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**To:**
Dockets Management Branch (HFA-305)
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**From:**
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**Re:**
Docket no. **01D-0044**

Medical Devices Draft Guidance for Clinical Laboratory Improvements Ammendments of 1988 (CLIA) Criteria for Waiver

Date prepared: May 2, 2001

Please take account of the our comments below on Medical Devices Draft Guidance for Clinical Laboratory Improvements Amendments of 1988 (CLIA) Criteria for Waiver.

**Section III.**
Demonstrating "Insignificant Risk of Erroneous Result"

Design of simple test systems and incorporation of failure alert mechanisms are incompatible goals in some cases. For example, "dip-and-read test strips" are typically simple but addition of failure alert mechanisms would greatly complicate the reading of results and add substantial



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complexity and cost. Routine testing with positive and negative controls would be the most effective means of alerting users of failure.

General Recommendations for Designing QC

Some products can be designed to withstand freezing temperatures and periods of unusually high temperatures. Adding temperature monitors and indicator desiccants will add substantial expense. These issues can be addressed adequately with studies that define the effects of stress conditions on each product.

**Section IV Demonstrating "Accurate"**

Untrained/Professional Agreement Study for Qualitative Tests

The draft guidance recommends that 300 aliquots be tested by 300 untrained users, one sample per user, and each sample be tested simultaneously by a professional. This protocol is impractical for several reasons:

1. Recruiting 300 untrained users would be nearly impossible and extremely expensive. In most cases the analytical specimens would need to be treated as biohazards and the untrained users would have to be trained on handling of biohazardous materials. They would also have to be clothed with gloves and other personal protection.

2. It is not necessary for each of the 300 aliquots to be tested by a professional analyst. Every aliquot at a particular concentration is identical; therefore, a professional analyst can run several replicates on each concentration of the analyte and these results can be compared to the untrained user data.

3. Why does the draft guidance specify that each untrained user test only one aliquot at one concentration? Each untrained user can test one aliquot at each of the four concentrations. Then 300 data points can be collected with 75 untrained users. This scheme would reduce the expense discussed in item 1 above.

4. The draft guidance emphasizes that the untrained users should not have prior experience with the test system under study. This requirement does not recognize the real world situation. First, medical personnel who are running a test for the first time are advised to read the product insert and run controls to familiarize themselves with the procedure and gain experience in obtaining the expected results. Second, the vast majority of tests will be run by personnel who have used the procedure previously, i.e. once they have conducted a test a few times they are experienced. Thus, the emphasis on untrained users for the studies is misplaced. The objective here is to ensure that untrained users can become trained to run tests properly by reading the insert and running controls.

The protocol suggested by the guidance would be too expensive for manufacturers of low volume diagnostic tests. Some tests have small markets but the tests are very beneficial to patient care. The cost of obtaining waived status under the guidance protocol would make the development and manufacture of the tests uneconomic and deprive patients the benefits such test provide. An example, is tests used by home dialysis patients annual sales of many beneficial tests are less than $50,000/year. Home dialysis allows patients to dialyze themselves daily and this frequent treatment improves their health. Daily dialysis in clinics is impractical but home dialysis necessarily requires self-testing by patients.

Performance Target for Qualitative Tests

This section recommends calculation of "odds ratios" and the 95% confidence interval without explaining the calculation. Statistics reference texts use various terminologies for similar calculations and this makes the guidance ambiguous on what is expected. The guidance should include references, the rationale for using this statistical approach and detailed examples of how the calculations should be applied.

Untrained/Professional Agreement Studies for Highly Sensitive or Specific Qualitative Tests

This section recommends that tests that perform well be tested to more rigorous standards than tests that perform poorly. This recommendation is illogical because it punishes good performance. The strategy could encourage manufacturers to "dumb down" their tests.

The section also recommends that manufacturers seek agreement with DCLD on criteria for conducting studies on high performance tests. If this recommendation is retained the guidance should name a specific contact at DCLD with a phone number, e-mail address and postal address. From experience it is impossible to communicate with DCLD on a issue unless a responsible individual is designated. DCLD does not respond to communications that are not directed to specific individuals.

**V. Waiver Labeling**

Quick Reference Instructions

The guidance requests that Quick Reference Instructions be written at 7$^{th}$ grade level. A standard is needed to define "7$^{th}$ grade level".

**VI. Voluntary Safeguards for Waived Tests**

Item #3

The guidance recommends that manufacturers submit a surveillance plan describing how they will detect unacceptable analytical bias and precision in the field. This would require customers

to run reference assays on specimens in parallel with the waived device and report the results to the manufacturer. This type of surveillance would be extremely expensive and very difficult to administer on a scale that would give meaningful data, e.g. a large number of customers would have to be monitored to give an adequate sampling of the customer population. Customers who agree to participate in the effort might not be typical of the average customers.

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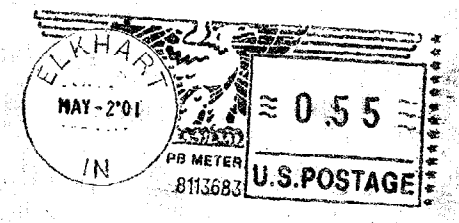


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