July 16, 2014

VIA ELECTRONIC SUBMISSION AND FEDERAL EXPRESS

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

Dear Mr. Deese,

These comments are submitted on behalf of the undersigned, who practice anatomic and clinical pathology at academic medical centers and whose laboratories develop and perform laboratory developed tests (LDTs).

As licensed, board-certified physicians and non-physician doctoral level laboratory directors practicing academic anatomic and clinical pathology, we write in opposition to FDA regulation of LDTs. Our respective academic laboratories perform millions of tests each year, and have served as centers of innovation, developing thousands of LDTs in response to unmet clinical needs, sometimes for miniscule patient populations, in order to provide the best care possible to the patients we serve.

Significantly, as lab directors and laboratorians at academic medical laboratories, we work at nonprofit entities and are singularly associated with what's in the best interest of the patient, patient care, the public health and health care innovation.

LDTs are not medical "devices" that are subject to regulation under the Federal Food, Drug, and Cosmetic Act (FDCA). We urge the Food and Drug Administration (FDA) to refrain from issuing any draft, proposed, or final guidance document or rule that would purport to regulate LDTs as medical devices.

1. LDTs Are Ubiquitous and Vital to the Practice of Medicine

LDTs are laboratory tests that hospitals, academic, and clinical laboratories develop as testing services according to their own procedures. These tests are often created in response to unmet clinical needs, and are commonly used for early and precise diagnosis, monitoring, and guiding patient treatment. LDTs are also used to diagnose and assess diseases and disorders for which no FDA-authorized test-kit currently exists, such as rare and emergent diseases, or those with small patient

populations. Nearly all diagnostic tests and FDA-approved test kits begin as LDTs, and in many cases, LDTs represent the standard of care. The ability of laboratories to develop custom diagnostic tests has been critical to the growth of personalized medicine and keeping pace with the changing face of disease to best serve patients and clinicians.

Over the last few decades, laboratory medicine has seen many exciting advances in the areas of cancer, infectious and rare disease, and numerous other health conditions. These advances have fundamentally changed our understanding of the mechanisms of disease, enabling physicians to diagnose conditions more precisely, detect the onset of disease earlier, target patient treatments more effectively, monitor disease progression, and predict individual predisposition to disease due to genetic or molecular factors. These came about because of, and would not have been possible without, the current regulatory framework governing LDTs.

2. LDTs Are Not Medical Devices

LDTs are laboratory testing services, not devices, under the Food, Drug and Cosmetics Act (FDCA). Not only are these testing services not sold into interstate commerce, but these essential laboratory services are the practice of medicine, not the manufacturing of medical devices, and accordingly, our laboratories are not medical device manufacturers. We physicians practice laboratory medicine, providing medical services to patients at the request of their primary care providers, similar to the practice of an orthopedic surgeon, or other specialists. The FDA is not authorized to regulate the practice of medicine; that oversight is left to CMS and state medical licensing boards.

3. LDTs and Performing Laboratories Are Already Highly Regulated Under A Comprehensive Regulatory Framework

America's clinical laboratories are complex health care operations staffed by highly skilled and specialized pathologists, geneticists, laboratorians and technologists operating in heavily controlled and strictly regulated environments. LDTs, and the laboratories and personnel that develop and perform them, are highly regulated under a three part framework consisting of federal regulations under the Clinical Laboratory Improvement Amendments (CLIA), state laws, and accreditation by deemed authorities such as the College of American Pathologists. As part of this oversight, clinical laboratory physicians and scientists, including most of the signatories to this letter, perform careful inspections of lab facilities, exhaustive review of test protocols and validation, and continually monitor laboratory performance. This regulatory framework requires both extensive validation and continuous monitoring to ensure the performance, quality and

reliability of diagnostic services, yet allows laboratories the flexibility to develop and validate lab tests quickly and, thus, more quickly adopt new scientific knowledge and rapidly respond to unmet public health needs.

4. FDA Regulation of LDTs Would Stifle Innovation, Be Contrary to Public Health

FDA regulation of LDTs would be contrary to the public health. Numerous critical tests are only available as LDTs, including many "gold standard" DNA sequencing assays, newborn screening tests, and tests for rare diseases. If FDA were to require clearance or approval for LDTs, laboratories may be unable to continue offering them. Some testing currently performed at laboratories as LDTs will never generate the financial returns to justify the costs of obtaining FDA clearance or approval. Patients served by these tests would be left with no testing options. Similarly, critical testing would be unavailable in the "lag time" between development of new tests and FDA authorizing them, and subsequent improvements on existing tests would slow significantly under the rigid, inflexible, and duplicative FDA regulatory scheme.

As academic medical centers, our laboratories are often called upon to meet the needs of small patient populations with a rare disease or condition. Typically there is no FDA-approved or FDA-cleared device available for testing in these rare diseases or conditions, including DNA tests for the organisms that cause Malaria and Babesia, inherited mitochondrial diseases, and severe combined immunodeficiency. The total volume for such a test may not even reach 100 tests per year.

These patient populations are often far too small to support the commitment of finances and human resources to pursue the FDA regulatory process. Even the FDA's Humanitarian Device Exemption (HDE) regulations do not adequately address this concern, because obtaining designation as a Humanitarian Use Device (HUD) and then approval of an HDE application can take years, and then use of the HUD must be under the scrutiny of an institutional review board (IRB) and subject to various FDA reporting and other requirements. This HDE process would add a burdensome and unnecessary layer of regulation on top of the CLIA regulations already applicable to the small-population LDT.

LDTs have long addressed emerging public health risks, such as HIV. For example, no HIV-1 antibodies confirmatory test was available when the HIV-1 screening test was introduced in 1985. Clinical laboratories developed and validated an LDT Western blot to meet the critical need to establish definitive diagnoses of HIV-1. It took two years before an FDA-approved Western blot test became available.

Even now, the FDA-approved Western blot kit has not significantly changed since its first approval. Because obtaining additional FDA approvals for test kit modifications would be so burdensome, the manufacturer has not modified the test to keep up to date with the medical science. As a result, FDA regulation has stifled that test's improvement and product innovation.

Academic medical centers have also developed LDTs to address other emerging infectious diseases, such as SARS and H1N1. The immediate or near-immediate response by the medical center laboratories in developing these LDTs is critical to the welfare of patients and the public health. Although FDA may authorize the use of a device under its Emergency Use Authorization (EUA) regulations, that process remains subject to time constraints, such as awaiting a declared emergency or threat and following the procedures and criteria established in the EUA regulations.

Lastly, LDTs have been instrumental in addressing some of the most widespread health crises facing our population over the last half century, particularly in the cancer space. For some of the most widely characterized cancer biomarkers, including KRAS, and others, such testing was available as an LDT long before an FDA-approved or cleared test ever reached the market, in some cases, by almost a decade. It was the validation and demonstrated viability of these vital cancer diagnostics as LDTs which made the subsequent development and commercialization of an FDA-approved or cleared diagnostic possible.

Conclusion

LDTs play a vital role in the delivery of high quality health care to patients, and have produced some of the most stunning advancements in diagnostic medicine over the course of the last 25 years. FDA regulation of laboratory developed tests would stifle the medical innovation occurring in academic medical centers today, and interfere with our ability to care for patients. We are writing you as individuals with long-standing affiliations with academic medical centers and commitment to patient care through the practice of laboratory medicine. For all of these reasons, in the best interest of the relevant agencies, Congress, stakeholders, and the American people, we collectively urge the Administration not to proceed with issuance of any guidance or regulation under which LDTs would be regulated by the FDA as medical devices.

Should you have any questions regarding this letter, please feel free to contact our spokesperson on this matter,

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cc: Howard Shelanski, Administrator of Office of Information and Regulatory Affairs (OIRA)