



Clinical Laboratory Improvement Amendments of 1988 (CLIA)

Test Categorization and Waiver

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Federal Agencies

- Health Care Financing Administration
- Centers for Disease Control and Prevention
- Food and Drug Administration



Key Features of CLIA

- Law applies to virtually all clinical laboratories
- Standards based on complexity of testing
- Special provisions for cytology
- Sanctions include remedial actions
- User fees



CLIA Statute and Test Complexity

- Requires laboratory regulation on the basis of test complexity, not test site
- Specifies waiver criteria
- Exempts laboratories performing waived tests from regulation



Guiding Principles

- **Assure quality testing**
- **Specify minimum standards**
- **Ensure access**
- **Accommodate new technology**



Complexity Model

Type of Laboratory Testing

Requirements

Very Simple (Waived)

**Registration and Good
Laboratory Practice**

Moderately Complex

**QC, QA, PT, Limited
Personnel**

Highly Complex

**QC, QA, PT, Stringent
Personnel**



Waiver Requirements

■ Waived laboratories

- must register
- not routinely inspected
- exempt from CLIA standards

■ Standards (personnel, PT, QC, and QA requirements) do not apply to waived testing



Test Categorization and Waiver

- **All tests are categorized – high or moderate complexity**
 - Concurrent with 510K, PMA, and licensure notice
 - Categorization level depends on score using 7 criteria

- **Sponsors (manufacturers) may request waiver determination**
 - General criteria defined in the law
 - Tests reviewed and determinations made



CLIA Criteria for Test Categorization

- Knowledge
- Training and Experience
- Reagents or Materials Preparation
- Characteristics of Operational Steps
- Calibration, Quality Control, Proficiency Testing Materials
- Troubleshooting and Maintenance
- Interpretation and Judgment



Waiver Criteria (Law)

- **Approved by the FDA for home use, or**
- **Simple tests that have an insignificant risk of an erroneous result , including those that --**
 - **employ simple, accurate methodologies with negligible likelihood of erroneous results by the user, or**
 - **HHS has determined pose no unreasonable risk of harm to patients if performed incorrectly**



Waiver Chronology

- 10/88 CLIA law
- 02/92 waived tests listed in CLIA regulations
- 11/94 categorization delegated to CDC
- 09/95 proposed rule published
- 11/97 FDAMA revised CLIA waiver provisions
- 03/00 waiver process transferred from CDC to FDA
- 08/00 public workshop meeting
- 09/00, 2/01 CLIAC recommendations on waiver issues
- 03/01 FDA draft guidance published
- 04/01 CLIAC waiver workgroup meeting
- 05/01 CLIAC recommendations relative to FDA draft guidance



1995 NPRM Clarified Waiver Criteria

■ **Simplicity**

- unprocessed specimens
- no analyst intervention or troubleshooting
- fail safe mechanism
- step by step instructions

■ **Accuracy and precision (low risk)**

- field studies at 3 sites with 20 participants (each site)
- reference materials
- statistical evaluation



Tests Categorized and Waived by CDC

From February 1992 until January 2000

- 25,708 test systems categorized

- 733 test systems (includes 27 analytes) approved for waiver
 - 612 specified by regulation (9 analytes/tests)
 - 109 proposed rule 9/95
 - 12 approved for home use



CDC Waived Tests- Listed in Regulations

1. Dipstick/tablet reagent urinalysis (143)
2. Fecal occult blood (33)/gastric occult blood (1)
3. Ovulation tests (37)
4. Urine pregnancy tests (252 = 35% of all waived tests)
5. Erythrocyte sedimentation rate, nonautomated (4)
6. Hemoglobin (copper sulfate) (1)
7. Blood glucose devices (FDA-cleared for home use) (130)
8. Spun microhematocrit (5)
9. Hemoglobin single analyte instruments (2)



CDC Waived Tests- Approved for Home Use

1. Bladder tumor antigen (1)
2. Catalase, urine (1)
3. Cholesterol (5)
4. Fructosamine (2)
5. HDL cholesterol (1)
6. Ketone, blood (1)
7. Prothrombin time (1)

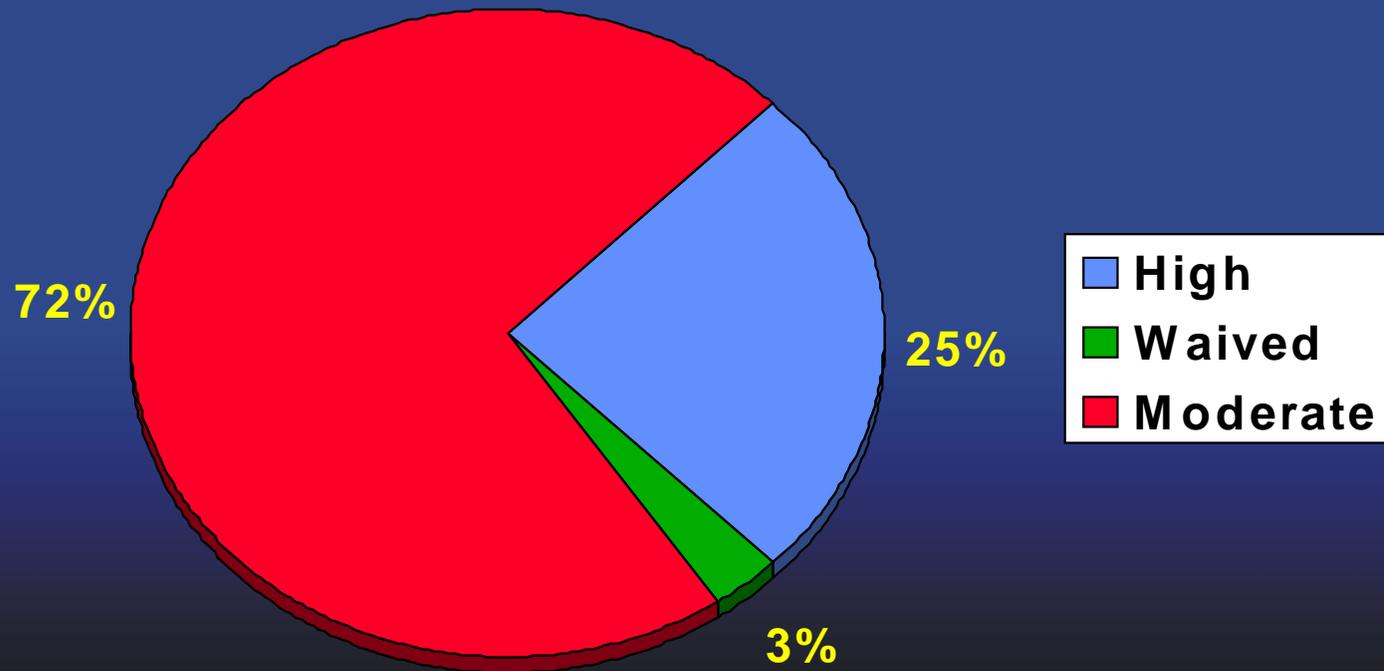


CDC Waived Tests- 9/95 Proposed Rule

1. Amines (1)
2. Cholesterol (4)
3. Creatinine, urine (1)
4. Ethanol (2)
5. Fructosamine (1)
6. Glucose (2)
7. Glycosolated hemoglobin (3)
8. hCG, urine (1)
9. HDL cholesterol (1)
- H. pylori (4)
- H. pylori antibodies (13)
- Hematocrit (2)
- Inf mononucleosis (13)
- Microalbumin, urine (3)
- Nicotine (1)
- Prothrombin time (4)
- Strep A, rapid (14)
- Triglyceride (1)
19. Vaginal pH (1)



Test Categorization





Waiver Processes

	<u>9/95 Proposed Rule</u>	<u>3/01 FDA Draft Guidance</u>
Simplicity	Characteristics	Similar
Risk	Accuracy/Precision studies	Stress/flex studies
Accuracy	Reference material, method	Precision, agreement studies
Fail-safe	QC required	QC recommended
Flex Studies	Modify steps/temp etc.,	(See Risk)
Post-approval Surveillance	None	Recommended



Waiver Challenges

- **Maintaining consistency in decisions**
- **New tests and technology**
- **Increasing complexity of waiver reviews**
- **Public health benefits and concerns**