THE PEW CHARITABLE TRUSTS

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August 20, 2018

The Honorable Larry Bucshon, M.D.
U.S. House of Representatives
Washington, DC 20510

The Honorable Orrin Hatch
U.S. Senate
Washington, DC 20510

The Honorable Diana DeGette
U.S. House of Representatives
Washington, DC 20510

The Honorable Michael Bennet
U.S. Senate
Washington, DC 20510

Re: FDA Technical Assistance to the Diagnostic Accuracy and Innovation Act

Dear Representatives Bucshon and DeGette, and Senators Hatch and Bennet:

The Pew Charitable Trusts is pleased to offer comments on the technical assistance issued by the Food and Drug Administration (FDA) in response to the Diagnostic Accuracy and Innovation Act (DAIA) discussion draft. Pew is an independent, nonpartisan research and policy organization with a longstanding focus on the quality and safety of medical products, and our work includes research and policy analysis on issues related to the regulation of diagnostics.

The current regulatory regime for diagnostics was largely established through the Medical Device Amendments of 1976 and the Clinical Laboratory Improvement Amendments of 1988. In the intervening decades, the diagnostics market has significantly evolved. Technology, coupled with our growing understanding of molecular genetics, has enabled diagnostics to become more sophisticated, driving significant breakthroughs in diagnosis and treatment, and enabling the practice of precision medicine. However, given the growing range and complexity of these tests, as well as their importance in guiding key treatment decisions, robust oversight is important to ensuring that providers and their patients can trust the results of diagnostic tests.

Currently, diagnostics come to market via one of two divergent regulatory pathways. *In vitro* diagnostics (IVDs) are developed by device manufacturers, approved or cleared by FDA based on clinical evidence of validity, and marketed largely to laboratories. By contrast, laboratory-developed tests (LDTs)—which in many cases are substantially similar to IVDs—undergo no premarket review. This regulatory structure undermines the incentive for test developers to invest in robust premarket clinical research, and can result in tests that are neither accurate nor reliable being introduced into the health care system. LDTs are also not subject to adverse event reporting requirements, so it can be difficult to know if patients have been harmed as a result of an inaccurate test.

Over the last two decades, many stakeholders have called for reform to the current regulatory regime, with some arguing that FDA should play a greater role in overseeing LDTs.[iii] Others have raised concerns that unnecessary regulatory oversight would stifle innovation, limit patient ac-

cess to high-quality tests, and impede labs' ability to respond to public health threats and academic medicine's translation of cutting edge research to new diagnostics that directly benefit patients.[iii,iv]

Given this longstanding policy debate, Pew appreciates the attention both you and the FDA have devoted to this issue. In a market as driven by scientific and technological discoveries as diagnostics, regulations must adapt over time to meet the goals of ensuring patient safety and bringing innovative tests to market expeditiously. Policymakers should bear in mind the implications that new regulatory schemes will have on patient safety and product innovations. From our analysis of the potential risks and benefits of the various regulatory approaches that have been proposed, we submit that policymakers should consider the following principles:

Health care providers and their patients should be able to trust the results of a test, no matter where it is assembled or performed. Regulatory requirements tailored to product characteristics, as opposed to where the product is made, will provide assurance that *all* tests are of sufficient quality and reliability.

Tests should be accurate, and provide meaningful information. Patients and providers must be able to trust that a test accurately detects or measures what it seeks to measure (analytical validity), and that the information provided is relevant to the condition being diagnosed or treated (clinical validity). These are key standards that should be applied to all diagnostics.

Regulatory oversight should be tailored to risk. If an inaccurate test result is unlikely to have serious or long-lasting implications for a patient, the balance of regulatory review should favor speed to market and broader patient access. However, if the consequences of an inaccurate test are potentially serious, there should be a correspondingly greater burden on developers to demonstrate a test's analytical and clinical validity. Thus, regulatory requirements should correlate to the consequences that flow from an inaccurate test result.

The regulator overseeing tests needs access to information and the scientific and regulatory expertise to review that data. Diagnostics should be overseen by personnel with the experience and expertise necessary to ensure that tests are accurate and reliable. In order to do this, however, regulators must be able to access and evaluate information about those tests. This includes, where necessary, access to the full slate of evidence supporting the validity of tests, including those already on the market and those under development.

To promote compliance and protect patients, enforcement authority must be adequate and clear. When tests pose unacceptable risk, the agency should have the authority to take action, including the ability to remove a test from use.

Regulators need sufficient resources to ensure effective review without unnecessary delay. Whatever the funding mechanism, effective and efficient oversight requires reliable resources. As we can see in other contexts, insufficient resources leads to backlogs in application review, which in turn, leads to delays in treatment. This fails to serve the interests of patients, providers, industry, or the public health.

FDA's technical assistance proposes an oversight regime that appears to be largely consistent with these principles. The proposal would subject diagnostic tests to the same regulatory regime regardless of where they are assembled, and would establish regulatory requirements based on a test's risk. It contains broad exemptions to maximize access, but also includes a process for the agency to gather and review information about exempted tests when necessary to ensure public health. The proposal FDA has outlined is not the only possible regulatory regime that would further the principles outlined above, and though certain provisions raise questions, it contains many important elements essential to protecting patients and consumers.

Pew appreciates this opportunity to comment on your efforts to modernize the oversight of diagnostic tests. Should you have any questions, or if we can provide any assistance, please do not hesitate to contact Sarah Despres at sdespres@pewtrusts.org or (202) 540-6601.

Sincerely,

Elizabeth Jungman, J.D., M.P.H.
Director, Public Health Programs

CC: Chairman Michael C. Burgess, M.D., Ranking Member Gene Green, Chairman Greg Walden, Ranking Member Frank Pallone, Jr., Chairman Lamar Alexander, Ranking Member Patty Murray

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[i] Multi-stakeholder letter to Senate HELP and House Energy & Commerce Committees (May 9, 2018)
[ii] Sharfstein, Joshua. "FDA Regulation of Laboratory-Developed Diagnostic Tests." *JAMA* 313, no. 7 (2015): 667. https://jamanetwork.com/journals/jama/fullarticle/2089188.
[iii] Multi-stakeholder letter to Senate HELP and House Energy & Commerce Committees (June 21, 2018)
[iv] Evans, James P., and Michael S. Watson. "Genetic Testing and FDA Regulation." *JAMA* 313, no. 7 (2015): 669. https://jamanetwork.com/journals/jama/fullarticle/2089189.