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Commissioner Robert Califf, M.D., MACC.
U.S. Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

December 1, 2023

Re: Docket No. [FDA-2023-N-2177](#) Medical Devices; Laboratory Developed Tests

Dear Commissioner Califf:

On behalf of the U.S. PIRG (Public Interest Research Group) and our two dozen state affiliates, I am submitting comments on the U.S. Food and Drug Administration (FDA) proposed rule on laboratory developed tests, published October 3, 2023 in the Federal Register.¹

U.S. PIRG is a 50 year old nonprofit consumer advocacy organization. We speak out for a healthier, safer world which includes promoting policies that support the delivery of the high value healthcare we deserve. For laboratory tests, high value is achieved when diagnostic tests, which patients, insurers and our government health care programs pay for, deliver reliable and accurate results that result in improved patient care. Diagnostic tests can be expensive and their results drive even larger amounts of avoidable health care spending if they inaccurately point to a diagnosis that leads to unnecessary (and potentially dangerous) care. The public relies on the mission of the FDA to ensure the medicines and devices used by health care professionals are safe and effective.² We applaud the aims of this proposed rule to drive higher value care for laboratory tests by developing a regulatory scheme to improve their usefulness and accuracy.

The proposed rule is essential to patient safety and recognizes the modern LDT market.

Overall, U.S.PIRG supports this proposed rule to clarify and strengthen the agency's enforcement role over laboratory-developed tests (LDTs). We have been advocating for changes in FDA oversight and enforcement of quality standards for the many LDTs used by health care professionals and sometimes by consumers themselves. We applaud the FDA for recognizing that health practices have changed over the four decades since the Medical Device

¹ Federal Register, 88 FR 68006, October 3, 2023, <http://www.federalregister.gov/documents/2023/10/03/2023-21662/medical-devices-laboratory-developed-tests> accessed on November 30, 2023.

² FDA Mission, FDA: What we do, <https://www.fda.gov/about-fda/what-we-do#:~:text=FDA%20Mission,-The%20Food%20and&text=FDA%20is%20resp onsi ble%20for%20advancing,maintain%20and%20improve%20their%20health> accessed on November 30, 2023.

Amendments of 1976³ (the MDA) established FDA regulation of devices intended for human use. This proposed rule will clarify that LDTs are medical devices and will phase out FDA “enforcement discretion” - two important steps to regain FDA’s power to ensure safety and efficacy of *all* medical devices, including those developed and manufactured in laboratories.

LDTs have operated outside of key regulatory oversight for decades. This proposed rule will require the same level of scrutiny of LDTs as other medical devices. With the adoption of this rule, patients and their doctors will be assured that the tests used for diagnosis and treatment of medical conditions and diseases are reliable, accurate, effective and safe.

Over time, LDTs have gotten more complex and are being used in larger patient populations than before. And LDTs are used to develop treatment plans for complex conditions. LDTs are no longer being used only on small patient populations in one site of service. Today, laboratories are taking in large numbers of testing samples from around the country so the impact of even one inaccurate test can be affecting thousands of lives. It is crucial to have accurate and reliable tests. For these reasons and more, there is much more at stake when LDTs are allowed on the market without needing to prove clinical validity, demonstrating that the results show the presence or absence of the condition or disease. This proposed rule will set the FDA on the path to enforcing important standards of validity that are imposed on other medical devices. And greater oversight will better enable the FDA to identify and quantify problems with LDTs already on the market.

The FDA must ensure that LDTs are reliable because patients and their doctors develop treatment plans based on their results.

PIRG and other patient and public health advocates have called for stronger regulatory oversight of LDTs to ensure accuracy because LDTs are used to determine patient treatment plans. These tests must be highly reliable and not lead to misdiagnoses. It is the only way to prevent harm to patients. Consider the impact of inaccuracy:

- LDTs that present a “false negative” result by inaccurately “clearing” a patient of a serious condition, cause delay in treatment, with serious and sometimes deadly consequences for the patient.
- LDTs that show a “false positive” result by inaccurately diagnosing a condition that the patient doesn’t have or by measuring levels of a condition inaccurately can result in unnecessary or inappropriate care that could result in physical and psychological harm to the patient.

The extensive impact of unreliable LDTs.

A recent example demonstrates the broad impact when LDTs are marketed without proper oversight to determine clinical validity, reliability and accuracy. During the COVID-19 pandemic, people in the U.S. relied on LDTs to determine whether they had the contagious virus. One

³ Medical Device Amendments of 1976, Public Law 94-296, <https://www.govinfo.gov/content/pkg/STATUTE-90/pdf/STATUTE-90-Pg539.pdf> accessed on November 30, 2023.

study showed that of 152 LDTs, 82 had design or validation problems.⁴ Health care and social decisions were made based on the results of those tests. We won't be able to quantify how many were exposed to the virus because someone relied on a false negative COVID test and how many weddings, funerals and other important life moments were missed because of a false positive test. We can't even begin to quantify the wasted taxpayer dollars spent providing families with free COVID tests that were inaccurate or unreliable.

The wasted costs of inaccurate LDTs.

When measured, the cost to patients and the government can be astronomical if a test inaccurately makes a diagnosis. One study “assessed the clinical and economic impact of inaccurate test results between laboratory developed tests (LDTs) and a US Food and Drug Administration (FDA)-approved test for detection” of a marker for metastatic non-small cell lung cancer. The analysis showed an additional \$7.3 million in treatment costs could be avoided if the more accurate FDA test had been used for the cohort of 60,500 patients.⁵ This doesn't attempt to capture the cost of the patient and family anguish for those who were misclassified and thereby mistreated.

Key strengths of the proposed rule.

- The proposed rule includes LDTs created in academic medical centers (AMCs) to be regulated as medical devices. Despite strong opposition from the AMCs to regulation of LDTs, the proposed rule is correct in refusing to carve-out these centers. As the proposed rule itself states, “This amendment would reflect that the device definition in the FD&C Act does not differentiate between entities manufacturing the device...” It is inappropriate, therefore, to exempt from oversight those LDTs developed in AMCs. An exemption makes no sense. Every entity that creates a LDT should be held to the same standard to allow patients and their providers to trust in the tests they use. How are patients to know which tests are from an AMC and therefore have not undergone the process to prove clinical validity? Patients deserve accurate tests, regardless of *where* that test originates.
- The proposed rule includes tests for rare diseases to be regulated as medical devices. Patients with rare diseases should be equally protected from inaccurate tests, especially because the options for treatment might be difficult and expensive to obtain. Misdiagnosis is unacceptable in any circumstance and can be even more deadly when the disease is not as common and health practitioners have only a test, and no personal experience to rely on.
- The proposed rule would mean that all tests would be registered and listed to allow the FDA and the public to know which tests are available and have undergone review. LDT manufacturers under this rule would now be required like other medical devices, to

⁴ Jeffrey Shuren, MD and Timothy Stenzel, MD, Covid-19 Molecular Diagnostic Testing — Lessons Learned, New England Journal Of Medicine, October 22, 2020, <https://www.nejm.org/doi/full/10.1056/NEJMp2023830>

⁵ Mindy M. Cheng, et al. The Clinical and Economic Impact of Inaccurate EGFR Mutation Tests in the Treatment of Metastatic Non-Small Cell Lung Cancer, Journal of Personalized Medicine Sept 2017, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5618152/>

publish performance data, improving transparency about the clinical and analytical validity for their tests.

We recommend that a swifter time frame for full implementation be adopted.

Our one concern is that the proposed rule means that patients won't be able to fully rely on accurate LDTs until at least four years from the date this proposed rule is finalized and implemented. A phased-approach will ensure a comprehensive roll out of this important program. However, we would expect, if LDT manufacturers were doing the right thing from the beginning, they would not need a long ramp-up time to prove that their tests are accurate and reliable. LTD creators are under a professional code of honor to make sure that their tests do what they claim they do. This rule merely asks them to provide FDA the very information they should have relied upon to put the test into the market.

FDA should prioritize its own work to ensure the process is clear and science-based. However this long lead time for full implementation means that patients and their doctors will be operating under uncertainty for another four years at a minimum. Lives are at stake when patients are misdiagnosed. Dollars are wasted with every inaccurate test on the market. We urge an accelerated time frame for implementation than proposed in the year.

We applaud the rule and urge the FDA to finalize the rule swiftly so the process to improve diagnostic accuracy of laboratory developed tests will begin.

The information gleaned from accurate LDTs is as important to patient care and safety as the drugs or medical devices used to treat them. The proposed rule sets up a patient-centered regulatory framework by establishing greater scrutiny over LDTs to avert misdiagnosis and inappropriate treatment as well as result in more timely diagnosis by eliminating from the market those tests that don't pass the regulatory standards. As an added bonus, more reliable testing will prevent wasted health care spending by our public health programs, insurers and patients. Ensuring more accurate lab test results will eliminate the need for unnecessary treatment and procedures.

Thank you for your consideration.

Respectfully submitted,



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