January 24, 2017

The Honorable Paul Ryan
Speaker
US House of Representatives
Capitol Building, H-232
Washington, DC 20510

The Honorable Nancy Pelosi
Minority Leader
US House of Representatives
Capitol Building, H-204
Washington, DC 20510

Dear Speaker Ryan and Minority Leader Pelosi:

The undersigned organizations, representing patients, scientists, advocates, caregivers and health care professionals, urge you to make updating the oversight framework for all molecular diagnostic tests, including laboratory developed tests (LDTs), a priority early in the 115th Congress. We also believe strongly that FDA should play a critical role in a modernized framework that supports patient safety and access to valid tests.

Molecular tests have become essential tools in the delivery of 21st century medicine, helping to diagnose patients, providing prognostic information, guiding therapy selection, and helping to monitor disease trajectory. It is imperative that patients and physicians are assured of the accuracy and reliability of these test results when making vital health decisions. Currently, diagnostic tests undergo widely different levels of oversight depending on whether they are submitted to FDA for review or are offered as LDTs. Originally, the rationale for lack of FDA premarket review for LDTs was that the tests were relatively simple – like Pap smears – and generally done within the same facility where the patient was treated. As science and technology have progressed, tests are increasingly being sent to centralized labs, and the development and complexity of LDTs has grown substantially. As a result, tests that play a direct role in determining the care patients receive currently circumvent oversight.

Due to this gap in oversight of LDTs, there is no systemic way to be sure of the accuracy and reliability of these tests. Several cases illustrate the challenges with this lack of oversight. Researchers sent samples from the same cancer patients to different LDT providers for cancer testing, and found only 25 percent of the drug recommendations based on test results overlapped.[i] In perhaps one of the most shocking examples, a company performing LDTs invalidated two entire years' worth of test results after it discovered problems with tens of thousands of tests it had administered.[ii] Patients already made treatment decisions based upon invalid high-risk tests. This is an example of why proactive oversight by FDA based on a risk-based approach paradigm is necessary. The current oversight framework creates inconsistencies in oversight and can leave FDA with limited options to catch and address problematic LDTs other than public warnings when it identifies flawed LDTs.[iii]

Prevailing regulations that govern laboratory practices (Clinical Laboratory Improvement Amendments or CLIA) do not directly assess the safety and effectiveness of individual tests offered by laboratories. Under CLIA, laboratories are required to demonstrate the analytical validity of the tests they offer, that is, that the test accurately and reproducibly measures what it claims to measure. However, analytical validation of LDTs under CLIA is not as comprehensive as that required by FDA, and is not designed to ensure consistent performance for measuring the same analyte across laboratories. Moreover, CLIA does not evaluate the clinical validity of a test, i.e., the test's ability to detect the clinical condition for which the test is intended. FDA oversight of tests – including premarket review for high-risk tests – is critical to ensuring the analytical and clinical validity of LDTs.

In summary, the current system of LDT oversight is inadequate and in urgent need of updating. FDA had proposed addressing this need with a new draft oversight framework issued in 2014. FDA engaged the public in consideration of its draft proposal through numerous public forums, workshops, a lengthy comment period, and countless meetings with patients, providers, test developers, labs, and other stakeholders. Congress subsequently initiated discussions with stakeholders on a legislative proposal to update LDT oversight. Since the finalized proposal did not come to fruition through the administrative route, we urge the new Congress to continue its efforts to work with all stakeholders to craft a consensus proposal to update FDA oversight of all diagnostics, including LDTs. While we recognize that molecular diagnostics are complex and that changing the oversight paradigm will be difficult, we also know that ensuring good science will lay a strong foundation for innovation. We also believe strongly that FDA should play a critical role in any new framework. We stand ready to work with you on this important patient safety issue.

Sincerely,

Alliance for Aging Research
American Cancer Society Cancer Action Network
American Heart Association
American Medical Student Association
American Society of Clinical Oncology
American Society of Plastic Surgeons
Breast Cancer Action
C-Change
Coalition of State Rheumatology Organizations
Colon Cancer Alliance
Cure CMD
Dermatology Nurses' Association
Fight Colorectal Cancer
Friends of Cancer Research
Intercultural Cancer Council Caucus
International Foundation for Autoimmune Arthritis
LUNGevity Foundation
Lung Cancer Alliance
Lupus Foundation of Northern California
Lupus LA
Lupus and Allied Disease Association, Inc
MLD Foundation
MPN Research Foundation
National Brain Tumor Society
National Down Syndrome Society
National Infusion Center Association
National Lymphedema Network
Oncology Nursing Society
Ovarian Cancer Research Fund Alliance
The ALS Association
The Leukemia and Lymphoma Society
United Spinal Association
US Pain Foundation

cc: The Honorable Greg Walden
The Honorable Frank Pallone

[i] Kuderer, Nicole, et al., "Comparison of 2 Commercially Available NextGeneration Sequencing Platforms in Oncology," JAMA Oncology, Dec. 15, 2016. http://jamanetwork.com/journals/jamaoncology/article-abstract/2593039

[ii] John Carreyrou, "Theranos Voids Two Years of Edison Blood-Test Results," Wall Street Journal, May 18, 2016.http://www.wsj.com/articles/theranos-voids-two-years-of-edison-blood-test-results-1463616976

[iii] "The FDA recommends against using screening tests for ovarian cancer screening: FDA Safety Communication," Sept. 7, 2016. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm519413.htm