December 10, 2014

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Re: Docket No. FDA-2011-D-0360: Framework for Regulatory Oversight of Laboratory Developed Tests; Draft Guidance for Industry, Food and Drug Administration, Staff, and Clinical Laboratories

Dear Sir or Madam:

As leading organizations representing the interests of patients, providers and other stakeholders in a wide range of disease areas, we are writing to commend the release of the draft guidance on the framework for regulatory oversight of laboratory developed tests (LDTs). The draft guidance represents a critical turning point in the development of advanced diagnostics and it is essential that the FDA move forward with a transparent and open comment period to ensure appropriate and efficient oversight of safe and effective diagnostics.

Diagnostic tests play an important role in the advancement of patient care, from detection of new emerging infectious diseases and identification of effective antibiotics to the advanced molecular diagnostics that are accelerating the development and application of personalized medicine. These tests represent one of the most effective areas of healthcare, efficiently providing a wealth of information that is used by doctors and patients to make critical decisions at every stage of care. Especially because of the continuing development of new molecular diagnostics, there is a growing reliance on these tests by doctors and patients to make diagnosis and treatment decisions. This growing reliance, however, means that the risks to patients are much higher if these tests do not perform as expected. False results, or missed or incorrect diagnoses, could mean that patients either will not receive the therapy they need, or will be subject to the adverse effects and costs of a therapy that will not work for them.

Currently, a diagnostic test produced by a manufacturer and sold to a laboratory must first obtain pre-market clearance or approval from FDA to support the safety and effectiveness of the test. These tests are also subject to comprehensive quality system requirements from design through distribution, as well as post-market oversight that includes mandatory adverse event reporting and FDA's recall authority.

Laboratories that develop, manufacture and use a similar test, however, do not obtain pre-market approval for tests offered and are also not subject to a post-market surveillance system. Yet these LDTs are widely used as interchangeable with FDA-approved or cleared diagnostics, with patients or even doctors often unaware of the regulatory status of the test being used to make critical treatment decisions.

Laboratories are subject to regulatory oversight under the Clinical Laboratory Improvement Amendments (CLIA), which is run by the Centers for Medicare and Medicaid (CMS). CLIA

ensures that labs are following good lab practices including the employment of credentialed lab personnel and testing procedures set out laboratory quality standards. Unlike FDA oversight of diagnostics, CLIA **does not** regulate the safety and effectiveness of diagnostic tests, **does not** require pre-market review or a regulatory review process for tests, **does not** require demonstration of clinical validity, **does not** require independent review of clinical claims, **does not** require adverse event reporting system for tests, and **does not** have a process for corrections or recalls.

CMS, the agency that oversees CLIA, released a FAQ in October 2013 highlighting the differences between CMS review of LDTs and FDA review of IVDs. In particular, CMS itself notes:

- "[T]he regulatory schemes of the two agencies are different in focus, scope, and purpose…"

- "CLIA and its implementing regulations do not affect FDA's authority under the FDCA to regulate LDTs or other devices used by laboratories."

- "LDTs … have not undergone FDA premarket review, which assures both the analytical validity (e.g., analytical specificity and sensitivity, accuracy and precision) and clinical validity of IVDs."

- "The FDA's processes also assess clinical validity…as part of the review that is focused on the safety and effectiveness of the test system."

Congress gave FDA authority over all in vitro diagnostic (IVD) tests, including LDTs, in the Medical Device Amendments of 1976. FDA chose to exercise enforcement discretion of LDTs because, at the time, these tests were generally low-risk tests, or used for rare conditions for which adequate validation would be difficult, if not impossible. Over 30 years later, LDTs are now being used to assess high-risk and relatively common diseases and conditions and to inform critical treatment decisions. As a result, there are significant and well recognized gaps in the current regulatory environment for LDTs, including a pre-market review process to ensure safety and effectiveness of tests and a post-market surveillance system that is designed to assure quality and patient safety throughout the product lifecycle.

It has become clear that the historical paradigm that led to enforcement discretion is no longer valid. Patients and other stakeholders have recognized the growing use of LDTs and the likelihood that doctors and patients may not know whether the test they are relying on for course of treatment has been vetted for safety and effectiveness. A modernized regulatory process that encourages timely and efficient oversight of all diagnostics, regardless of where they are developed, is needed to promote innovation and ensure patient safety.

The draft guidance therefore represents a significant step forward in addressing this regulatory gap and resolving the uncertainty surrounding this critical area of medicine by reaffirming FDA's oversight of diagnostics. As proposed, the risk-based approach would allow the agency to focus its resources while supporting both innovation and the public health. This approach allows

the agency to implement a flexible, efficient regulatory approach for all diagnostics. In doing so, it balances the need for access to safe and effective tests from low-risk, small population tests, tests for unmet needs, to high-risk tests used for broad populations or as the sole determinant of a treatment decision.

The draft guidance details agency thinking into the types of tests that would be regulated and how they would be regulated. We are encouraged by this critical first step. The open comment period is an important next step. We urge the FDA to engage all stakeholders in a public and transparent process as you work toward a final guidance document in a timely manner.

Sincerely,

AIDS Institute
Alliance for Aging Research
American Association for Cancer Research
American Cancer Society Cancer Action Network
American Heart Association
American Society for Clinical Oncology
Colon Cancer Alliance
Facing our Risk of Cancer Empowered (FORCE)
National Down Syndrome Society
Ovarian Cancer National Alliance
United Spinal Association
ZERO - The End of Prostate Cancer