LEUKEMIA & LYMPHOMA SOCIETY®
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Division of Dockets Management
US Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

RE: Docket No. FDA-2011-D-0360, Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)

Dear Associate Commissioner Lurie:

LLS appreciates this opportunity to submit comments on the Food & Drug Administration (FDA) Draft Guidance regarding the Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs) and supports the agency's efforts to ensure that patients have access to accurate, safe, and effective diagnostic tools.

As the world's largest voluntary organization dedicated to the needs of blood cancer patients, LLS is a strong supporter of actions that will facilitate the discovery, development and delivery of new, safe, effective therapies and diagnostics for blood cancer patients.

Our mission is to cure leukemia, lymphoma, Hodgkin's disease and myeloma and improve the quality of life of patients and their families. We advocate on behalf of all blood cancer patients to ensure they have sustainable access to quality, effective, affordable, coordinated healthcare. LLS has provided more than $1 billion for research aimed at discovering, developing and delivering blood cancer cures since its founding. LLS-funded research has been part of nearly all of the FDA-approved therapies for blood cancer treatment.

Recent scientific advances have changed the way that diseases can be treated. Greater understanding of the genetic drivers of cancer have enabled the practice of precision medicine. The potential to identify and treat disease variants is becoming increasingly sophisticated. Increased diagnostic precision will allow the identification of patient sub-populations that will respond to treatment with greater benefit. In vitro diagnostics (IVDs), including laboratory developed tests (LDTs), are essential to this vital area of medical practice impacting patients across the country.

The FDA's draft guidance on LDTs is an important first step to ensuring the accuracy, effectiveness and safety of the diagnostic tools that patients need. LLS welcomes the FDA's risk based approach as well as their efforts to engage various stakeholders, including patient groups, in the development of this guidance.

As molecular and genetic tests are increasingly used to guide treatment decisions, patients should have confidence that the tests being used represent the best quality science. While the draft guidance represents an important beginning, certain issues require additional clarity or modification to ensure the continued development and availability of these critical tools that are needed in the treatment and diagnosis of blood cancers.

Scope of the Guidance

FDA's draft guidance defines an LDT as "an IVD that is intended for clinical use and [is] designed, manufactured and used within a single laboratory." However, the FDA also notes that many tests do not meet this strict definition of an LDT but are nevertheless marketed as LDTs. LLS appreciates the FDA decision to apply its LDT regulation to all of these tests in an effort to maintain uniformity in the market. The FDA's decision helps to ensure that the world of IVD regulation in not further splintered, and that there are in effect only two classifications of IVDs, i.e. IVDs developed by traditional manufacturers and LDTs created in labs.

LLS also appreciates the FDA's decision to allow LDTs to remain on the market during its review and consideration of applications, and the FDA's understanding of the need to provide continuity in the care for patients. LDTs assist many treating physicians in making important, and immediate, treatment decisions. The sudden removal of these tests from the market would present an immediate increase in the risk of misdiagnosis or delayed diagnosis for blood cancer patients.

FDA Registration and Notification Requirements

LLS supports the FDA determination to continue enforcement discretion regarding registration and listing requirements if laboratories notify FDA of their existing LDTs within six months of the publication of the final LDT guidance, and the requirement to notify the FDA of new LDTs prior to offering the LDT for use. Collecting this information is necessary for the FDA to classify LDTs and prioritize the enforcement of premarket review requirements.

Proposed Factors for Enforcement Discretion – Unmet Medical Needs

Throughout the draft guidance, the FDA lists the factors that will be considered when determining whether to apply enforcement discretion to traditional LDTs, LDTs for rare diseases and LDTs for unmet medical needs. As stated by the FDA, these factors were considered means to mitigate the potential risks posed by these LDTs. These factors include, for both traditional LDTs and LDTs for "unmet needs", a requirement that the LDT be both manufactured and used by a health care facility laboratory (such as one located in a hospital or clinic) for a patient that is being diagnosed and/or treated at that same health care facility or within the facility's healthcare system.

LLS requests that the FDA clarify further the circumstances for the use of enforcement discretion regarding LDTs for unmet medical needs outside of a single healthcare system. It is critical to recognize the importance of cancer treatment in the community setting. Many doctors, rely on existing relationships between health centers to perform uncommon diagnostic tests in the blood cancer space. This relationship ensures that blood cancer patients continue to have access to the most up-to-date testing available in a timely manner. Patients should not be required to transfer between providers in order to receive the right diagnostic or treatment. LLS believes that the current standard of care for many patients is dependent upon sharing and collaboration between academic centers and the physicians in the community, and that this collaboration is critical for the timely and accurate treatment of patients. LLS is concerned that requiring LDTs for unmet medical needs to be performed within the same healthcare facility will present potential access barriers for blood cancer patients.

Clarity Regarding the definition of an Unmet Medical Need

LLS proposes that the FDA issue further clarification regarding when an LDT will be considered an LDT for an unmet medical need. The guidance states that once the FDA approves an IVD for the same intended use as an LDT, the FDA will no longer consider that LDT to be an LDT for an unmet need. However, the guidance is unclear on how broadly or narrowly the intended use for an LDT will be construed when compared to the intended use of a newly approved diagnostic. For example, will a genetic test that examines a genetic marker for one disease state be considered to have the same "intended use" as an LDT that examines that marker for a separate disease state? Similarly, will an approved test for a larger population prevent the development of an LDT that identifies a subpopulation? LLS urges the FDA to clarify how these determinations will be made.

Proposed Factors for Enforcement Discretion - LDTs for "Rare Diseases"

In the draft guidance, the FDA has proposed continued enforcement discretion from premarket review and quality system requirements for LDTs used for rare diseases. These tests are defined as those that meet the definition of LDT and meet the definition of a Humanitarian Use Device (HDE), meaning that the number of persons who may be tested is fewer than 4,000 per year in the United States. While LLS agrees that the FDA must balance the need to mitigate the risks associated with these tests with their potential benefit for patients, LLS is concerned that limiting the rare disease exception to fewer than 4,000 persons tested per year is unduly restrictive and will prevent access to important LDTs.

Though nearly 150,000 Americans will be diagnosed with blood cancer this year, many blood cancers are diagnosed in fewer than 20,000 people per year. In the case of blood cancers, there are no screening tests, and patients are generally not tested until they present with symptoms.

Given these numbers, there is often a lack of financial incentives to conduct the large scale clinical trials required for FDA approval of tests for these conditions.

LLS requests that the FDA consider the following categories when determining whether to exercise enforcement discretion regarding LDTs for rare diseases: confirmatory tests and screening tests. Confirmatory tests are those tests performed after a patient presents with symptoms. For blood cancers, exercising enforcement discretion on confirmatory tests for rare diseases will help to ensure that these important diagnostic tools remain available. In determining whether to exercise enforcement discretion for screening tests, the FDA should consider whether the use of the test is based on an established predictive factor or if the test is widely used despite a low incidence rate of the disease. LLS requests that the FDA consider enforcement discretion for the former.

Clarity Regarding Devices Acting like Companion Diagnostics

Throughout the guidance the FDA emphasizes that it will be focusing on specific high risk tests, including "LDTs with the same intended uses as a cleared or approved companion diagnostic" and "devices that act like companion diagnostics." How clinical validity is demonstrated in IVD's and LDTs is an important focus for LLS. We request that the guidance provide additional clarity on how the FDA intends to determine clinical validity.

LLS believes that the draft guidance represents a significant step in ensuring the safety and accuracy of these critical tests for blood cancer patients. The risk-based approach outlined in the draft guidance will permit the agency to focus resources and permit the agency to continue to exercise enforcement discretion where appropriate. With additional clarifications or modifications, the guidance will both support innovation and promote the public health. Once again, LLS appreciates this opportunity to represent the voice blood cancer patients to the FDA.

Sincerely,

Bernadette O'Donoghue

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