Regulatory Oversight of Laboratory Testing[2]
Clinical Laboratory Improvement Amendments (CLIA)

CDC Consultation on Rapid HIV Testing
September 10-11, 2002

Background

In 1988, Congress enacted the Clinical Laboratory Improvement Amendments (CLIA). CLIA established "quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed." The Centers for Medicare and Medicaid Services (CMS) is responsible for implementing CLIA, including laboratory registration, fee collection, on-site surveys, and enforcement. CMS contracts with state agencies and private accreditation agencies to carry out the provisions of CLIA.

Under current law, all laboratories must be certified under CLIA[3] to perform testing on human specimens. The CLIA regulations define a laboratory as

> *[a] facility for the . . . 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. These examinations also include procedures to determine, measure, or otherwise describe the presence or absence of various substances or organisms in the body.*

Laboratories enroll in the program by completing an application and paying a certificate fee to CMS. Fees are based on type of certificate, annual volume, and types of testing reported in the application. All laboratories are required to keep CMS informed of major changes in testing, laboratory ownership, or directorship. All CLIA-certified laboratories must also comply with all state laws governing laboratories.

Types of CLIA Certificates

Each laboratory must have a certificate appropriate for the complexity of the testing conducted. All laboratory test methods have been categorized by the Food and Drug Administration (FDA) into 4 categories based on testing complexity[4]: high complexity, moderate complexity, provider-performed microscopy procedures, and waived (see Figure 1).

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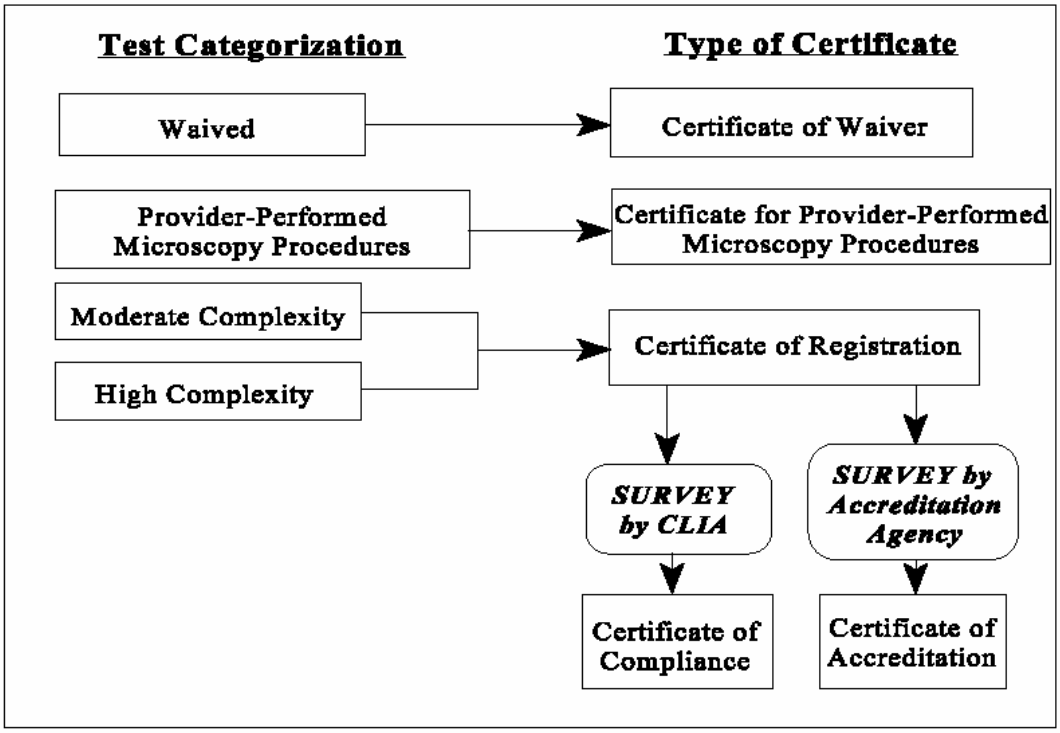
[2] Source for most of this summary: DHHS, Office of the Inspector General. *Enrollment and Certification Processes in the Clinical Laboratory Improvement Amendments Program.* August 2001. Report OEI-05-00-00251. Available at: http://www.hhh.gov/oigoei. Update with data current as of October 2001 from the CMS Web site available at: http://www.cms.hhs.gov/clia.

[3] The regulations allow for some exceptions, including forensic laboratories, research laboratories that "do not report patient-specific results," drug-testing laboratories certified by the Substance Abuse and Mental Health Services Administration, and some federal laboratories.

[4] CDC held this responsibility until January 2000.

Figure 1: Relation of test categorization to CLIA certificate type



As of October 2001, 173,191 laboratories were registered under CLIA.[5] About 91,500 laboratories (55%) had been issued a certificate of waiver (see Figure 2). Certificates of waiver are issued to laboratories that use specific test methods approved by the FDA for this category. A test may be categorized as waived if it is (a) approved by FDA for home use or (b) determined to have an insignificant risk of erroneous result, including those that

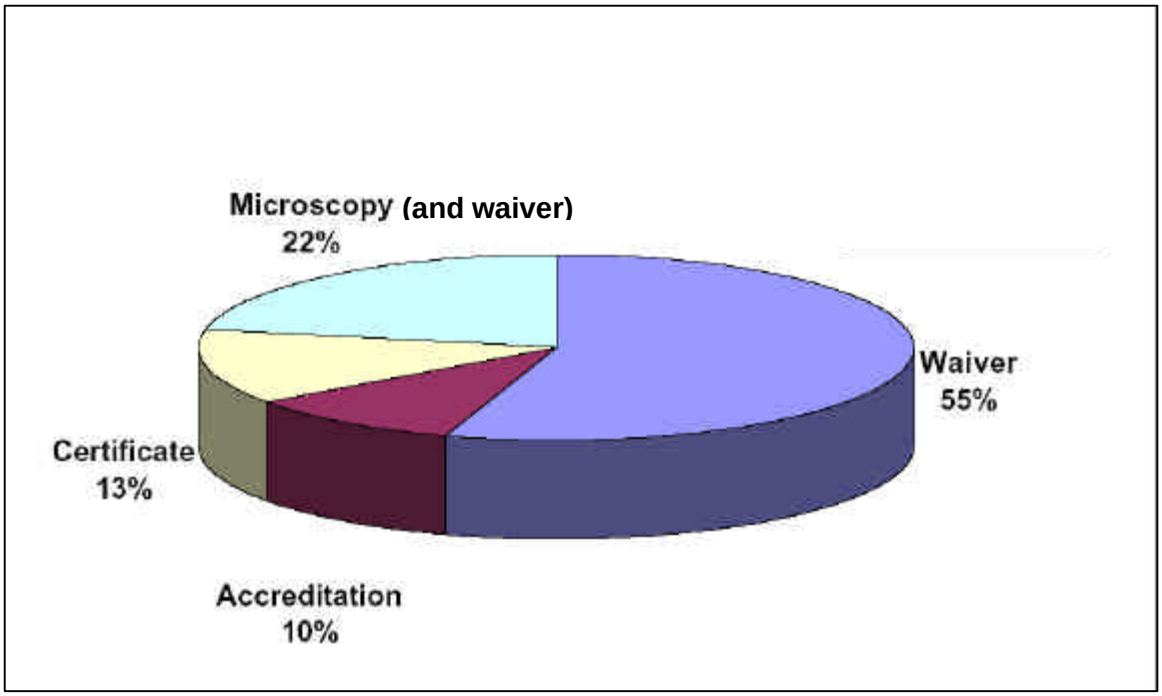
- "are so simple and accurate as to render the likelihood of erroneous results negligible, or
- the Secretary has determined pose no reasonable risk of harm to the patient if performed incorrectly." [6]

These laboratories may be surveyed if complaints are filed against them, but waived laboratories are not routinely surveyed. Approximately 36,000 (21%) laboratories hold certificates for provider-performed microscopy procedures. These certificates are issued to physicians and other approved providers who meet CLIA requirements to perform specific microscopy procedures of moderate-complexity. Laboratories with these certificates may also conduct waived tests. Like waived laboratories, laboratories with a provider-performed microscopy certificate may be surveyed if complaints are filed but are not otherwise routinely inspected by CLIA surveyors.

[5] This includes about 5400 laboratories in New York and Washington, which are exempt states. These states must show CMS that the state program meets or exceeds the requirements for laboratories under CLIA.

[6] Laboratories Performing Waived Tests, 42 CFR §493.17 (2001).

Figure 2. Percentage of CLIA laboratories by type of certificate



Source: CLIA database (as of October 2001) [CMS Web site]. Available at: http://www.cms.hhs.gov/clia.

The remaining 38,800 (22%) laboratories conduct testing of moderate or high complexity. When these laboratories initially apply for CLIA certification, they are issued a certificate of registration and a CLIA number. Laboratories with a certificate of registration can conduct testing until they are inspected. On-site inspections occur within 24 months of the filing of an application and are used to verify compliance with CLIA standards. Once the laboratory has proven to surveyors that it meets all requirements, it is issued a certificate of compliance or a certificate of accreditation. These laboratories are revisited every 2 years to verify compliance with CLIA standards.

Surveys: State Agencies, Accreditation Agencies, and CMS Regional Offices

More than half (56%) of moderate- and high-complexity laboratories are surveyed by state agencies. The CMS contracts with state survey agencies to carry out the oversight provisions of CLIA, including routine visits to laboratories as required under CLIA law. State agencies also investigate complaints and maintain records of laboratory applications and surveys in CMS databases.

Laboratories can elect to be surveyed by an accreditation agency. Accreditation agencies must be approved by CMS and demonstrate that their requirements are equivalent to, or more stringent than, CMS's regulatory requirements. CMS has contracts with 6 such agencies to provide surveys of laboratories. Examples of accreditation agencies are the College of American Pathologists and the Commission on Office Laboratory Accreditation (which primarily accredits physicians' office laboratories).

CMS's regional offices assist states in their oversight functions. Regional office staff performs on-site surveys of federally operated laboratories, state laboratories, and some county laboratories. Regional office surveyors also conduct monitoring surveys of laboratories that the state has inspected to ensure the accuracy of state inspections. In addition to surveys, regional offices provide advice to states and laboratories regarding CLIA regulations and procedures.

Waived Laboratories: Requirements

Waived laboratories are exempted from routine site visits under CLIA law and regulations, although states are not prohibited from requiring site visits to waived laboratories. The main reason there are no site visits at these laboratories is that waived tests are those that are simple, accurate, and unlikely to pose harm to the patient if performed incorrectly. For laboratories conducting these simple tests, waived (and later provider-performed microscopy) categories minimized regulatory and financial burdens. Without the cost of surveys, CMS was able to set very low CLIA fees for waived and provider-performed microscopy laboratories.

Laboratories that want to conduct waived testing must apply for a certificate of waiver. The application must describe the characteristics of the laboratory operation and test procedures performed by the laboratory, including

- The qualifications (educational background, training, and experience) of the personnel directing and supervising the laboratory and performing the test procedures

In addition, laboratories that perform waived tests must

- Make records available and submit reports to the Department of Health and Human Services (DHHS)
- Agree to permit both announced and unannounced inspections by DHHS

Under CLIA, waived laboratories are required only to follow manufacturers' instructions for waived tests and to limit testing to methods approved by the FDA as waived.

Moderate-Complexity Laboratories: Requirements and Exceptions

All laboratories performing moderate-complexity testing must obtain a separate registration certificate for each laboratory location, with 3 exceptions:

1. Laboratories that are not at a fixed location, such as **mobile** units providing laboratory **testing**, health screening fairs, or other temporary testing locations, may be covered under the certificate of the designated primary site.
2. Not-for-profit or federal, state, or local government laboratories that engage in **limited** (not more than 15 moderately complex or waived tests per certificate) **public health testing** may file a single application for a certificate.
3. Laboratories in a hospital or in buildings on the same campus may file a single application or multiple applications for sites at the same street address.

The steps required for a laboratory to obtain a CLIA moderate-complexity certificate are outlined in Table 1. Some states may have additional requirements.

Table 1. Steps for Obtaining a Moderate-Complexity Certificate for HIV Testing

Enroll in the CLIA program.

1. Complete an application for certification.
    - Form is on the CMS Web site. Description of the laboratory must include the name and number of tests and examinations performed annually, methodologies for each test, personnel qualifications.
    - Form must be signed by the laboratory owner or authorized representative
    - Once issued, the certificate is valid for 2 years.
2. Pay fee.
    - Fee is based on the annual volume and types of testing performed. .For small laboratories, the fee is about $150 for the 2-year period.

Satisfy CLIA Technical Requirements: Personnel.

1. Director[7]: responsible for the overall management and direction of the laboratory. A broad range of experience and education is acceptable, for example:
    - A physician with 1 year of experience directing or supervising a nonwaived laboratory or with 20 continuing medical education units in laboratory practice;
    - A person with a bachelor's degree and 2 years of laboratory training or experience plus 2 years of supervisory experience in nonwaived testing.
2. Technical consultant: responsible for the technical and scientific oversight of the testing. Minimum requirement is a bachelor's degree plus 2 years of laboratory training or experience in nonwaived testing.
3. Clinical consultant: provides clinical consultation. Minimum requirement is a doctoral degree plus board certification.
4. Testing personnel: responsible for specimen processing, test performance, and reporting test results. Minimum requirement is a high school diploma or the equivalent and training in the testing performed.

Satisfy CLIA requirements for quality management. The laboratory must

1. Have procedures that ensure proper patient preparation, specimen identification and integrity, monitoring and evaluation of the testing process, and a quality management system
2. Have a manual of procedures
3. Follow manufacturer's instructions for performing the test
4. Test a positive and negative control each day patient specimens are tested
5. Enroll and participate in proficiency testing (available for $135 per year in 2001)
6. Identify and correct problems or errors, and record remedial actions taken
7. Maintain test requisitions and laboratory records for 2 years

Undergo biannual inspection by CLIA or a private accrediting agency.

[7] The director, technical consultant, and clinical consultant are not required to be on-site at all times of testing. The director could, depending on education and experience, qualify for all other positions.

Categorization of Test Complexity

The complexity of each laboratory test is categorized according to 7 criteria specified in the CLIA legislation[8]:

1. Scientific and technical knowledge required to perform the test
2. Training and experience necessary to perform the test
3. Requirements for preparation of reagents and materials
4. Characteristics of the operational steps (e.g., the need for monitoring, precise timing, or extensive calculations)
5. The need for and stability of calibration, quality control, and proficiency testing materials
6. Requirements for troubleshooting and maintenance of the test system or equipment
7. Requirements for interpretation and judgment while performing the test or reading the results

Each test is graded for level of complexity by assigning scores of 1, 2, or 3 for each criterion. A score of 1 indicates the lowest level of complexity, a score of 3 the highest. Test systems receiving a score of more than 12 are categorized as high complexity. Those with a score of 12 or less are categorized as moderate complexity unless the manufacturer applies for waived categorization and the test meets the criteria for waiver.

The Health Care Financing Administration (now CMS) published proposed guidelines in 1995 to clarify the criteria for waived categorization.[9] No final rule has been published. To meet the requirements for simplicity and ease of use, the proposed guidelines require that the test system

1. Use direct unprocessed specimens, require no specimen manipulation before analysis or operator intervention during analysis, and provide a direct readout of results
2. Incorporate a fail-safe mechanism so that no result is produced when the test system malfunctions
3. Require no invasive test system troubleshooting or electronic or mechanical maintenance
4. Have instructions written at a comprehension level no higher than seventh grade. Instructions must include step-by-step information for operating the test system and for maintenance procedures, reagent preparation; storage; and action to be taken if control results are out of range.

In addition, the guidelines require field studies to ensure the accuracy and precision of the test regardless of the environment in which the testing is performed. These studies must be performed at nonlaboratory sites to ensure that all users – professionals as well as lay persons – can perform waived testing with the same competence. Study participants cannot have any laboratory experience or training.

[8] Test Categorization, 42 CFR §493.17 (2001).
[9] Categorization of waived tests: proposed rule. *Federal Register* 60:177 (September 13. 1995).

Office of the Inspector General Report on Waived Laboratories and Tests[10]

The number of waived laboratories and waived tests has increased significantly since the beginning of the CLIA program. In 1992, waived laboratories accounted for about 20% of all CLIA-certified laboratories. Today, 77% of all laboratories perform only waived tests or a combination of waived tests and microscopy. In 1992, the waived category covered 9 tests (e.g., urine pregnancy, glucose and urine dipstick or tablet analysis). Currently, about 50 tests are in the waived category. Test systems are created by manufacturers and given brand names, resulting in multiple test systems for each type of test. There were 250 waived test systems in 1995; that number increased to approximately 900 by October 2001.

During 1999-2000, the Office of the Inspector General, DHHS, conducted an analysis to identify vulnerabilities in the CLIA certification processes.[11] Among their findings are the following:

1. Significant vulnerabilities exist in CLIA's oversight of waived laboratories.

Waived laboratories are not surveyed. Therefore, surveyors do not have the opportunity to identify and correct problems or to educate untrained laboratory staff at these laboratories. During routine visits at moderate- and high-complexity laboratories, CMS uses an educational survey process by which surveyors educate noncompliant laboratories about the CLIA requirements applicable to their particular setting. About 90% of state respondents believed that the lack of routine site visits to waived laboratories presents program vulnerabilities. Fifteen states mentioned concerns about testing at waived laboratories, for example:

- failure to follow manufacturers' instructions
- failure to identify incorrect results
- testing beyond the laboratory's CLIA certificate
- untrained staff
- lack of quality controls
- poor equipment
- poor storage of reagents
- poor record keeping
- misunderstanding of CLIA requirements

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[10] DHHS, Office of the Inspector General. *Enrollment and Certification Processes in the Clinical Laboratory Improvement Amendments Program.* 2001. Report OEI-05-00-00251. Available at: http://www.hhh.govoig/oei.

[11] The Office of the Inspector General interviewed CMS central office staff and regional office staff in five regions and contacted state agencies in all 50 states, the District of Columbia, and Puerto Rico. In-person interviews were conducted with state agency staff in the District of Columbia and 11 states: Arizona, California, Delaware, Illinois, Kansas, Maryland, Missouri, New Jersey, New York, Pennsylvania and Wisconsin. The remaining 39 states and Puerto Rico completed written surveys. Overall, 52 state agencies participated in this study. Similar discussions were held with representatives from 3 accreditation agencies: the College on Office Laboratory Accreditation, the Joint Commission on Accreditation of Healthcare Organizations, and the College of American Pathologists. These 3 agencies surveyed more than 95% of the accredited laboratories in the CLIA program. Staff at the CDC and at the FDA were also interviewed (these agencies play a role in advising and assisting CMS in carrying out the provisions of the CLIA law).

2. Waived tests conducted at moderate- and high-complexity laboratories are vulnerable to noncompliance.

Routine surveys of moderate- or high-complexity laboratories do not include reviews of waived testing. Therefore, any problems with these tests would not be identified and corrected through the routine CLIA survey process. In Colorado, surveyors found that 40% of moderate- and high-complexity laboratories failed to follow manufacturers' instructions for waived tests. Surveyors had expected to find few compliance problems with waived tests in moderate- and high-complexity laboratories because laboratories are routinely surveyed to ensure quality testing. Laboratories with major compliance problems such as failure to follow manufacturers' instructions and lack of quality assurance may produce inaccurate test results and thus affect patient health.

3. Some state laboratory licensure requirements may mitigate CLIA vulnerabilities.

In most states with laboratory licensure programs, laboratory regulations are identical to, or similar to, CLIA's regulations. However, there are exceptions. Some states have processes that go beyond CLIA regulations.

About half of the states surveyed reported having a state laboratory licensure program in addition to the CLIA program. Many state programs parallel CLIA, but some allow additional actions that minimize CLIA program vulnerabilities. Ten state programs require surveys of some or all waived and provider-performed microscopy laboratories. Four states also require that all accredited laboratories be surveyed by their program.

Maryland is an example of a state with regulations and processes that bolster surveyors' ability to ensure compliance. Maryland routinely conducts initial surveys of all accredited laboratories and routine surveys of some waived and provider-performed microscopy laboratories. Unlike most states, Maryland also reviews waived and provider-performed microscopy testing conducted at moderate- and high-complexity laboratories. Maryland staff reported finding the same types of deficiencies in waived and provider-performed microscopy testing that were found in CMS studies (see following section). They reported that repeated surveys are effective in bringing laboratories into compliance. On the basis of these findings, the Office of the Inspector General made the following recommendations with regard to waived laboratories:

1. Provide educational outreach to laboratory directors of waived laboratories. Directors should be periodically informed about the CLIA requirements for the testing they conduct, as well as the limitations involved in the waived certificates.
2. Periodically, use paper self-assessment tools to help ensure compliance by laboratories that are not routinely visited. This could be a checklist of compliance requirements for waived laboratories.
3. CMS encouraged to conduct random surveys of some waived and provider-performed microscopy laboratories each year.

CMS Project: Survey of Laboratories with Certificates of Waiver or Provider-Performed Microscopy Procedures

The states of Colorado and Ohio initiated on-site inspections of a random sample of laboratories with certificates of waiver or of provider- performed microscopy procedures. These pilots consisted of focused on-site inspections (Ohio did 100, Colorado did 95) with prior notification and screening of the laboratory. Significant quality and certification problems were found in more than 50% of these laboratories. If quality problems were found, the inspectors provided assistance to the laboratories to achieve accurate results.

To follow up and verify the scope and seriousness of these initial findings, CMS expanded this pilot to include 8 additional states across the nation during October 2000 through January 2001[12]: Arizona, Idaho, Iowa, Massachusetts, Mississippi, New Mexico, New York, and Pennsylvania. Using Colorado and Ohio's pilot as a model, CMS inspected 436 (2.5%) of laboratories with certificates of waiver or provider-performed microscopy procedures in the 8 selected states. The inspections were conducted like routine compliance inspections, which entail an educational approach.

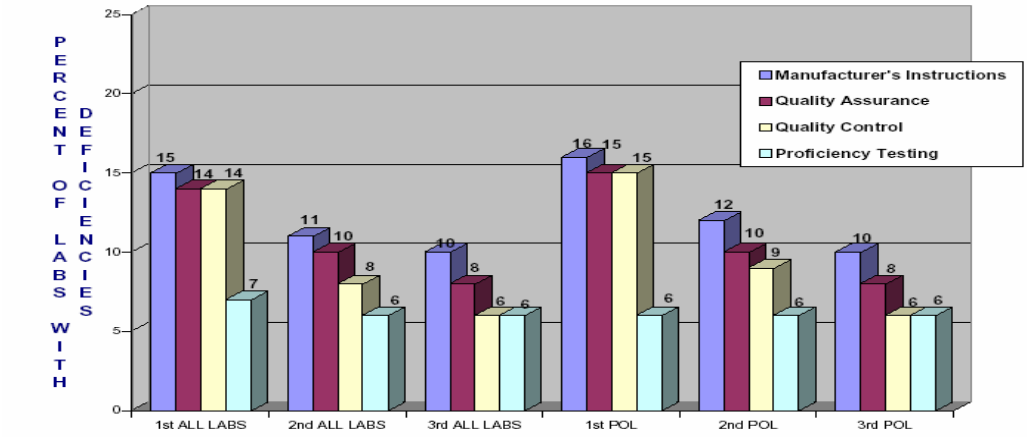
Project Findings

The information gathered during this project was separated into 2 categories: waived and provider-performed microscopy. Some of the quality problems found in waived laboratories follow:

- 32 % failed to have current manufacturer's instructions
- 32% did not perform quality control as required by manufacturer or CDC
- 16% failed to follow current manufacturer's instructions
- 7% did not perform calibration as required by manufacturer

These problems were similar in scope to those found during regular surveys of moderate-complexity, high-complexity, and physicians' office laboratories (POLs) (see Figure 3).[13]

Figure 3. TOP FOUR CLIA DEFICIENCIES CITED - 3 SURVEY CYCLES



[12] Source: CLIA database [CMS Web site]. Available at: http://www.cms.hhs.gov/clia/cowppmp.asp.
[13] Source: CLIA database [CMS Web site]. Available at http://cms.gov/clia/stat4def.pdf.

The survey project was unable to ascertain whether the quality problems in the waived laboratories were associated with poor outcomes (i.e., inaccurate test results).[14] Consistent with the findings of the Office of the Inspector General, quality problems were found much less often in waived laboratories located in states that require licensure and oversight in addition to that required by CLIA (see Table 2).

Table 2. CMS survey: comparison of results for state-licensed waived laboratories and nonlicensed waived laboratories[15]

Survey Results	State Licensure Number (%)	Non-Licensure Number (%)	Total
Lab does not have current manufacturer's instructions	18 (17%)	68 (42%)	86 (32%)
Lab does not follow manufacturer's instructions	5 (5%)	39 (24%)	44 (16%)
Lab does not perform calibration or function checks as required by manufacturer's instructions	0	20 (12%)	20 (12%)
Does not follow manufacturer's storage or handling instructions	0	23 (14%)	23 (9%)
Lab does not use reagents in prescribed order	0	0	0
Uses reagents past expiration date	1 (1%)	15 (9%)	16 (6%)
Lab does not use appropriate specimen	0	0	0
Lab does not perform QC as required by manufacturer's instructions	7 (6%)	46 (28%)	53 (20%)
Lab does not meet additional QC requirements as prescribed by CDC	2 (2%)	31 (19%)	33 (12%)
Does not provide training for testing personnel	11 (10%)	7 (4%)	18 (7%)
No evaluation of staff for accurate and reliable testing	21 (19%)	12 (7%)	33 (12%)
Testing beyond certificate level	4 (4%)	13 (8%)	17 (6%)
Operating in a manner that poses immediate jeopardy	0	0	0
Has testing personnel ever been asked to repeat a waived test	6 (6%)	30 (19%)	36 (13%)
Lab participates in PT voluntarily	11 (10%)	2 (1%)	13 (5%)
Lab performs QC beyond manufacturer's instructions	35 (32%)	8 (5%)	43 (16%)
Total of Waived Labs Surveyed	108 (100%)	162 (100%)	270 (100%)

[14] Minutes, Clinical Laboratory Improvement Advisory Committee Meeting, May 30-31, 2001. Available at: http://www.phppo.cdc.gov/cliac/pdf/CLIAC501.pdf.
[15] Presented at the Clinical Laboratory Improvement Advisory Committee Meeting, May 30-31, 2001.