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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Subject Comments regarding Draft Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications, **Docket No. 2001D-0044** issued on: September 7, 2005

Focus appreciates the opportunity to comment on the above guidance document, and applauds FDA's efforts to clarify this challenging area. We understand that the document represents the efforts of many dedicated individuals.

Focus Diagnostics, Inc., has served the healthcare community for nearly three decades as an innovative developer and provider of an array of specialized testing services, diagnostic products and anti-infective surveillance and consultative services oriented to the diagnosis, treatment and management of infectious diseases.

Since its founding Focus has evolved into a national reference laboratory that now offers its clients over 1200 infectious disease laboratory tests. It is often the first laboratory to introduce new and innovative laboratory tests. Focus' reference laboratory clients include all major US reference laboratories, many major US medical schools, hundreds of community medical centers, and many public health facilities. The laboratory is CLIA, CAP and ISO certified. Focus' ISO-certified in vitro diagnostics business is primarily comprised of products originally developed for us in its reference laboratory that were subsequently transferred into a commercial product once market demand increased and other laboratory clients wished to internalize testing. Today Focus' niche, diagnostic product line includes products for 17 infectious diseases. Focus' product portfolio includes the number one products on the market for West Nile Virus and for Herpes Simplex Virus type-specific antibody detection, HerpeSelect®.

Focus would like to comment on two items:

1. Diseases that are reportable to public health authorities should not be excluded from CLIA waived tests.
2. The study design should be clarified because many risks are already evaluated as part of the 510(k) studies.

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1. Diseases that are reportable to public health authorities should not be excluded from CLIA waived tests.

Background

In the DEMONSTRATING "SIMPLE" section, the Guidance states

" We believe that a test that is simple should not have the following characteristics:

Results need to be reported to a public health department at the state or local level e.g., tests for sexually transmitted diseases, since this is not a requirement that would be explained in the device labeling"

Summary

Focus believes that diseases that are reportable to public health authorities should not be excluded from the CLIA waived list because:

- a) The Oraquick HIV test is already a CLIA waived test.
- b) Physicians already have a legal duty to report.
- c) Reportable diseases are often the diseases that most need a quick a result so that patients get results and more effective counseling.
- d) Monitoring local authorities is burdensome and subject to local abuse.

Reasoning

- a) Diseases that are reportable to public health authorities should not be excluded from the CLIA waived list because the Oraquick HIV test is already a CLIA waived test. See "Frequently Asked Questions About the OraQuick Rapid HIV-1 Antibody Test", at <http://www.fda.gov/cber/faq/oraquickfaq.htm>. HIV is a reportable disease and a different rule for tests cleared through CDRH would cause confusion and disrespect for authority.
- b) Diseases that are reportable to public health authorities should not be excluded from the CLIA waived list because physicians already have a legal duty to report. Since the physician already has a duty to report then they should already be trained. The physicians are already reporting if they get a positive test result from a separate test site (e.g., a high complexity laboratory), and lab reports don't train how to report.
- c) Diseases that are reportable to public health authorities should not be excluded from the CLIA waived list because reportable are often the diseases that most need a quick a result. In Sexually Transmitted Diseases Treatment Guidelines 2002, CDC states that "The accurate identification and timely reporting of STDs are integral components of successful disease control efforts." Liang, et al, report that post-test counseling rate for clients tested for Oraquick was 89% for infected and 93% for uninfected, versus 11% of infected clients and 40% of uninfected clients tested for traditional ELISA test were post-test counseled. Excluding reportable diseases from being tested with waived tests will impair the public health's ability to fight these diseases.
- d) Diseases that are reportable to public health authorities should not be excluded from the CLIA waived list because monitoring local authorities is burdensome and subject to abuse. "Local authorities" is indefinite, and could be construed to include townships or authorities representing less populous areas. There are potentially innumerable authorities, requiring a major effort to identify each. There is no centralized list. Additionally, the "local authority" can be subject to persuasion by major companies to adopt new reporting requirements after the company's product was FDA cleared, thus barring competition.

Alternative Approach

In the warning section and/or the interpretation section of the package insert, include a statement "If appropriate under local or national requirements, the physician should report positive results to the public health authorities".

If the disease is a nationally reportable disease, then require that the test's intended use be limited to use by a "clinical laboratory" as defined by For CLIA's definition of a clinical laboratory. see [493.257 FR 7139, Section 493.2 Definitions](#).

2. The study design should be clarified because many risks are already evaluated as part of the 510(k) studies.

Background

Section 2. Clinical Study Design and Statistical Analysis in the IV. DEMONSTRATING INSIGNIFICANT RISK OF AN ERRONEOUS RESULT - "ACCURACY" describes studies for CLIA waiver.

Summary

Focus believes that the studies should be clarified because:

- a) Many elements of the design are already addressed in the 510(k) studies.
- b) The statistical justification for the sample size is unclear.

Reasoning

- a) Focus believes that the studies should be clarified because many elements of the design are already addressed in the 510(k) studies. 510(k) studies already address almost all risks that a waived device requires, for example, for microbiology IVDs:
 - indicated population studies estimate the risk of false positives and negatives in the most likely population,
 - sampling from different geographic areas estimates the risk of false positives and false negatives caused by geographic variation including strain variation,
 - cross-reactivity studies estimate the risk of false positives in analytes most likely to cause false positives,
 - reproducibility studies estimate the risk of lot, assay and lab variability.

The additional risk or variable that waived tests trigger is that there is a new intended user. The CLIA waived studies should focus on the new variable (new end-user) without adding risks that are already addressed in the 510(k) studies.

It is inefficient for the reviewer and the sponsor, if the CLIA studies to assess the same risks already evaluated in the 510(k) studies.

- b) The studies should be clarified because the statistical justification for the sample size is unclear. The sample size should vary with the test result's overall risk. For example, accuracy of a tuberculosis test should be higher than Lyme disease.

Alternative Approach

For high risk diseases, accuracy may have a default type 1 and 2 error of 10% or less, moderate risk diseases have a default type 1 and 2 error of 15% or less, and a low risk disease to have a default error of 20% or less. The default values impacted by the IVD's performance in the other risk assessments.

Thank you again for the opportunity to comment on the Guidance.

Please contact us if you have any questions.

Best regards,



Michael J. Wagner, Esq.
Regulatory Affairs
FOCUS Diagnostics, Inc.
10703 Progress Way
Cypress, CA 90630
T 714.220.1900
F 714.995.6921
mwagner@focusdx.com