



CLMA: Leadership in Clinical Systems Management

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August 18, 2000  
Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20850

Dear Madame/Sir

Thank you for the opportunity for CLMA: Leadership in Clinical Systems Management ("CLMA") to present to the Food and Drug Administration ("FDA") regarding the proposed rule and criteria for "waived" tests under the Clinical Laboratory Improvement Act of 1988 ("CLIA '88"). CLMA represents more than 6,500 laboratory managers, physicians and consultants working in all settings where clinical laboratory tests are performed. CLMA members also work for medical device manufacturers who have developed many of the assays that have been approved by the Food and Drug Administration ("FDA") for "home use" and as "waived" tests. Moreover, many of the medical device manufacturers actively participate in and support CLMA activities on behalf of its members.

The active participation of the medical device manufacturers in the activities of CLMA and the large number of CLMA members who work for these companies has exposed CLMA to many divergent points of view. This is certainly true regarding the FDA criteria for approving waived tests. Thus, our comments today will be more general in nature and are tempered by the disparate opinions of our members on the issues raised today by this conference.

FDA has posed a number of questions regarding the criteria and process that should be used to determine whether a particular test should be waived. The comments that we set out below are generally intended to respond to those questions on the basis of issues or concerns raised by CLMA members regarding the current approval process.

Our first comment is directed to the criteria that should be utilized to demonstrate that a waived test is a simple examination and procedure with "an insignificant risk of an erroneous result." In the past few years there has been an increasing number of tests that are approved as over-the-counter assays for "home use" which ultimately are used in clinical settings for the purpose of relying on the information generated to make a diagnosis decision for a patient.

CLMA is concerned about the trend to have assays achieve "waived" status through the "home use" exception rather than be subject to the "waived criteria" for approval. We appreciate the fact that this is due to "analyte anxiety" as coined by Glen Neuman. A device that is approved through the "home use" exception should clearly state that it was approved under the criteria for purposes of being determined to be a "waived" test. Likewise, an assay that is approved under the "waiver" criteria would also reflect this fact in the labeling. This would provide important information to a physician when utilizing this assay in a patient care setting.

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If analyte anxiety does exist, we believe that this should be addressed up-front before the manufacturer invests significant capital for an approval that will never be received.

Moreover, assays approved for home use that are expected to be used by elderly patients, the infirm or persons with debilitating conditions, should be subject to clinical trials involving these types of individuals prior to being approved by FDA for "home use." CLMA is concerned about the clinical trials being conducted for "home use" assays and whether adequate attention is being paid to the intended patient population.

Furthermore, there should be a different threshold for tests performed by a patient in the home as compared to the same test performed in a CLIA-certified lab. If the patient in the home receives a false positive, that person is likely to seek medical advice and will likely have a confirmatory test performed by trained personnel for which the likelihood of an erroneous result is diminished. Whereas if that same assay is used to treat patients in a near patient care, hospital emergency room or physician's office, the false positive can result in inappropriate treatment being rendered. Thus, CLMA believes that the test performed in the patient care setting should be subject to more stringent criteria because of the adverse consequences to the patient based on medical treatment rendered as a result of a false positive.

In response to question three regarding risk of harm, CLMA believes that both physical and emotional risk of an erroneous result should be considered. We recognize that this a subjective criteria, but the impact of a false negative or false positive result are very real for the patient that acts upon that information. Tests for which a false negative or a false positive could have a severe outcome for the patient, such as an HIV assay, should be carefully considered for whether a home use test should ever be approved. The emotional impact on the patient of an incorrect result could be substantial. Thus, this impact should be carefully considered by the FDA in addition to the scientific criteria that would be applied.

Further, CLMA believes that the criteria for sensitivity and specificity should, at a minimum, be as stringent for "home use" and "waived" tests. Otherwise, the different standards encourage medical device manufacturers to pursue the "home use" or over the counter exception for assays for which the manufacturer has no intention of marketing the assays to be performed in a patient's home. This seems to be contrary to the original intent of approving assays for over the counter use.

It has come to our attention that there is an inconsistent interpretation between the FDA for labeling purposes and HCFA for purposes of CLIA over the interpretation of the word "recommended" when used in product labeling. If it is FDA's intention under CLIA that an action be taken, such as the performance of quality control, then use words such as "shall," "must," or "require." If, there is no expectation, then use words like "recommend." If the use of quality control is truly part of the instruction of the device, then those instructions should be included in the step-by-step instructions for use of the device.



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We want to acknowledge our strong support for statements by Dr. Statland regarding his fourth "F" - follow through. We share Dr. Statland's concerns regarding the importance of follow-through to determine if users in a clinical setting are following through on manufacturers' instructions. In addition, that the users are consistent with the users that performed the testing in the clinical trials that led to the approval of a waived test.

We also acknowledge the value of the initial findings by HCFA from the pilot studies conducted in Ohio and Colorado, which indicate there is a failure to follow manufacturers' instructions in waived laboratories. We recognize that this can lead to poor patient outcomes. Therefore, we concur with an expansion of the pilot study to other states.

Finally, CLMA urges FDA to publish its decisions regarding home use and waived tests in the Federal Register to provide the opportunity for public, industry and professional to comment prior approval. The delay associated with publication will be offset by the valuable input FDA will receive from these different segments of the public. There is a concern that input into decisions regarding test categorization is confined to a limited set of organizations and companies, while the process would benefit from a much broader range of input.

Thank you for your consideration of our comments.

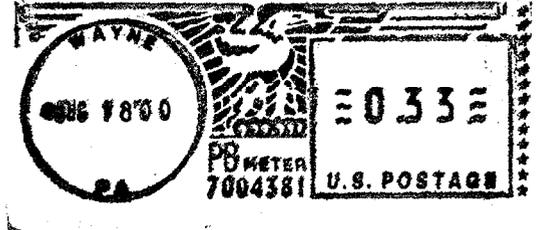
Sincerely,

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Leadership in Clinical Systems Management

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