CENTER FOR Science IN THE Public Interest
Your Food and Health Watchdog

May 9, 2025

Martin A. Makary, MD, MPH
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Submitted via email to: Commissioner_Writein@fda.hhs.gov

Dear Dr. Makary,

We write to you regarding the District Court for the Eastern District of Texas's March 31 decision in an industry-initiated lawsuit challenging FDA's authority to regulate Laboratory Developed Tests (LDTs). As you know, the court ruled, in its primary finding, that LDTs are services, not devices, thereby setting aside a final rule that had been in the works at FDA for years.[1] We expect the Agency is concerned about an opinion that removes authority from FDA over an important subset of medical products and erodes the Agency's authority to ensure safe and effective diagnostics are on the market.

As the Agency considers next steps, we urge you to keep in mind that the regulation of LDTs is a public health issue, not something to be solved through a district court decision that is riddled with factual errors in a cherry-picked jurisdiction. Of course, we understand that there are strategic concerns involved in the decision to appeal, including the potential for an adverse decision at the appellate level. We write to offer our insights into the District Court opinion so that all sides of the argument are available to you to determine how best to proceed.

Founded in 1971, the Center for Science in the Public Interest (CSPI) advocates for evidence-based and community-informed policies on nutrition, food safety and health; holds government agencies and corporations to account; and empowers consumers with independent, unbiased information to live healthier lives. CSPI has advanced efforts towards LDT regulation, including filing an amicus brief in support of FDA's position in the district court litigation over the LDT final rule. We accept no corporate donations. We are joined in this letter by a number of leading academic physicians and scholars.

We trust that you recognize the importance of accurate diagnostics and companion diagnostics based on your experience as a physician who has cared for countless cancer patients. Tests that may be useful in determining the course of a pancreatic cancer patient's

[1] *Am. Clinical Lab'y Ass'n v. United States FDA*, No. 4:24-CV-479-SDJ, 2025 U.S. Dist. LEXIS 59869 (E.D. Tex. Mar. 31, 2025).

treatment, such as NTRK1/2/3 or MSI-H, must be accurate and reliable.

However, the court's opinion was based on a number of misinterpretations and erroneous readings of facts, resulting in a misapplication of the law. We summarize these concerns below:

Role of CLIA

The court misunderstood the role of the Clinical Laboratory Improvement Amendments ("CLIA"), a statute enforced by the Centers for Medicare & Medicaid Services (CMS), stating that CLIA was enacted to create a "single…system for the federal regulation of laboratory test services." FDA and CMS have, for more than a decade, attempted to clarify the role of CLIA with respect to LDTs—that only FDA can review a test before it is introduced on the market, before patients and providers have been exposed to potentially erroneous results.[2] In 2015, a Deputy Administrator of CMS, Dr. Patrick Conway, testified before a House Subcommittee:

> *On the other hand, CMS does not have scientific staff capable of reviewing complex medical and scientific literature in determining clinical validity. This expertise resides within the FDA, which assesses clinical validity in the context of premarket reviews and other activities aligned with their regulatory efforts under the Food, Drug, and Cosmetic Act.*[3]

CLIA does not ensure clinical validity of tests before they are performed—it only ensures analytical validity, and even then only *after* the tests are already being performed on patients[4]— but FDA regulation does.

Authority

The court stated that FDA "first suggested that it might possess authority" to regulate LDTs in 1992.[5] However, as noted in our *amicus* brief, FDA published a notice of its intent to

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[2] CMS, *LDT and CLIA FAQs* (2013) *available at* https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/ldt-and-clia_faqs.pdf.

[3] Testimony of Dr Conway before the House Energy & Commerce Committee, Subcommittee on Health, Nov 17, 2015. *available at* https://docs.house.gov/meetings/IF/IF14/20151117/104127/HMTG-114-IF14-20151117-SD015.pdf.

[4] "CMS regulates laboratories that perform testing on individuals in the U.S. through the [CLIA] by establishing quality standards for all laboratory testing to help ensure the accuracy, reliability and timeliness of patient test results. In 2013, CMS published a fact sheet on LDTs, outlining each agency's authority and the complementary roles of the two regulatory schemes. That said, a decade later, in connection with the FDA's notice of proposed rulemaking, we are – together – reiterating that CMS's CLIA program is separate in scope and purpose from FDA oversight." CMS Press Release, *FDA and CMS Statement: Americans Deserve Accurate and Reliable Diagnostic Tests, Wherever They Are Made*, Jan 18, 2024 available at https://www.cms.gov/newsroom/press-releases/fda-and-cms-statement-americans-deserve-accurate-and-reliable-diagnostic-tests-wherever-they-are.

[5] The opinion also reads "In the approximately thirty-five years since the 1988 CLIA amendments, FDA has occasionally claimed authority to regulate laboratory-developed test services as "devices" under the FDCA, but failed to act on such claims until the issuance of the final rule in 2024" which is not true. Supra note 7

regulate in vitro diagnostics (IVDs; a category that includes LDTs) in 1972, and proposed a rule on IVDs in 1973.[6] In its description of IVDs in that notice, FDA did not distinguish IVDs offered as LDTs as a distinct category of tests to be regulated differently.[7] The Hematology and Pathology Devices Final Rule, published in 1980, included LDTs assessing sickle cell disease, partial thromboplastin time,[8] and erythrocyte sedimentation rate (ESR).[9] These tests are still performed using both LDT and non-LDT IVDs.[10] The court thus erred in its recounting of the history of LDT regulation by 20 years, significantly mischaracterizing FDA's most recent action as a deviation from the norm, rather than what it truly is: part of a long line of relevant FDA notices, rules, guidances, and public meetings.[11]

The court further misinterpreted FDA's legal authority when it wrote that Congress was not clear that FDA had authority to regulate LDTs. The opinion discussed VITAL,[12] a bill that would put authority over LDTs under CLIA; that legislation would not be necessary if FDA did not have authority over LDTs currently.[13] A recent example involves non-invasive prenatal tests (NIPTs), which are tests performed on blood samples from pregnant people to determine if the fetus has certain microdeletions or genetic mutations. After a 2022 New York Times article cast doubt on the reliability of those tests,[14] more than 90 Republican members of Congress asked FDA why these products had not been reviewed by the

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[6] Brief for Center for Science in the Public Interest as Amicus Curiae, Appendix A, AMP v FDA CIVIL NO. 4:24-CV-479-SDJ (2024) and ACLA v FDA CIVIL NO. 4:24-CV-824-SDJ (2024) *available at* https://www.cspinet.org/sites/default/files/2024-11/2024%2011%2004%20CSPI%20Amicus%20Brief%20with%20exhibits%20%282%29.pdf.

[7] *Id.*

[8] For example, ARUP offers a partial thromboplastin time test as an LDT https://ltd.aruplab.com/Tests/Pub/0030235 and US Diagnostics offers one as an IVD https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pmn&id=K862669.

[9] 45 Fed. Reg. 60576 (Sep. 12, 1980) available at https://www.govinfo.gov/content/pkg/FR-1980-09-12/pdf/FR-1980-09-12.pdf.

[10] For example, LabCorp offers an ESR tests as an LDT https://www.labcorp.com/tests/005215/sedimentation-rate-modified-westergren and Becton-Dickson offers one as an IVD https://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=pmn&id=K953994.

[11] FDA held a public meeting in 2010, released draft guidance in 2014 and released a discussion paper in 2017, among other actions.

[12] S. 1666 Verified Innovative Testing in American Laboratories (VITAL) Act (2021).

[13] "VITAL, by contrast, expressly deemed laboratory services to be 'professional health care activity' that would be regulated under CLIA. VITAL expressly excluded laboratory-developed test services from the FDCA. Neither the VALID Act nor VITAL were passed. And new versions of both bills have been introduced in subsequent Congresses without success. In sum, Congress has considered but declined to enact several bills over the past two decades that would have reshaped the regulatory framework over laboratory-developed test services. Under the circumstances, agencies cannot circumvent, and courts must enforce, the statutory framework Congress enacted as it exists under the FDCA and CLIA." *Am. Clinical Lab'y Ass'n v. United States FDA*, No. 4:24-CV-479-SDJ, 2025 U.S. Dist. LEXIS 59869 (E.D. Tex. Mar. 31, 2025).

[14] Sarah Kliff and Aatish Bhatia, *When They Warn of Rare Disorders, These Prenatal Tests Are Usually Wrong*, N.Y. Times, Jan 1, 2022, available at https://www.nytimes.com/2022/01/01/upshot/pregnancy-birth-genetic-testing.html.

Agency.[15] Nowhere in that letter did Congress question FDA's authority over NIPTs or other LDTs. No similar letter was sent to CMS regarding CLIA's authority over NIPTs. Congress' recent actions thus clearly acknowledge that oversight of LDTs is within FDA's purview.

Criminal Penalties

The court was concerned that doctors developing and performing LDTs could be considered criminals and could be persecuted for their previous behavior.[16] However, the Final Rule is not retroactive, thereby invalidating the plaintiff's argument that pathologists could be jailed for their previous actions.[17] While FDA has authority to impose criminal penalties for violations of the FDCA, it typically begins with inspections, warning letters, seizures and injunctions; it does not immediately seek jail time and, even then, only for egregious misconduct.

The court's opinion has far-reaching implications for public health and safety. Of critical importance, the court's opinion, should it stand, would prohibit FDA from taking action regarding problematic tests. FDA has documented issues with tests[18] for conditions such as ovarian cancer,[19] Lyme disease, and COVID-19.[20] In the case of COVID tests, FDA has documented that, of 125 Emergency Use Authorization requests, the Agency "identified 82

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[15] Roy C. Daines et al., *Letter from Congress to Commissioner Janet Woodcock* (Jan. 21, 2022). Available at: https://tinyurl.com/mr2phrk7.

[16] "FDA's interpretation of the FDCA is troublesome for another reason—it turns on the assumption that a breathtaking amount of criminal activity has been occurring in the clinical laboratory field for many years. No one disputes that the FDCA has not only civil but criminal applications, including offenses that carry penalties of years of imprisonment. *See, e.g.*, 21 U.S.C. § 333(a). FDA's final rule takes the interpretive position that, in 1976, when Congress expanded FDA's authority to regulate medical devices in the MDA, it also quietly intended to outlaw—and subject to substantial civil and criminal monetary penalties—any professional laboratory-
developed test services that were not first approved or cleared by FDA.
…
The logic of FDA's position is that tens of thousands of professionals across the country performing millions of diagnostic testing services every year, working with thousands of doctors and patients, have done so for decades in open and direct violation of the law." *Am. Clinical Lab'y Ass'n v. United States FDA*, No. 4:24-CV-479-SDJ, 2025 U.S. Dist. LEXIS 59869 (E.D. Tex. Mar. 31, 2025).

[17] "First, under FDA's approach, Your Honor, the Court would have to conclude that Congress outlawed unapproved laboratory tests more than 50 years ago, at least in 1976 -- although, I think the position now is all the way back to 1938 -- and that thousands of professionals across the country are and have been openly engaged in criminal conduct that whole time." *Am. Clinical Lab'y Ass'n v. United States FDA* (Transcript of Oral Argument)

[18] The Public Health Evidence for FDA Oversight of Laboratory Developed Tests: 20 Case Studies, *available at* https://wayback.archive-it.org/7993/20171114205911/https:/www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm472773.htm.

[19] See one write up of the report by Rachel Sachs *at* https://petrieflom.law.harvard.edu/2015/11/23/fda-releases-report-detailing-problematic-laboratory-developed-tests/.

[20] Jeff Shuren and Tim Stenzel, *Covid-19 Molecular Diagnostic Testing — Lessons Learned,* N Engl J Med (2020) *available at* https://www.nejm.org/doi/full/10.1056/NEJMp2023830.

with design or validation problems."[21] The Agency has sent warning letters,[22] provided public information[23] and worked with manufacturers of these tests to improve them.[24] If LDTs are no longer considered "devices," then FDA will no longer be able to take these corrective post-market actions regarding LDTs, even if the products threaten public health or safety.

Tests are Devices not Services

FDA has long held that tests, whether IVDs sold as kits or IVDs offered as LDTs, are medical devices.[25] In 1977, FDA promulgated a rule, now codified at 21 USC § 807.65, which provides exemptions from registration and listing for certain manufacturers. The rule includes "clinical laboratories." No exemption would be needed if clinical laboratories did not already fall under the registration and listing requirements for device manufacturers.[26]

The court's decision also fails to distinguish medical services from the devices (such as LDTs and cardiac stents) that are integral to their delivery. Different facets of the same service may fall under the purview of different regulators, each with their own requirements. For example, CMS regulates the quality of operating rooms where cardiac procedures are performed and FDA regulates the devices used during these procedures. By the same token, CMS oversight of laboratories under CLIA does not negate the authority of FDA to regulate the safety and efficacy of diagnostic tests performed within those facilities.

Economics of Accurate Tests

Lastly, industry has repeatedly argued that the industry's size makes regulation too expensive.[27] We would ask that you consider why this large swath of medical products

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[21] *Id.*

[22] See, for example, Warning Letter to Inova Genomic Laboratory, Apr 4, 2019 *available at* https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/inova-genomics-laboratory-577422-04042019.

[23] *See*, for example, Shelia Kaplan, *FDA warns against widely used ovarian cancer screening test*, STATNews, Sep 7, 2016 *available at* https://www.statnews.com/2016/09/07/ovarian-cancer-screening-test/.

[24] *See*, for example, 23andme and the FDA, *available at* https://customercare.23andme.com/hc/en-us/articles/211831908-23andMe-and-the-FDA.

[25] Supra note 6

[26] As explained in detail by FDA in its Combined Summary Judgment Reply for this case.

[27] "And what we're talking about there is 1.65 billion testing procedures a year and, even by their low estimates, costing well over a billion a year. But as you can see, Your Honor, before they engaged in their questions of phasing it in, we're talking about hundreds of billions. This is a huge impact on the economy and our healthcare system." *Am. Clinical Lab'y Ass'n v. United States FDA* (Transcript of Oral Argument).

should be exempt from regulation merely because it is large.[28, 29] Conversely, the economic impact indicates the ubiquity of testing, and its importance, making regulation paramount. The LDT industry has come a long way from the 1970s, when FDA first exercised enforcement discretion and the tests were uncommon, uncomplicated, and involved relatively few patients.

Conclusion

This letter does not include all concerns we have with the court's opinion. However, it outlines a number of reasons why we stand with the FDA in its efforts to ensure that only safe and effective tests are on the market. Tests should not be regulated differently based on where they are manufactured; they should instead be regulated based on the risk to patients. We ask that you take this information into consideration as you decide whether to appeal this decision. We remain ready to continue our work with the Agency, Congress and other stakeholders on this important issue.

Sincerely,

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[28] "LDTs represent a longstanding, significant part of the U.S. healthcare system and play a critical role in delivering dynamic healthcare solutions to patients. Yet with no express statutory authorization, FDA has proposed to regulate this important sector in a manner that would fundamentally alter the market. As in Brown & Williamson, it is implausible that Congress chose to delegate to FDA an issue of 'such economic and political significance ... in so cryptic a fashion.' The Supreme Court has recently and repeatedly counseled that federal agencies should 'hesitate before concluding that Congress meant to confer [rulemaking] authority" regarding issues of vast "economic and political significance' where the statutory basis for such a regulatory action is unclear. [citations omitted]. ACLA Complaint.

[29] "The economic significance of the statutory interpretation on which the Final Rule is based hardly can be overstated. FDA itself estimates that enforcing its interpretation would affect an estimated 1.65 billion LDT-based medical procedures per year by subjecting up to 160,800 currently used LDTs and up to another 15,550 new LDTs per year to FDA regulation at a cost of up to $114 billion in one-time expenditures and another $14.31 billion in annually recurring costs—nearly all of which then would be passed onto the hundreds of millions of Americans who benefit from these billion-plus laboratory procedures each year" AMP Complaint.

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