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April 28, 2021

The Honorable Xavier Becerra
Secretary
United States Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Secretary Becerra,

The Pew Charitable Trusts (Pew) is a global research and policy organization dedicated to serving the public. Operated as an independent, non-partisan, non-profit organization, Pew applies a rigorous, analytical approach to improve public policy, inform the public, and invigorate civic life.

Pew's Health Care Products project advances data-driven policies that improve patient safety by reducing the risks posed by U.S. Food and Drug Administration (FDA)-regulated products. The project's current efforts focus on diagnostic tests, dietary supplements, and regenerative medicine, among others.

While the FDA plays a central and irreplaceable role in ensuring that the benefits of these and other products outweigh their risks, recent policy changes and ambiguities in the law have created serious challenges for the agency that limit its ability to respond to the current pandemic, as well as conduct other essential oversight functions. We appreciate the administration's temporary regulatory freeze announced on January 20[1] and commend the recent joint decision from the Department of Health and Human Services (HHS) and the FDA to withdraw a previous proposal exempting 84 devices from premarket review[2] which would have posed a major threat to public health if enacted. Further, we applaud the HHS decision to postpone the implementation of the Securing Updated and Necessary Statutory Evaluations Timely (SUNSET) rule.[3] If implemented, the SUNSET rule would have been an incredibly burdensome project for any federal agency to undertake, and we appreciate that HHS recognized this and took steps to address the issue. We urge the administration and HHS to permanently rescind this harmful policy and others highlighted below, and to prioritize legislative reform so the FDA can fulfill its public health mission.

**Some new HHS policies do very little to advance transparency, efficiency, or accountability within FDA and should be immediately rescinded.**

[1] https://www.whitehouse.gov/briefing-room/presidential-actions/2021/01/20/regulatory-freeze-pending-review/
[2] https://www.federalregister.gov/documents/2021/04/16/2021-07760/making-permanent-regulatory-flexibilities-provided-during-the-covid-19-public-health-emergency-by
[3] https://www.federalregister.gov/public-inspection/2021-05907/securing-updated-and-necessary-statutory-evaluations-timely-administrative-delay-of-effective-date

- **A final rule mandating job reviews be conducted every five years for FDA Center Directors** and their equivalents across all operating divisions in HHS.[4] Placing career civil servants under formal review on a regular basis to determine whether they should be retained or reassigned could have a range of negative consequences, both for the FDA and for public health. Most concerningly, it could make senior staff more susceptible to political pressures, particularly if they know their position may be threatened by taking a politically unpopular stance. One of the key lessons of the pandemic is the need for strong public health agencies that are driven by science—this policy could further undermine confidence in the FDA's independence from politics as well as confidence in the safety or effectiveness of products reviewed by the agency.

- **The August 2020 announcement declaring that FDA could not require premarket review of lab-developed tests (LDTs)**.[5] This not only eliminated a critical quality check on those COVID-19 tests developed by labs, but also stripped FDA's ability to require premarket review for any LDT—whether for COVID-19 or for other areas where such tests are widely used, such as cancer and prenatal screening. This decision is extremely shortsighted given that the FDA recently evaluated 125 Emergency Use Authorization applications from labs—the main producers of LDTs—and found that among them, 82 had design or validation problems that needed to be addressed before they could be offered to patients.[6] Now, LDTs for the novel coronavirus are not required to be subject to even these baseline FDA quality checks and could make it to market unabated.

  Furthermore, this sudden change in HHS policy casts doubts on FDA's ability to protect patients if it does learn of a faulty LDT on the market. The statement announcing the decision indicated that the FDA could undertake formal rule-making—a process that often takes years—to establish premarket review requirements for LDTs, but it failed to specify whether FDA's other regulatory authorities for diagnostics—such as the power to conduct lab inspections or recall tests—were still in effect. In a subsequent statement, the Department later clarified that LDTs remain subject to FDA regulation under the Public Health Services Act. However, legal and regulatory analysts question whether the oversight and enforcement authorities necessary to shield patients from bad tests are available to the agency under this statute.

**Legislation is needed to update FDA's regulatory oversight of diagnostic tests and to provide regulatory certainty.**

The question of FDA's jurisdiction over LDTs has been debated for many years, and was only complicated by the HHS announcement last year. While it is important to immediately reinstate FDA's ability to review COVID-19 LDTs prior to their use on patients, the administration

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[4] https://www.hhs.gov/about/news/2021/01/15/hhs-issues-final-rule-increase-professional-development-opportunities-career-civil-servants-harmonize-hr-practices.html

[5] https://www.hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html

[6] https://www.nejm.org/doi/full/10.1056/NEJMp2023830

should also prioritize reforming the entire diagnostic testing regulatory regime under the oversight of FDA.

There are several reasons why current diagnostics oversight is insufficient. First, LDTs perform the same clinical function as commercial diagnostics, but are not held to the FDA's standards for quality or validity. Instead, they are primarily regulated under the Clinical Lab Improvement Amendment (CLIA) regulations that govern laboratory operations. Regulatory oversight should correspond to a test's risk and complexity, rather than where it is developed. Second, the lack of transparency in the diagnostics market makes it difficult to identify risky LDTs once they have been introduced. LDT developers are not required to register their tests with the FDA or publicly disclose any adverse events arising from their use. This makes it challenging for federal regulators to identify emerging risks to public health and respond appropriately.

Finally, excluding a large proportion of tests from FDA review distorts the diagnostics market. Holding comparable tests to different standards based on where they are developed and used creates an uneven playing field between LDT developers and other diagnostic developers. The cost of demonstrating safety and effectiveness through FDA's approval process limits developers' incentive to invest in the research that could make a test more accurate and clinically meaningful, and instead provides an incentive to simply market an LDT.

The current crisis has further highlighted the urgent need for a uniform, commonly understood regulatory framework for all in vitro clinical tests and one that appropriately balances the need for rapid innovation with the need to ensure test quality. For example, in the early weeks of the pandemic, several laboratories reported difficulties in navigating the FDA review process, in many cases because they were unfamiliar with the agency's requirements. Device companies, by contrast, were in some cases able to obtain emergency use authorizations (EUAs) in as little as 24-48 hours after they submitted their applications.

Rather than forgoing FDA review of all tests developed and used within the same laboratory—the approach adopted by HHS in August—the administration should establish a universal framework for all tests that would help to avoid such challenges in the future and improve regulatory oversight of these important public health tools. FDA has a critical role to play in ensuring test reliability and quality. This was made particularly clear last spring when the agency briefly waived EUA requirements for antibody tests. Many of these tests produced unreliable results and within weeks, the agency reversed its policy.[7] FDA's validation and review procedures, through EUAs and the existing 510k frameworks, are designed for this purpose and should not be circumvented.

COVID-19 is not the only example of when LDT oversight has fallen short. In June 2008, LabCorp began offering a new test called OvaSure, which was marketed as an LDT that could detect ovarian cancer at an early stage in high-risk populations—such as women with a family history of the disease. Unfortunately, subsequent evaluations found that the test developer had miscalculated the degree to which a positive test result was predictive of cancer. In fact, only 1 of every 15 positive results was accurate, potentially leading to unnecessary and invasive surgery

[7] https://www.politico.com/news/2020/05/04/fda-enacts-stricter-rules-for-antibody-tests-after-congressional-investigation-233867

to remove the ovaries.[8] Four months after the test's introduction on the market, the FDA sent a warning letter to LabCorp, outlining its concerns about the test's lack of clinical validation.[9] LabCorp stopped offering the test the following month. However, because the test was offered as an LDT, the company did not report any adverse events associated with its use, so the scale of its impact on patients is not fully known. Another well-known example is Theranos, a diagnostics start-up that deployed LDTs, claiming they could diagnose a range of diseases using just a few drops of blood. The company was ultimately sanctioned by CMS and two of its leaders were charged with fraud, but it was able to operate for many years before the problems with its test were brought to light.[10] Though Theranos was not representative of the broader laboratory industry, like any other test developer, the company had an incentive to offer their tests as LDTs because this meant they would not be subject to FDA's premarket requirements. Both of these examples highlight the risks associated with CLIA, which does not require premarket review even for high-risk tests. Patients may be exposed to unreliable tests for years before regulators learn of any potential issues.

**Conclusion**

These recent policies by HHS undermine our health agencies at a time when our country needs them most. In order to unleash the full potential of the FDA, it will be vital to reinstate authorities such as premarket review of LDTs, while also rescinding burdensome mandates like sunsetting regulations every ten years. Furthermore, given the central role that diagnostics play in informing treatment decisions for conditions such as infectious diseases and cancers, it is imperative that the administration prioritize the establishment of a risk-based regulatory framework that governs all diagnostics, regardless of where they are developed and used.

Please consider us a resource and should you have any questions or if we can be of assistance, please contact Elise Ackley at 202-540-6464 or eackley@pewtrusts.org.

Sincerely,

Liz Richardson
Project Director
Health Care Products
The Pew Charitable Trusts

[8] https://www.nature.com/news/2011/110323/full/471428a.html
[9] https://wayback.archive-it.org/7993/20170112200113/http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2008/ucm1048114.htm
[10] https://www.justice.gov/usao-ndca/us-v-elizabeth-holmes-et-al