AMERICAN SOCIETY for HISTOCOMPATIBILITY AND IMMUNOGENETICS (ASHI)

POSITION ON FDA REGULATION OF LABORATORY-DEVELOPED ASSAYS

January 27, 2015

Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Re: Response to Request for Comments on the draft guidance entitled "Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)", Date Posted: Oct 3, 2014
Federal Register Number: 2014-23596. [Docket Nos. FDA-2011-D-0360 and FDA-2011-D-0357]

Dear Commissioner Hamburg:

Thank you for the opportunity to comment on the Draft Guidance Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs). We are writing to you on behalf of the American Society for Histocompatibility and Immunogenetics (ASHI). ASHI is an international society of professionals dedicated to advancing the science, education, and application of immunogenetics and transplant immunology. As such, ASHI accredits laboratories nationally and internationally for compliance with our standards for histocompatibility and immunogenetics testing. This testing includes both HLA and non-HLA transplantation related testing and testing related to non-transplant clinical assessment of risk for certain diseases, risk for drug hypersensitivity reactions and immune function status. The Centers for Medicare and Medicaid Services have determined that ASHI's accreditation standards meet or exceed applicable CLIA requirements (Federal Register. Vol. 76, No. 78, page 22711).

We are writing to you both regarding the extent of the proposed FDA review of HLA LDTs for transplantation and regarding the extent of the proposed FDA review of our laboratories' non-transplantation LDTs. In relation to transplantation, we strongly agree with your proposal to "continue to exercise enforcement discretion for all applicable regulatory requirements for LDTs used for transplantation when used in certified, high-complexity histocompatibility laboratories".

ASHI accredited laboratories also perform histocompatibility testing for non-transplant purposes such as disease association; celiac disease, diabetes, ankylosing spondylitis, arthropathies and narcolepsy all of which have well established associations with specific HLA alleles. Other HLA alleles are important for determining possible drug sensitivities, for example HLA B*57:01 predispose patients to possible adverse reactions to abacavir, B*15:02 to carbamazepine, and B*58:01 to allopurinol. Another non-transplant purpose includes determination of vaccine eligibility such as testing for HLA-A*02:01 to determining cancer vaccine eligibility.

Additionally, HLA labs perform testing of other polymorphic loci such as KIR (Natural-Killer Cell Immunoglobulin-like Receptor), and Single Tandem Repeat (STR) polymorphisms which lie outside of the HLA region that are informational in some transplant settings (such as for critical chimerism testing after stem cell transplant) and also for other clinical purposes.

As we have previously noted, our very stringent requirements for certification of histocompatibility laboratories ensures that the tests performed in our laboratories have been subject to rigorous test validation and need to be able to be changed quickly, with appropriate additional validation, in response to changes in available reagents and new methodologies.

The development, validation and proficiency testing are all well covered under both ASHI standards and CLIA regulations. It is a point of great pride to ASHI and our member laboratories that LDTs developed in ASHI-accredited laboratories have provided reliable testing for decades, enabling countless successful transplants and great patient safety.

We are requesting that FDA continue to exercise enforcement discretion in full over all LDT histocompatibility testing for transplantation and immunogenetics testing for non-transplant clinical purposes performed in an ASHI-accredited laboratory with appropriate external proficiency testing to ensure the accuracy of their results. This would be a great help in maximizing the efficiency in which clinical testing could be provided to patients, especially considering the extensive validation these tests undergo in the course of accreditation for clinical testing purposes.

Clinical Laboratory professionals are not manufacturers; but highly trained and qualified health care providers; our laboratory testing services are dissimilar from traditional medical devices and in vitro diagnostic test kits. Therefore, the FDA should carefully evaluate its plan to channel significant personnel and monetary resources into providing an additional layer of oversight to organizations that meet or exceed applicable CLIA requirements. A health care system that is already struggling to control costs should be spared these additional financial burdens. If the FDA has a concern that CLIA fails to assess the safety and effectiveness of LDTs and does not evaluate clinical validity, these requirements can be added to existing CLIA regulations without imposing a second layer of oversight over the entire laboratory operations.

On behalf of the ASHI Board of Directors and the Accreditation Review Board, we would like to thank you for reading this letter and recognizing that ASHI-accredited laboratories, utilizing standards which meet or exceed CLIA requirements, provide outstanding clinical service and safety for patients in our institutions. After all, patient safety and successful transplant outcomes are what ASHI is all about. ASHI is available to provide any further information that may be helpful to the implementation of the proposed guidance.

Sincerely,

Malek Kamoun, MD, PhD

President

American Society for Histocompatibility and Immunogenetics.

Linda Buckert, MT(ASCP), SBB, CHS

Program Director

ASHI Accreditation Review Board