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VIA E-MAIL

Nancy Anderson, Chief
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Division of Laboratory Science and Standards
Laboratory Science, Policy and Practice Program Office
Office of Surveillance, Epidemiology and Laboratory Services
Centers for Disease Control
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Re: Oral Comments for CLIAC Meeting

Dear Ms. Anderson:

I am writing to provide a copy of comments that I would like to deliver orally at the November 5, 2014 meeting of the Clinical Laboratory Improvement Advisory Council ("CLIAC"). I will be attending in-person, and will present the comments within the five-minute timeframe requested by the CLIAC.

Comments for Oral Presentation

My name is James Boiani. I am a regulatory attorney and chemist, and I truly appreciate the opportunity to address the CLIAC on an important public health issue: CLIA waiver reform.

As you know, CLIA grants waived status to a test that is "so simple and accurate as to render the likelihood of erroneous results by the user negligible." In 2001, FDA stated "[b]ased on the legislative history and ['by the user'] language" added to CLIA in 1997, a test is "accurate" if it "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."[1]

[1] Guidance for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Criteria for Waiver; Draft Guidance for Industry and FDA (Mar. 2001).

In 2005, FDA moved away from CLIA's focus on equivalent performance by professional and untrained users when it proposed to add a requirement for the inherent accuracy of the test – that is, accuracy which depends upon both the user *and* the technological limits of the diagnostic. With this new requirement, which was adopted in final guidance by changing FDA's interpretation of "accurate,"[2] performing equally well in the hands of professional and untrained users is not enough to demonstrate accuracy for waiver purposes; FDA may also require a level of inherent accuracy that not even a laboratory professional could achieve with the test, thereby keeping the diagnostic from ever reaching certificate of waiver labs.

The new accuracy requirement followed on the heels of CDC and CMS surveys of certificate of waiver labs which led those agencies to conclude that some survey findings "raise[d] quality concerns about [laboratory] practices that could lead to errors in testing and poor patient outcomes."[3] (It should be noted that CMS and CDC also found that certificate of waiver laboratories "generally take measures to perform testing correctly."[4]) The new requirement seemed to be an attempt to address potential laboratory practice concerns by limiting access to waivers, but it did not address the root cause of the concern: potential for user error. Also, associated changes FDA made in recommendations for trial design to accommodate its new requirement created a variety of practical problems, and contributed to very lengthy, and in many cases unsuccessful, pursuits of CLIA waiver status.

In the years that have followed, there has been good news and bad news. The bad news: FDA's inherent accuracy requirement and associated changes have created significant barriers to approval of novel CLIA-waived tests, severely limiting access to new point-of-care testing ("POCT") options. The good news: Within the device industry as a whole, there has been an evolution in risk management thinking and human factors engineering[5] that, coupled with advances in technology, has led to the development of more user-friendly devices. Within POCT, this has meant diagnostics are now designed with more fail-safes and safeguards to guide the proper use of a test even in the hands of the most novice users.

Now is the time to revisit the inherent accuracy requirement for CLIA waivers. One reason is that newer tests address the very concerns that CMS and CDC raised previously about potential

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[2] Recommendations: Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices (Jan. 2008).

[3] Good Laboratory Practices for Waived Testing Sites: Survey Findings from Testing Sites Holding a Certificate of Waiver Under the Clinical Laboratory Improvement Amendments of 1988 and Recommendations for Promoting Quality Testing (Nov. 2005), *available at* http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5413a1.htm.

[4] *Id.*

[5] *E.g.*, AAMI/ANSI HE75:2009 (Human Factors Engineering – Design of Medical Devices), ISO/IEC 62366:2007 (Medical Devices – application of engineering to medical devices), and ISO 14971:2007 (Medical Devices – Application of risk management to medical devices). *See also* Draft Guidance for Industry and Food and Drug Administration Staff - Applying Human Factors and Usability Engineering to Optimize Medical Device Design (June 2011).

for misuse. Because waivers are being limited by a requirement that goes beyond CLIA's intent, labs may be forced to use older tests that have not been designed with modern thinking and technologies that prevent misuse. Thus, the requirement may actually perpetuate the problem it was intended to address.

Another reason to revisit the requirement is the potential public health value of expanded CLIA-waived POCT. Recognition of POCT's value was recently on display in a September 2014 Executive Order which attempts to create new incentives for POCT development.[6] With certificate of waiver laboratories accounting for the vast majority of POCT labs, expanding the armamentarium of CLIA-waived tests is essential to realizing POCT's true potential in advancing healthcare.

The benefits of POCT may come in many forms, from improved patient outcomes to reduced healthcare costs, depending upon the particular test. However, one benefit I would like to highlight today which often goes unrecognized is reducing "loss to follow-up" – a phenomenon in which patients will come in for testing but never follow-up to get results. For example, in North America, 25-30% of patients who present at health clinics for STD testing are lost to follow-up, in large part due to the time it takes to get certain test results.[7] The benefit of more CLIA-waived testing options at clinics that can provide results while the patient is in the exam room speaks for itself.

CLIA-waived tests can also benefit the 25% of Americans,[8] including 36% of veterans,[9] who live in rural communities. For these individuals, each visit to a physician or clinic can pose a challenge due to distance and limited access to transportation. Making the most of each healthcare visit by facilitating access to more in-office POCT options, thereby limiting the chances of loss to follow-up, could be a substantial benefit to many individuals in these communities.

With all of that said, I would like to make three recommendations for your consideration.

First, the CLIAC should offer its support for returning to the 2001 definition of "accurate," and the straight-forward study designs for determining accuracy, described in FDA's 2001 Draft Guidance. There should no longer be a requirement on inherent accuracy as part of the CLIA waiver process.

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[6] *Available at* http://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria.

[7] Nitika Pant Pai, MD, MPH, PhD, McGill University, CN, *Self-Testing for HIV: A Game Changer, Really?*, *presented at* AACC Critical and Point-of-Care Testing: Real World and Emerging Applications for Improved Clinical Outcomes (Sept. 2014).

[8] *See* http://www.ruralhealthweb.org/go/left/about-rural-health.

[9] *See* http://www.ruralhealth.va.gov/.

Second, the CLIAC should facilitate release of complete data regarding the CLIA Waiver Project. Although summary data have been given to the public, these might not provide a complete picture of certificate of waiver laboratory performance. For example, CMS has said that the Project suggested some concerns with laboratory practice, but it is unclear what specific tests were associated with each concern. Knowing this is important, because other studies suggest modern POCT designs help prevent most, if not all, analytical use errors.

Finally, if there is evidence that additional requirements for certificate of waiver laboratory practice are needed, the CLIAC should work with laboratories, consensus and voluntary accreditation bodies, CMS, and Congress to develop proposals that address those concerns directly through new laboratory practice standards.

I appreciate your time, and would be happy to help in any way I can to further access to point-of-care testing.

Sincerely,

James A. Boiani, M.S., J.D.
General Counsel, Coalition for CLIA Waiver Reform