manufacturers' QC instructions for compliance with CLIA
- Sets QC standards for nonwaived testing.
- Reduces QC frequency in most of the subspecialties
- Merges moderate & high complexity QC requirements
- Uses plain language

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Highlights

- Reorganizes to mimic the flow of a specimen through the lab.
- Studies show most lab errors are pre-analytical
- Requires mod. complexity labs to validate a test once before use
- Ensures the test works accurately before pts. tested.
- Onus on laboratory
- CMS drafting inspector guidelines

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Who are the Players?

- Centers for Medicare and Medicaid Services (formerly HCFA) oversees CLIA
- Authority for regulation and policy
- CLIA self-funded
- User fees from regulated labs
- CMS pays FDA to categorize commercially marketed tests
- CDC categorizes lab procedures
  - -Provider performed microscopy
  - -Gram stain

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CMS

- Reimbursement
- CLIA certificate
- HIPAA – Privacy Act
- CLIA regulations, lab sends report to authorized person
- CLIA defines as individual authorized under State law to order tests or receive test results, or both.
- HIPAA-- patient requests their records from a lab, results should be sent to them.

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CMS CLIA Contact

- Kathy Todd, CMS
  ktodd@cms.hhs.gov
- Phone: 410.786.3385
- Fax: 410.786.1224

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OIVD's CLIA Players

- Renita Hoard, CSO
- Dr. Joe Hackett, founding father
- Don St. Pierre, Deputy Director
- Dr. Steve Gutman, Director
- CLIA team – represents OIVD
- CBER devices – Clara
- CBER waiver tests - Clara, lead reviewer, OIVD CLIA team

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Key Features

- Standards based on complexity of testing, not the laboratory site
- The key to understanding categorization;

  -the analyst/operator

  -how complex it is for the analyst to run the test

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FDA and CLIA

- 1992 CLIA regulations
- FDA responsible for complexity categorization
- 1993-94 FDA categorized >900 tests
- 1994 CDC delegated responsibility
- Resources, funding issues

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FDA and CLIA

- Impetus for change
- Manufacturers
- Congress
- “Confusion and duplication of effort”
- CDC, CMS, FDA consensus
- Interagency agreement 2/27/99
- Tri-agency team – CMS, CDC, FDA

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What Regulations Govern Categorization

- 42 CFR 493.17, categorization of specific laboratory tests by level of complexity
- Moderate, high
- 7 Criteria

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Moderate, High

42 CFR 493.17

- Knowledge
- Training and experience
- Characteristics of operational Steps
- Calibration, QC, PT materials
- Troubleshooting, Maintenance
- Interpretation and judgment

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Moderate, High

42 CFR 493.17

- **7 criteria scored as 1, 2, or 3**
- **Score of 1 = minimum**
- **Score of 3 = specialized**
- **Total scores of 12 or less = moderate**
- **13 or higher = high**
- **e.g. PCR = high complexity**

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Categorization Regulations

42 CFR 493.15 (c)

- **Lists the 9 generic test groups**
- **Categorized by regulation**
- **Automatically waived**
- **But still requires categorization notification letter from FDA**
- **Requires posting categorization on website**

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Generic 9

493.15 (c)

- dipstick and tablet reagent urinalysis
- fecal occult blood
- ovulation tests
- urine pregnancy tests
- erythrocyte sedimentation rate
- hemoglobin (copper sulfate)
- blood glucose devices (FDA-cleared for OTC use)
- spun microhematocrit
- hemoglobin single analyte instruments (1993)

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Most Common Waived Tests

- Urine pregnancy – 34%
- All other tests – 20%
- Blood glucose (OTC) – 18%
- Urine dipstick/tablet chemistries-19%
- Ovulation tests – 5%
- Fecal occult blood – 4%

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Categorization Regulations

- CMS and PHS Sept 13, 1995 Notice of Proposed Rulemaking
- Clarified statutory criteria for obtaining waiver
- Guidelines list the criteria
- Final rule pending
- CMS leads tri-agency team

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CMS/PHS Waiver Criteria

- Defined simplicity, low risk
- Defined accuracy as comparison to reference materials, methods
- Precision field studies in hands of lay user
- Flex studies, different environments
- Studies distinct from FDA premarket review

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Categorization Regulations

- Food and Drug Modernization Act Nov. 21, 1997
- clarifies tests cleared for over-the-counter are automatically waived.
- But still requires categorization notification letter from FDA
- Requires posting categorization on website

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OTC

- Growing number of OTC tests
  - -drugs of abuse
  - -cholesterol, HDL chol
  - -vaginal ph
  - -microalbumin
  - -FSH, qual.
  - -HgbA1C
  - -fern test, saliva.
  - -semen, male fertility

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Prescription Home Use

- **Prescription home use is an Rx device physician instructs patient to use in home**
- **FDA devices are OTC or Rx**
- **Any device used in the home that is not OTC**
- **Examples – prothrombin time, hemoglobin A1c**

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What is Categorization?

- **Process of assigning new commercially marketed tests to one of 3 CLIA categories:** *waived, moderate, high*
- **The key to understanding categorization; the** *analyst/operator* **and the** *complexity* **of testing**
- **Regulations that govern categorization**

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What Requires Categorization

- Categorization applies to all laboratory test systems on materials derived from the human body conducted for the purpose of diagnosis, prevention or treatment, or assessment of the health

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What Requires Categorization

- Plain Language
- Commercially marketed test systems that produce a result
- This includes 510(k) exempt tests

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Not Categorized

Produce no test result

- **Quality Control**
- **Calibrators**
- **Test tubes**
- **Collection kits**
  - **--drugs of abuse**
  - **--Hepatitis C, HIV**

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Not Categorized

Not currently regulated under CLIA

- **Non-invasive (laser hematocrit)**
- **Breath tests (h. pylori, alcohol)**
- **Drugs of abuse – Workplace**
- **Monitoring devices (Minimed)**

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How FDA Categorizes

- Center for Devices and Radiological Health
- Center for Biologics Evaluation and Research

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CDRH Categorizes

- Pre-amendment
- 510(k) exempt tests
- New Premarket Notification 510(k)

  e.g. special 510(k)s
- New Premarket Approvals (original, supplements)

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CDRH Categorizes

- New Humanitarian Device Exemptions (original, supplement)
- 510(k) add-to-files
  - -Replacement reagents
  - -Manufacturer name change
  - -Relabel
- Previously uncategorized test systems

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Automatic Categorizations

- Manufacturer submits premarket submission to Document Mail Center
- Categorization performed in conjunction with product review
- CLIA notification accompanies clearance, approval order or follows shortly after

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Automatic Categorization, Replacement Reagents

- *Well characterized lab analyzers for use by laboratory professionals.*
- *Previously cleared instruments and reagents, when a claim is made for a new reagent/instrument combination.*
- *Introduction of new instrument family members of a previously cleared instrument family.*

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Automatic Categorization

- **Replacement reagent**
  - *Replacement reagents require a package insert with the new instrument/reagent combination*
  - **CLIA notification follows shortly after**

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Categorization by Request

- Change in company name
- Additional trade name
- Modification?
- Not previously categorized
  -defaults to high complexity

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Categorization by Request

- Submit new labeling to FDA
- Document Mail Center, HFZ-401, 9200 Corporate Blvd., Rockville, MD 20850
- "For CLIA Categorization Only"
- Reference original 510(k) number
- CLIA categorization performed
- Notification letter to manufacturer
- Categorization posted on website

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Categorization by Request

- Exempt from 510(k), CLIA required
- Submit new labeling to FDA's DMC
- "For CLIA Categorization Only"
- OIVD assigns "X" document number

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Categorization by Request

- "X" number accessible through CLIA database
- CLIA categorization performed
- CLIA letter issued
- Categorization posted on CLIA website

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Categorization by Request

- Waiver via CMS/PHS 1995 Criteria
- Test cleared or approved to apply for waiver through process
- FDA approves waiver protocol
- Waiver studies begin
- Timeframe depends on queue

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CBER:

- Manufacturer submits request for product review to CBER
- When test is cleared, approved, licensed CBER sends test instructions to Clara Sliva
- CBER test logged into CDRH CLIA database using CBER document number: BK, BP, BLA, PL

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Rapid HIV Waiver

- Manufacturer submits waiver application to CDRH
- CBER reviewer consults
- CMS consults
- CDRH issues letter
- CDRH posts categorization on CLIA website

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Categorization Notification Letter

- FDA's document number is the key
- "k001111" – new 510(k) CDRH
- "BLA002222 – new BLA CBER
- "k001111/A1" – new trade name
- complexity
- test system name
- analyte name

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Categorization Notification Letter

- Call – don't be shy
- No letter 3 weeks after clearance
- Incorrect letter
- Website updates monthly

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FDA's CLIA Workload

- 10/1//02 – 4/18/03
- 1,125 categorized
- 912 - moderate
- 87 - high
- 126 - waived

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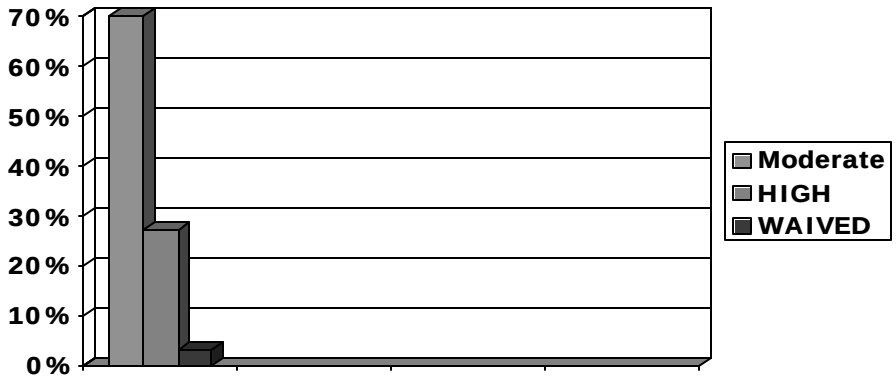
>1,125 Tests Categorized



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FDA's CLIA Website

- http://www.fda.gov/cdrh/clia/
- "Government Google" for current CLIA information
- Lists all waived analytes and tests
- Links to CMS, CDC websites
- CLIA database

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CLIA Database

- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCLIA/search.cfm
- Contains all commercially marketed tests categorized by CDC and FDA
- Several ways to search

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Search CLIA Database

- Search for CLIA records by
  - -test system name
  - -specialty/subspecialty
  - -analyte
  - -document number
  - -qualifier (reagent application)
    e.g. SLIVA Analyzer/St. Pierre reagent
  - -effective date
  - -complexity

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Tips

- **You may enter the entire test name**
- **But most successful if you enter the first word or two**
- **Or just the first few letters**
- **e.g. first few letters of manufacturer name**

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Mastering the CLIA Database

- **Manufacturer Test System**
- **Qualifier**
- **Analyte**
- **Document Number**
- **Complexity**
- **Analyte**
- **Specialty**
- **Effective Date *(mm/dd/yyyy)***
- **Sort *one* or a *combination* of the values and select Search:**

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Publication of Categorizations

- Monthly on FDA's CLIA Home Page
- Federal Register Notice, interval to be determined

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What We Have Learned

- Multiple stakeholders
- Labs
- Providers
- Patients
- Manufacturers
- Government

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Over 31,000 Categorizations

Laboratory Inspectors, Laboratories, Manufacturers, and Other Stakeholders Want to Know

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CLIA INFORMATION

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