AMERICAN SOCIETY FOR CLINICAL LABORATORY SCIENCE

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President 2000-2001

May 29, 2001

Dockets Management Branch (HFA-305)
Docket No. 01D-0044
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Dear Sir/Madam:

The American Society for Clinical Laboratory Science (ASCLS) is writing in response to the FDA's request for comment on the draft guidance document entitled "Guidance for Clinical Laboratory Improvement Amendments (CLIA) of 1988 Criteria for Waiver; Draft Guidance for Industry and FDA". We applaud the FDA for seeking such broad input and commit to continue to work with the agency on this and other related topics.

ASCLS is the nation's oldest and largest non-registry professional association for non-physician clinical laboratory professionals. The Society's mission includes promoting high standards of practice in the workplace and ensuring professional competence, while its ultimate goal is to ensure excellent, cost-effective laboratory services for consumers of health care. Our membership of nearly 13,000 includes clinical laboratory directors, managers, administrators, supervisors, and staff at all levels of practice.

We have reviewed the entire guidance document and offer the following comments and suggestions:

DEMONSTRATING "SIMPLE"

We believe that the statements, "Requires only basic, non-technique-dependent specimen manipulation" and "Requires only basic, non-technique-dependent reagent manipulation", need clarification so that it is clear what the agency means by "basic, non-technique-dependent" manipulation. ASCLS believes that the language used in the guidance document must be very specific and state that "only direct unprocessed specimens be used for waived tests", and that "waived tests should have self-contained reagent packs or pre-prepared reagents, controls, etc". ASCLS believes that any specimen

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manipulation by untrained personnel introduces the potential for error. We also believe that such personnel should not be allowed to manipulate controls, calibrators, or reagents. The remainder of the characteristics for demonstrating "simple" is very descriptive and we believe this suggested language would help manufacturers better understand the agency's intent.

DEMONSTRATING "ACCURATE"

The agency is interpreting "***accurate*** to mean test performance (i.e., the test performs the same in the hands of untrained users is it does in the hands of laboratory professionals when using the device under realistic conditions)". This interpretation is not consistent with the definition of accuracy that is acceptable in good laboratory practice. Accuracy is how close to the true value a method's results will come and is therefore an indication of the quality of the result. Precision is an indicator of the scatter of data or the quality of the method or instrument. A method can be precise but not accurate (the results are very similar but do not reflect the true value). These are the definitions and concepts upon which quality judgements of all measurements, not just the laboratory, are made.

ASCLS believes that the FDA's interpretation of accurate, as stated in this document, actually represents the precision of the method. While precision should be an important factor in determining the categorization of the test method, this interpretation eliminates the requirement, on the part of the manufacturer, to demonstrate the accuracy of their method. In proposing to use comparability studies (i.e., whether an untrained user, using the same device, can get the same result as a moderate or high complexity laboratory), the agency is using reproducibility, in lieu of sensitivity, specificity and repeatability, as the primary means for assessing the "accuracy" of a device and determining its categorization status. We believe that this is dangerous.

ASCLS commends the FDA for the precision testing requirements (number of samples, levels and sites coupled with testing done by laboratorians and lay users). They appear to be rigid enough to ensure that the test system generates consistent results regardless of the testing environment or the skills of the testing personnel. We are pleased that fail-safe mechanisms are required so that no results are produced when a system malfunction occurs.

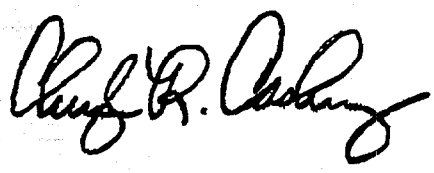
ASCLS suggests that the FDA incorporate the CDC evaluation criteria for waived tests published in 1995. Those criteria asked for a 90% specificity and sensitivity rate for diagnostic testing; we believe this requirement to be appropriate for waived systems since there will be no experienced laboratorian to assess the success of the test. The establishment of accuracy using data generated in a laboratory setting by professionals who can recognize potential pitfalls in the procedure is also appropriate. We also support the

establishment of reproducibility in the hands of lay users, including relatively untrained personnel at the point of care who will be the end users of the test. In addition, ASCLS joins the CLIAC in recommending that the FDA require manufacturers of waiver devices replace the terms "should" or "may" in their labeling instructions with "must". This would eliminate some of the confusion among certificate of waiver laboratories about whether QC is required or not for their level of testing.

Clearly defining the criteria for waived tests will likely encourage manufacturers to develop more accurate and safe technologies for waived testing, as definite market incentives exist. The growth of the current list of waived tests is, in our opinion, a testament to the ingenuity, commitment, and technological innovations of manufacturers. We congratulate all of the manufacturers who have done so much to improve the public's access to quality testing. These same manufacturers, and many new companies, are on the brink of introducing revolutionary technology that can explode the menu of waived tests. The analytes that will be tested, chemical or infectious agents, will stretch the waived criterion of "posing no reasonable risk of harm if performed incorrectly", will determine diagnostic pathways, and will be used as a basis for a clinical decision. Therefore, we must formalize a process that ensures that the tests are simple, accurate and precise. As additional tests are categorized as waived, patient access to testing should continue to improve. Absent the perceived regulatory burden of moderate complex testing, waived testing should be performed in more physician office laboratories and other sites. However, the test characteristics and criteria must be carefully evaluated so that the resulting improved access to testing truly benefits the public. If lesser standards or alternatives are allowed and test results are not reliable, then the consequences will certainly be negative.

Thank you for the opportunity to submit our comments.

Respectfully submitted,



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