AACC
Advancing
Clinical Laboratory
Science Worldwide

May 30, 2001

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sir/Madam:

The American Association for Clinical Chemistry (AACC) welcomes the opportunity to comment on the Food and Drug Administration's (FDA's) "Guidance for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Criteria for Waiver; Draft Guidance for Industry and FDA," which outlines the agency's alternative criteria for waiving tests under the laboratory standards. We support FDA's effort to clarify the regulatory language, ensuring that the criteria are consistent with recent statutory changes.

In recent years, technological advances have allowed manufacturers to develop new and simpler devices, which make it easier for individuals with less training to accurately perform tests that were previously performed in more sophisticated laboratories. This technology-based trend is likely to accelerate in the near future. There are great benefits to simple, waived tests, such as the potential for diagnosing and treating the patient earlier and reducing overall health care costs.

However, as we move forward in this dynamic and fast growing area, it is important to remember that no device is "foolproof" and that errors can occur. Therefore, it is imperative that the FDA, Health Care Financing Administration (HCFA) and Centers for Disease Control and Prevention (CDC)—the federal agencies responsible for administering CLIA'88—remain vigilant in fulfilling their duties by ensuring that laboratories using these devices are complying with existing federal requirements.

We are particularly concerned by recent findings of the Health Care Financing Administration (HCFA) and its state survey agencies, which indicate that a significant percentage of waiver (and provider performed microscopy) laboratories are not following the manufacturer's instructions—the only substantive requirement they are subject to under CLIA'88—when performing a test. AACC is concerned that these problems could lead to inappropriate patient care. Since CLIA'88 is a jointly administered program, we urge the FDA to coordinate its CLIA activities with the other federal agencies and that you establish means for ensuring appropriate and effective federal oversight of all laboratory testing, including waiver tests. Our specific comments follow:

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General Comments

AACC applauds FDA's efforts to provide manufacturers with guidance on what information needs to be submitted for a device to be considered for waived status. Although the current document is a good start, we believe it can be improved by providing manufacturers with clearer, more precise instruction. Too often, the agency uses such words as "should" or "may," which infers that a recommendation is optional, when it appears that the intent of the agency is to require specific action. For example, the agency states that manufacturers "should" provide clear and plain instructions, "should" include specific information on how to use and interpret a test and "may" choose to include good laboratory practice information in the package insert. If the agency believes this information is essential for the end user, then it must use words such "will" or "must," which will eliminate possible confusion and future disputes.

AACC also recommends that the FDA integrate the test clearance and characterization processes so that the same individual who reviews the device submission also determines its test categorization (including waiver). We believe this change would make the process more efficient while ensuring that the FDA reviewer who is the most knowledgeable about the device (by virtue of reviewing the PMA or 510(k) application) makes the classification decision. More importantly, a single integrated process will prevent duplicate work and prevent inconsistent or conflicting decisions and recommendations.

Demonstrating Simple and Insignificant Risk

The FDA states "waived test systems should contain failure alert mechanisms that produce no result when a test system malfunctions." AACC supports the agency's recommendation. We believe it is important that a waived device not produce a result when any of the operational specifications fail to meet standards established by the manufacturer.

AACC also believes that the FDA needs to address the use of internal controls to monitor quality control (QC). These controls can provide assurance that the reagent has not expired, that the lot number of the reagent (strip, cartridge, cassette, etc.) has been calibrated, that the calibration has not expired and/or that the electronic circuitry meets operational specifications established for the device. We are concerned, however, that internal controls may not verify reagent integrity, sample application and the deterioration of disposable components of the system. For those test/assay systems where the use of internal electronic controls fails to effectively monitor this appropriate use, the FDA should require the use of additional controls, as necessary, to meet this requirement.

In addition, AACC urges that the FDA guideline require an evaluation of the recommended QC process with regards to the extent to which it has or can be expected to verify instrument performance and operation. This should be done during the PMA or 510(k) process when a manufacturer is also seeking waived status. We urge FDA to require that QC systems or processes be designed to minimize the likelihood of error, taking into consideration operator error, reagent or device failure and sample inadequacy. Although no single QC strategy should be mandatory, use of alternative systems or processes should equal or exceed the assurance offered by external QC (i.e., traditional liquid controls).

However, when a new device includes internal operational and reagent function verification, which confirms that preset operational limits are met each time a patient sample is tested, the frequency of external QC testing may be reduced, or even eliminated. Further, we believe the agency should maintain the flexibility to waive the external QC provision, on a case-by-case basis, the manufacturer can demonstrate that a particular device can detect reagent deterioration as well as other reaction errors that could result in erroneous results being reported by the test system.

Demonstrating Accuracy

The FDA states that "based on the legislative history and language incorporated into FDAMA, we interpret accurate to mean test performance (i.e., the test performs the same in the hands of untrained users as it does in the hands of laboratory professionals when using the device under realistic conditions)." We believe this is an inappropriate use of the term "accurate" as understood by the vast majority of caregivers, policymakers and the public. Using this definition may needlessly confuse caregivers about the correctness of the result. What the FDA is describing under this section is performance comparability, not accuracy. Therefore, we believe this discussion regarding ease-of-use should be moved to the "Demonstrating Simple" section.

AACC believes that waived tests should have an insignificant risk of an erroneous result and, thus, be highly accurate—therefore manufacturers should demonstrate the analytical accuracy of the test. We recommend that manufacturers demonstrate analytical accuracy by (a) comparing the test to a generally accepted or approved method, and/or (b) by analyzing well-characterized reference materials. We believe the manufacturer should be required to make a claim of accuracy against (a) or (b) above, explaining why the approach chosen is appropriate. Such assertions should include claims regarding reliability and precision, using statistical or other appropriate descriptions. AACC further suggests that the manufacturer, who is most familiar with the product and its application, be given reasonable latitude in selecting the scientific evidence and method(s) to support its claims.

Waiver Labeling

AACC supports FDA's efforts to provide users of waived devices with easy-to-understand, useful information to ensure that the device is properly maintained and able to provide accurate results. We believe the agency needs to modify its recommendations, however, to ensure that manufacturers provide more specific guidance on what QC measures should be employed by end users in order to produce accurate results. Therefore, we recommend that "should" and "may," both in this document and the QC instructions, be replaced with words that connote direction, such as "will" and "must."

Voluntary Safeguards for Waived Tests

The agency states that manufacturers should "voluntarily" make a good effort to ensure that the users of their devices are educated on how to use their products properly, as well as monitor, and periodically report to the FDA (for the first three years), waived test performance under conditions of actual use. The FDA also recommends that manufacturers include materials on the MedWatch medical products reporting program in the product labeling.

AACC agrees with these concepts, but with modifications. We recommend that manufacturers be required to:

- make available training tools (e.g., internet programs, videos, website assistance) to educate users on how to use and maintain their devices and to inform users where to call if a problem occurs with the new device;
- monitor, and be prepared to report to the FDA, how a waived test is performing for the first three years of actual use; and
- include information about the MedWatch program with waived devices, when an erroneous result could result in death or serious harm to the patient.

In addition, we believe the FDA should assume responsibility for monitoring complaints regarding waived tests during their routine audits of manufacturers. Also, the agency should consider issues and findings identified by HCFA when prioritizing such audits.

However, we believe it should be noted that the manufacturer cannot provide the effective oversight necessary for ensuring public safety, nor should a manufacturer be expected to do so. Enforcement is the responsibility of the federal government and must remain so. Therefore, we urge the FDA to work closely with HCFA and CDC to ensure that some minimal regulatory safety net is in place to protect patients from inaccurate laboratory tests.

Related Compliance Issues

AACC believes it is essential, given the likely expansion of the waiver category, and recent HCFA reports about CLIA noncompliance by waiver labs, that federal oversight of such facilities be strengthened. We believe that many of the noncompliance issues can be addressed within the existing regulatory framework. For example, AACC recommends that HCFA:

- randomly inspect a percentage of waiver labs annually to evaluate program compliance (e.g., to verify that the laboratory is only performing those tests on its certificate and the facility's personnel are following manufacturers instructions);
- use their discretionary authority to conduct follow-up inspections, when deemed necessary, on facilities with serious problems (the costs of the follow-up inspection should be borne by the waiver facility);
- develop a self-assessment tool for waiver facilities to identify, correct and report problems; and
- require that the owner/authorized representative attest in writing that the individuals doing the tests can competently perform them.

AACC believes that these changes, if implemented, will assure safe patient testing and improve the overall quality of testing in waiver facilities without significantly increasing program costs. We look forward to working with the FDA, HCFA and CDC to maintain the quality of laboratory testing, while improving the effectiveness of the CLIA program.

By way of background, AACC is the principal association of professional laboratory scientists--including MDs, PhDs and medical technologists. AACC's members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and work in hospitals, independent laboratories and the diagnostics industry nationwide. The AACC's objectives are to further the public interest and educational activities and to help maintain high professional standards.

If you have any questions or we may be of any assistance, please call me at (215) 662-6575 or Vince Stine, Director, Government Affairs, at (202) 835-8721.

Sincerely,

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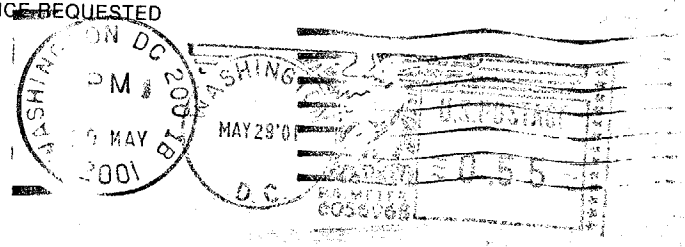

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