



Waiver Background and Previous CLIAC Recommendations

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CLIA Law



- Specifies waiver criteria
- Exempts laboratories performing waived tests from regulation



CLIA Law



Waiver Criteria

- Approved by the FDA for home use, or
- Simple, low risk tests that
 - ❖ Employ simple, accurate methodologies with negligible likelihood of erroneous results by the user
 - ❖ Pose no unreasonable risk of harm to patients if performed incorrectly



CLIA Regulations



- Published 2/92
 - ❖ Include waiver criteria specified in the law
 - ❖ Required laboratories to follow manufacturer's instructions for waived testing
- Listed 8 waived tests



Waiver Requirements



- Laboratories performing only waived testing
 - ❖ Must register
 - ❖ Not routinely inspected
 - ❖ Exempt from CLIA standards
- Standards (personnel, PT, QC, and QA requirements) do not apply to waived testing



Waived Test Systems Listed in Regulations



- Dipstick/tablet reagent urinalysis
- Fecal occult blood
- Ovulation tests
- Urine pregnancy tests
- Erythrocyte sedimentation rate
- Hemoglobin (copper sulfate)
- Blood glucose devices (FDA-cleared for home use)
- Spun microhematocrit
- Hemoglobin single analyte instruments (1993 addition)



Initial Waiver Concerns



- Criteria unclear
- Limited number of waived tests
- 2/93 CLIAC recommended
 - ❖ Clarify statutory criteria
 - ❖ Establish moratorium



Interim Waiver Process



CDC

- 2/93 Established a moratorium on waiver
- Developed an interim waiver process
 - ❖ 12/94 lifted moratorium
 - ❖ Required manufacturers to meet statutory criteria
 - ❖ Issued waiver guidelines



Proposed Waiver Rule



Published 9/95

- Clarified waiver criteria (included waiver guidelines)
- Solicited public comment
- Received 44 comment letters



Clarified Waiver Criteria



- Simplicity
 - ❖ Defined test system characteristics (simple)
- Insignificant risk of erroneous result
 - ❖ Accuracy – reference materials
 - ❖ Precision – field studies
 - ❖ Robust – stress/flex studies
 - ❖ Fail-safe mechanism – render no result, failure alert – QC testing



Waiver Review Process



- Three routes to waiver
 - ❖ Cleared by the FDA for home use
 - ❖ Matches a test system listed in the CLIA regulations
 - ❖ Meet clarified criteria/guidelines (9/95 NPRM)



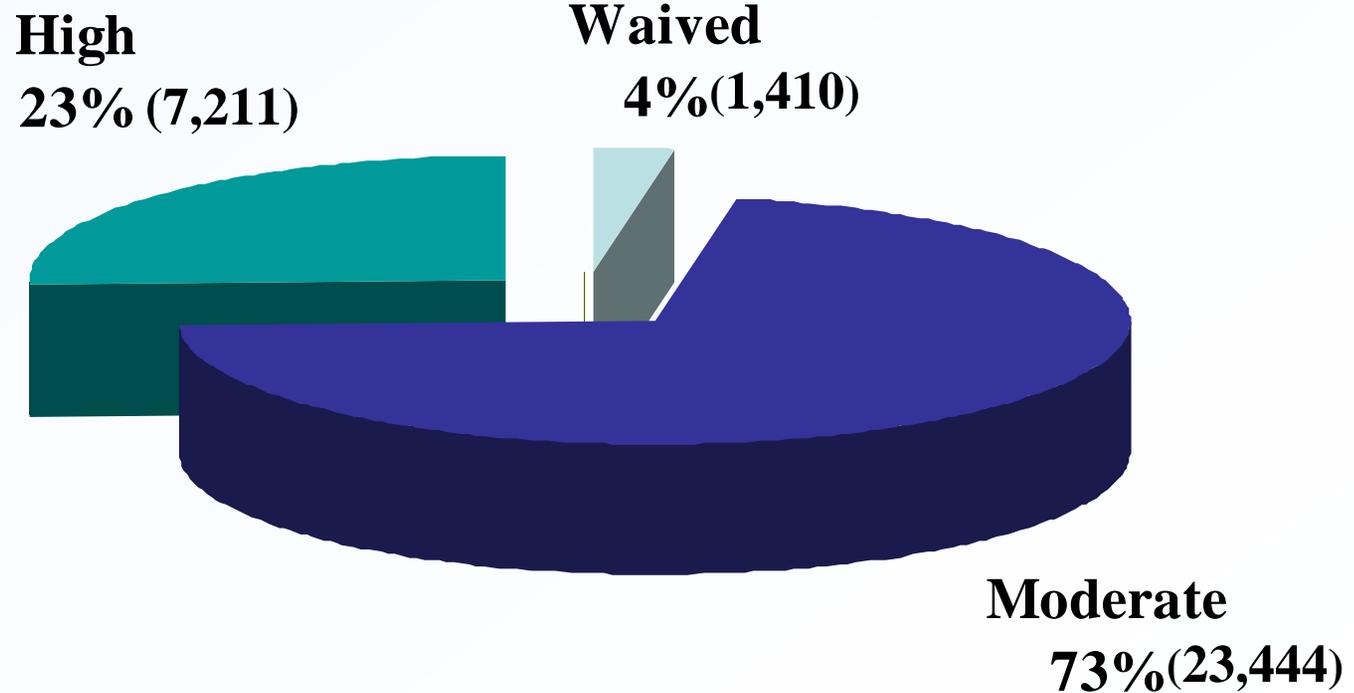
Waived Tests



- Currently, 32,065 test systems categorized (includes complexity categorizations, waiver determinations)
- 1,410 test systems waived, includes 72 analytes
 - ❖ 240 automatically waived due to home-use approval
 - ❖ 990 test systems waived by regulation (9 analytes/tests)
 - ❖ 180 waived through the review process



Percentage of Tests in Each Complexity Category





CLIA Challenges



- Ensure quality testing
- Preserve access to testing
- Cost-effective requirements
- Permit development of new technology



Waiver Challenges



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



Waiver Issues Considered by CLIAC



- Home use approval
- Accuracy
- Precision
- Risk of harm
- Appropriate tests for waiver
- QC testing
- Labeling
- Surveillance/post-approval monitoring
- General Recommendations



Home Use Approval



- Tests approved by the FDA for home use should not automatically be waived under CLIA (conflicts with the current statutory requirement)
 - ❖ Home use criteria not equivalent to other waiver approval criteria (“double standard”)
 - ❖ Home use approval should not be “back door” for waiver approval
 - ❖ Where possible, FDA should harmonize home use and waiver criteria
 - ❖ Clinical use of home use tests is off-label use - may have serious implications when home-use testing is performed in other settings



Accuracy



- Evaluate accuracy by comparing test performance to a measure of truth
- Measures of truth include reference methods, designated comparative methods, well characterized reference materials or well characterized working methods, and may include clinical evidence



Accuracy (cont.)



- Although accuracy studies are part of the FDA 510(k) clearance process, higher accuracy may be needed for waived tests than for moderate, high complexity tests
- Determine accuracy using laboratory professionals in a laboratory setting
- Use “accuracy”, “precision” and “comparability” appropriately



Accuracy – Qualitative Tests



Accuracy assessment should

- Include evaluation of
 - ❖ Clinical sensitivity
 - ❖ Clinical specificity
 - ❖ Predictive values
- Consider prevalence of disease



Precision Studies



- Studies should include a representative sample of intended user population in an intended-use setting
- Studies should show comparable performance between trained and untrained users (measure imprecision)
- To document untrained user ability to follow the package insert and perform the test correctly, the manufacturer must test the ability of the user to understand QC and test patient samples



Risk of Harm to Patients



- Impossible to objectively define “unreasonable,” “risk,” and “harm”
- All tests have some risk or harm if performed incorrectly
- tests that can’t harm a patient, can’t help a patient
- Data are needed on impact of erroneous results of waived testing
- Consider context of testing and clinical impact of waived tests
- Consider pre-analytic, analytic, and post-analytic phases of testing in assessing risk of harm and making waiver decisions



Appropriate Tests for Waiver



- Difficult to establish regulations for context of testing (e.g. use of test for screening vs. diagnosis)
- To consider waiver for screening tests requiring confirmation, need data on frequency of follow-up testing
- Screening tests should not automatically be excluded from waiver approval, but need to be evaluated on a case-by-case basis



Quality Control (QC) Testing



- Require lockout features, when feasible, to ensure QC performance and accurate results
- Require QC, rather than recommend, especially if used as a failure-alert mechanism (in lieu of fail-safe)
- Manufacturers should specify frequency and concentration levels in claims to FDA



QC Comments



- Waived laboratories tend to test QC, when kits contain QC
- Without inspections, unable to verify if QC is performed, even when required



Labeling



- Waived test instructions must be clear, easy to read and understand
 - ❖ Step-by-step instructions should be separate from other material – quick reference cards are useful
 - ❖ Visual aids (diagrams, charts, drawings) are helpful – also videos, websites, CD's
- POL's need education on test performance and importance of following test instructions, including QC testing



Labeling (cont.)



- Labeling should include
 - ❖ Test performance, and where relevant, sensitivity, specificity, predictive values
 - ❖ Prevalence data for infectious disease tests
 - ❖ Test limitations
- If testing is not appropriate for certain patients or populations, specify in labeling



Surveillance/Post-approval Monitoring



- Strong support for post-approval monitoring in rulemaking process, require surveillance of test performance following waiver approval
- Establish “sunset” provision to re-evaluate waived tests 3-5 years after approval, using field performance data
- Develop a mechanism for withdrawal of waiver approval, if post-approval performance data shows substantive variance from original waiver approval data



General Recommendations



- Base waiver decisions on science, not opinion
- Concerns about access should not outweigh issues of maintaining waived test quality
- Quality of waived tests needs to be high to offset inexperience of testing personnel
- Be conservative in establishing waiver criteria, rather than establishing permissive criteria to be upgraded later



General Recommendations (cont.)



- Since waived tests are exempt from standards and oversight, ensuring quality of this testing is critical
- Be flexible in waiver process by allowing manufacturers to show why certain criteria may not apply
- Consider requiring certificate of competence for testing personnel



AdvaMed Waiver Criteria Proposal



- 11/21/02 submitted to CMS, FDA
- 3/10/03 presentation/discussion with CMS, FDA, CDC
- Currently, seeking CLIAC comments/recommendations for HHS consideration of proposal

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