

United States Senate

WASHINGTON, DC 20510

July 02, 2014

The Honorable Brian Deese
Acting Director
Office of Management and Budget
Executive Office of the President
725 17th Street, NW
Washington, DC, 20503

Dear Mr. Deese:

I write to urge you to take prompt action in releasing draft guidance on the regulation of laboratory developed tests (LDTs), to ensure appropriate and efficient oversight of diagnostic tools can move forward in an open and transparent manner. Signed in 1993 by President Clinton, Executive Order 12866, recognized the need for a timely and transparent regulatory review process and set, among other things, a 90-day deadline for the Office of Management and Budget (OMB) Office of Information and Regulatory Affairs (OIRA) to conduct reviews of regulatory policies. President Obama affirmed his commitment to these standards in Executive Order 13563, stating that the regulatory system must promote predictability and reduce uncertainty. However, key standards have languished at OIRA, in some cases for several years. One such item is the Food and Drug Administration's (FDA) draft guidance on the regulation of laboratory developed tests (LDTs), some of which could help diagnose specific forms of cancer and other disease conditions.

According to the FDA, laboratories initially manufactured LDTs that were relatively simple, well-understood pathology tests that could be used for low-risk diagnostics or for rare diseases for which adequate validation would not be feasible. These tests were traditionally developed to be used for a small population of local patients being evaluated by physicians at the same facility where the laboratory was located. However, over the last decade, increased understanding of genetics and the role particular genes play in disease has led to the creation of new, more complex, medical diagnostic technology. Many of these new diagnostic tools, widely developed and marketed as LDTs, are intended to help diagnose disease earlier, more effectively, less invasively or in many cases, are the only pathology test available to diagnose a medical condition. These tests and their results are increasingly relied on by patients and medical professionals to help predict the most appropriate course of treatment and care. These tests hold great promise to customize healthcare to be more efficient and targeted for an individual patient.

Because these more advanced LDTs are a staple of clinical decision-making and are being used to diagnose, high-risk, but relatively common diseases, it is imperative that they perform as they are expected. Incorrect results mean that patients either will not seek out the care and therapy that is needed, or will be subject to treatments that do not work or are harmful. Recently, the Centers for Disease Control and Prevention (CDC) reviewed a frequently utilized LDT to detect Lyme disease and found "serious concerns" about false-positive results and misdiagnosis.¹ The CDC

¹Morbidity and Mortality Weekly Report (*MMWR*), April 18, 2014. Concerns Regarding a New Culture Method for *Borrelia burgdorferi* Not Approved for the Diagnosis of Lyme Disease.

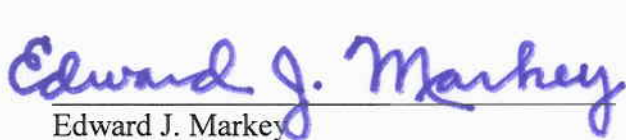
recommended that the diagnosis of Lyme disease should instead be left to tests approved by the FDA.

Currently, a diagnostic test produced by a manufacturer must first undergo an FDA pre-market review and approval to ensure the test is reasonably safe and effective. As a part of this review the FDA also assesses the clinical validity of a diagnostic test, which is the accuracy of the test in identifying, measuring or predicting the presence or absence of a clinical condition in a patient. However, an independent laboratory can develop and use a LDT diagnostic test, for an infinite number of patients, without ever being subject to these same pre-market reviews. This regulatory inconsistency can be confusing and is not always fully understood by either the patient or medical professional relying on LDTs for clinical decision-making.

Despite the fact that FDA has authority to regulate LDTs, under the Food, Drug and Cosmetic Act, historically the agency has exercised enforcement discretion—meaning that it generally did not enforce applicable regulatory requirements for these tests. According to the FDA, this enforcement discretion was used “because they were relatively simple, low-risk tests performed on a few patients being evaluated by physicians at the same facility as the lab.” However, with the advent of more sophisticated, complex, and high-risk LDTs coming to market, the FDA has recognized the importance of ensuring that all new and innovative diagnostic tools are safe and effective for use.

The FDA has developed what the agency has referred to as “risk based” draft guidance on how the agency will exercise its authority over LDTs, while recognizing the unique circumstances of the laboratory community. For years this draft guidance has languished at OMB causing continued unpredictability and uncertainty for industry, clinicians, patients and the general public. Once this draft guidance is released it will be open for public comment before being finalized by the FDA, a process that can take an additional significant amount of time. I therefore urge you to take prompt action in releasing this draft guidance on the regulation of laboratory developed tests (LDTs), to ensure appropriate and efficient oversight of diagnostic tools can move forward in an open and transparent manner.

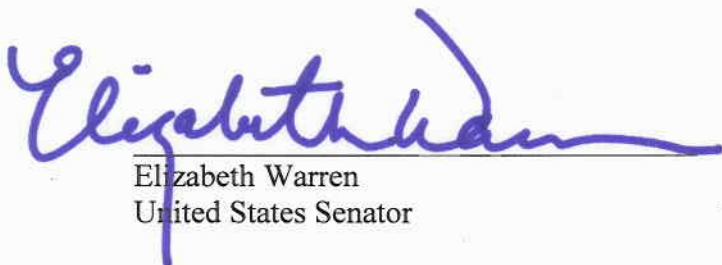
Sincerely,



Edward J. Markey
United States Senator



Richard Blumenthal
United States Senator



Elizabeth Warren
United States Senator



Sherrod Brown
United States Senator

A handwritten signature in blue ink, appearing to read "Dick Durbin", is written over a horizontal line.

Richard J. Durbin
United States Senator