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IN THIS ISSUE

Navigating the new norm: The FDA's final rule on laboratory developed tests (LDTs) and its impact on clinical laboratory operations

Rob E. Carpenter, *Soules College of Business, University of Texas at Tyler, 3900 University Blvd, Tyler, TX 75799, USA*
Chief Executive Officer, Advanta Genetics 10935 CR 159, Tyler, Texas 75703, USA

Abstract

On April 29, 2024, the U.S. Food and Drug Administration (FDA) issued a transformative final rule impacting the regulatory landscape for laboratory-developed tests (LDTs). This new regulation categorizes in vitro diagnostics (IVDs) used as LDTs under the same stringent oversight applied to other medical devices, thereby phasing out the agency's long-standing policy of enforcement discretion. This paper offers a concise historical overview and examines the FDA's revised regulatory framework scheduled for the next four years, examining its impact on laboratory operations in terms of safety, efficacy, and innovation. It explores how the new rule's increased compliance demands and economic implications impact laboratory operations, including economic stability, innovation, and patient safety. Also highlighted is how certain laboratories gain strategic advantages that could enhance their market stability and attract investors. The overall intent of this paper is not an in-depth analysis but instead it aims to inform stakeholders in health services about evolving laboratory standards. By doing so, it equips healthcare participants to strategically align with emerging regulatory demands, enhancing comprehension of how these changes influence healthcare delivery and laboratory procedures.

Introduction

Amidst a whirlwind of uncertainty and urgency, laboratories across the United States (U.S.) are grappling with the implications of a transformative regulatory shift. On April 29, 2024, the U.S. Food and Drug Administration (FDA) issued a final rule that significantly enhances its regulatory authority over laboratory-developed tests (LDTs). This decision aims to clarify and strengthen the FDA's oversight by amending existing regulations to explicitly categorize in vitro diagnostics (IVDs) as devices under the Federal Food, Drug, and Cosmetic Act, regardless of whether they are manufactured in a traditional industry setting or within a clinical laboratory [1]. Effectively, the FDA announced its intention to phase out its longstanding policy of enforcement discretion for LDTs over the next four years. The phaseout policy specifically targets IVDs that are produced as LDTs by laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) to conduct high complexity testing. This policy applies even if these IVDs are designed, manufactured, and used within the confines of a single laboratory [1]. This change means that IVDs produced by clinical laboratories will generally be subjected to the same regulatory standards and enforcement policies as other industry FDA regulated diagnostic devices and tests.

This move by the FDA represents a regulatory shift to apply the same standards of safety and efficacy to all diagnostic tests, including LDTs [2]. Dr. Jeff Shuren, director of the FDA's Center for Devices and Radiological Health (CDRH), emphasized that the rule is designed to protect patients from faulty tests by requiring more rigorous validation [3]. However, this increased

* *Corresponding author at: 10935 CR 159, Tyler, Texas 75703, USA.*
E-mail: rcarpenter@uttyler.edu

regulatory scrutiny is viewed by some as a potential barrier to innovation and accessibility in developing new diagnostic tests, particularly for emerging infectious diseases [4]. Laboratories fear that the stringent requirements may stifle their ability to respond quickly to public health emergencies, similar to their crucial role during the COVID-19 pandemic. Some stakeholders have raised concerns that the new rule may slow down the development of new tests and limit laboratories' ability to tailor diagnostics to evolving pathogens [5]. More recently, The U.S. House Appropriations Committee has requested that the FDA suspend its implementation of the new rule regulating LDTs [6]. This request expressed concerns that the rule, which significantly alters how LDTs are regulated, could disrupt patient care and innovation in diagnostic testing. The Committee has called for the FDA to work with Congress to modernize the regulatory approach to LDTs, suggesting that a legislative solution may be more appropriate to address the complexities of these tests without overburdening laboratories.

Background

Within these debates, it's important to understand the initial role of LDTs within the diagnostic landscape for healthcare delivery. Laboratory developed tests, originating in the 1970s and 1980s, emerged when clinical laboratories began developing custom assays to meet specific clinical needs not addressed by commercially available tests [7]. Initially regulated under the FDA's policy of enforcement discretion, which acknowledged FDA authority but generally did not enforce regulations due to their confined use within single laboratories, LDTs have historically operated with minimal oversight [8].

The importance of LDTs was starkly recognized during the recent COVID-19 pandemic, highlighting their critical role in responding to urgent public health needs [9]. As the pandemic unfolded, LDTs rapidly filled gaps left by traditional diagnostic development pipelines, which could not keep pace with the emerging crisis. Laboratories utilized their unique capabilities to develop and deploy tests that detected the SARS-CoV-2 virus, significantly accelerating the testing process when it was most needed [10,11]. Th ability of LDTs to innovate and be rapidly deployed during the pandemic highlighted their critical role in disease surveillance and control [12,13]. This demonstrated the importance of a regulatory framework that balances rapid development with the need for ensuring test accuracy and patient safety.

Under CLIA, which oversees U.S. laboratory testing, LDTs are categorized by complexity: waived tests, moderate complexity tests, and high complexity tests. Laboratory developed tests that are established in highly complex reference laboratories typically fall into the high complexity category due to their sophisticated analyses and significant interpretation requirements. Laboratories performing high complexity testing must meet stringent CLIA requirements, including higher personnel qualifications, participation in proficiency testing for each high complexity test, and implementation of comprehensive quality systems covering all aspects of laboratory operations [14]. Futhremore, a large percentage of these laboratories are also accredited by the College of American Pathologists (CAP). This accreditation is recognized by the Centers for Medicare & Medicaid Services (CMS), allowing CAP-accredited labs to bypass CMS inspections, and is also acknowledged by other significant healthcare oversight organizations like the Joint Commission and the United Network for Organ Sharing [15].

However, as the complexity and application of LDTs expanded, particularly with advances in genetics and personalized medicine, the regulatory landscape began to shift [16,17]. Concerns over the lack of stringent oversight increased, prompting debates about the level of regulation necessary to ensure safety and effectiveness without inhibiting innovation [18]. In response, recent proposals from the FDA suggest frameworks for more rigorous validation and oversight, especially for tests that present higher risks to patients [19]. These regulatory measures are meant ensure that LDTs used in high complexity laboratories provide reliable, accurate, and clinically relevant results, thereby safeguarding patient health while supporting medical advancements through innovative laboratory practices. This ongoing evolution in the regulatory framework reflects the complex balance needed between fostering innovation in laboratory medicine and ensuring test quality and patient safety [20].

Evolving laboratory standards

Laboratory-developed tests are classified as IVD medical devices under U.S. regulations [16]. Medical devices play a vital role in improving healthcare worldwide, with the global market projected to grow substantially from $471 billion in 2020 to an estimated $623 billion by 2026 [20]. The FDA oversees the regulation of these devices through CDRH. Before a medical device can be legally marketed in the U.S., a firm must navigate one of the FDA's regulatory pathways to demonstrate its safety and efficacy. Historically, the predominant pathway for this process has been the 510(k) route, established by the 1976 Medical Device Amendments. This pathway enables premarket submission for moderate-risk medical devices, with approximately 99% of FDA-approved or cleared devices utilizing it. The 510(k)-submission process is crucial for showing that a medical device is as safe and effective as a legally marketed predicate device, dictating how devices are introduced to the U.S. market. Initially, predicate devices were those marketed before the 1976 Amendments, forming foundational categories for subsequent device evaluations. The FDA classifies medical devices into three categories—Class I, II, and III—based on the risk they pose and the regulatory controls necessary to provide a reasonable assurance of safety and effectiveness.

Class I devices are deemed to pose the lowest risk to the patient and are often simpler in design. They are subject mostly to general controls and less stringent regulatory requirements. Many Class I devices are exempt from premarket notification requirements, relying instead on general controls to guarantee their safety and effectiveness [21]. Class II devices are subject to higher regulatory control than Class I and are designed to perform more complex functions. They require premarket notification and possibly special controls such as performance standards, post-market surveil-

lance, and guidelines to ensure proper performance and safety [22]. Class III devices are considered to have the highest risk and typically support or sustain human life, are of substantial importance in preventing impairment of human health, or present a potential, unreasonable risk of illness or injury. These devices are usually required to be approved by premarket approval (PMA), a scientific review to ensure the device's effectiveness and safety [22]. The FDA has classified about 1700 devices into 16 specialty panels based on risk levels, with regulatory controls increasing from Class I to Class III devices [20]. Class I and II devices benefit from the 510(k) pathway, allowing quicker market entry compared to the more rigorous PMA process required for Class III devices.

The transition from general controls for Class I devices to more rigorous premarket approval for Class III devices illustrates a critical stratification in medical device regulation based on risk assessment. The progression lays the groundwork for understanding the FDA's nuanced approach to LDT regulation through its new five-stage rule [1]. This rule outlines a phased implementation strategy, reflecting a thoughtful application of risk-based regulation tailored specifically to LDTs. Initially, the FDA will focus on basic compliance and reporting requirements, gradually escalating to more stringent measures that include full premarket reviews for the highest-risk devices. Each stage is designed to address specific aspects of regulatory compliance, from quality system (QS) requirements in the early stages to comprehensive premarket review processes in the later stages. This structured phase-in not only ensures that laboratories have adequate time to adjust to new requirements but also maintains a focus on patient safety at every step. Through this phased approach, the FDA effectively synchronizes the regulation of LDTs with the broader medical device regulatory framework, ensuring that all medical diagnostics, regardless of their complexity or risk level, meet the highest standards of safety and effectiveness. The FDA's decision is supported by its assertion that increased oversight will not only enhance patient safety but also foster innovation by ensuring that new IVDs introduced to the market are both safe and effective. The rule does, however, make accommodations for certain categories of IVDs, which may still fall under targeted enforcement discretion policies, reflecting a balance between regulatory oversight and the need to ensure continuous access to essential diagnostic tools [1].

Indeed, the FDA's new regulations serve as a pivotal bridge, transitioning from a broad commitment to enhanced safety and innovation to the tangible implications for laboratory operations. The enhanced oversight and structured compliance pathways established by the FDA ensure that laboratories are not only held to higher standards but are also clearly guided on how to meet these requirements. This regulatory guidance is essential as laboratories recalibrate their operational and development strategies to align with stringent safety and efficacy standards. Table 1 provides an overview of the FDA's phase-in stages and outlines potential strategies that laboratories might consider at each stage. Consequently, while the path to market may extend due to more comprehensive validation processes and increased documentation, these strategies are crucial for achieving higher standards of diagnostic reliability and patient safety. This creates a direct connection between the FDA's overarching goals and the practical realities faced by laboratories.

Strategic relief and economic benefits

Importantly, while new FDA regulations require a more rigorous compliance framework, there is an element of relief for those laboratories who have previously established LDTs. The "FDA intends to exercise enforcement discretion and generally not enforce premarket review and QS requirements…for currently marketed IVDs offered as LDTs that were first marketed prior to…" May 6, 2024.[1,p59]. Furthermore, the "FDA intends for this policy to apply to currently marketed IVDs offered as LDTs as long as they are not modified following the issuance of this final rule, or are modified but only in certain limited ways." [1,p59] Moreover, the CDRH has announced plans to reclassify high-risk IVD devices from class III to class II, aiming to streamline the approval process and expand accessibility. This shift primarily affects infectious disease and companion diagnostic IVDs, enabling manufacturers to pursue the less stringent 510(k) premarket notification pathway instead of the more demanding PMA pathway [23]. This reclassification is part of a broader, risk-based strategy to ensure that new IVDs provide a reasonable assurance of safety and effectiveness through special controls and general regulations.

The FDA's policy of enforcement discretion for existing LDTs allows laboratories to continue using previously marketed tests without undergoing the new premarket review process. This may help laboratories maintain operational continuity and avoid the need to withdraw tests for reapproval. By not requiring premarket review and certain QS requirements for LDTs marketed before May 6, 2024, laboratories potentially avoid the substantial costs associated with these processes. Premarket reviews, in particular, can be expensive, involving extensive data collection, documentation, and sometimes clinical trials. Savings on these fronts can be redirected towards other areas such as research and development or process improvement. The ability to continue marketing and using existing LDTs without undergoing the new, more rigorous approval process means laboratories can maintain steady revenue streams. This stability is crucial for financial planning and ongoing operations, as it avoids the potential revenue dips that come with pulling a product off the market for reevaluation and reapproval.

With the saved resources and reduced immediate regulatory pressures, laboratories can invest more in innovation. This could mean improving existing tests, developing new ones, or investing in advanced technologies that enhance test accuracy and patient outcomes. Over time, this reinvestment in innovation can lead to higher quality products that could command premium pricing or capture a larger market share. The policy allows laboratories to align with FDA standards at a more manageable pace. This strategic alignment without the immediate financial strain of full compliance means laboratories can plan more long-term investments in compliance and quality improvements, spreading out expenses in a way that supports sustainable growth. And finally, laboratories

Table 1. Stages and strategies for FDA oversight of LDTs for clinical laboratories.

Stage	Compliance Time Frame	Requirements	Operations Impact	Strategic Actions
Stage 1	Compliance Within 1 Year (April 6, 2025)	Beginning on May 6, 2025, which is 1 year after the publication date of the final LDT rule, FDA will expect compliance with medical device reporting (MDR) requirements, correction and removal reporting requirements, and quality system (QS) requirements regarding complaint files (specifically concerning complaint files under § 820.198).	Laboratories will need to establish or refine systems for tracking adverse events and device defects and ensure these systems can generate reports compliant with FDA requirements. This may involve upgrading IT systems and training staff to recognize and document reportable events.	*Establishment of Complaint Files:* Laboratories set up procedures to receive, review, and evaluate each complaint through a formally designated unit within the laboratory. The aim is to handle all complaints consistently and systematically. *Documentation and Processing:* All complaints, including oral ones, must be documented as soon as they are received. The process should be uniform and timely, ensuring that no complaint is overlooked and that each is handled according to predefined procedures. *Evaluation for Medical Device Reporting:* Complaints must be assessed to determine if they represent events that should be reported to the FDA under Part 803, Medical Device Reporting. This is critical for issues that could impact patient safety or device performance. *Investigation Requirements:* Not all complaints will necessitate a formal investigation. If a decision is made not to investigate, this decision must be documented, including the reasons and the name of the responsible individual. For complaints that do trigger an investigation, the process must thoroughly review whether the device, its labeling, or packaging failed to meet specifications. *Record Keeping of Investigations:* Investigations must be detailed, and their findings recorded. This includes the identification of the device, the nature of the complaint, investigation outcomes, and any corrective actions taken. The records should be easily accessible and maintained in an organized manner, especially if the complaint unit is located away from the manufacturing site. *Records*: If the designated complaint unit is outside the United States, the records must be accessible within the U.S. either where the laboratory's records are regularly kept or at the location of the initial distributor.
Stage 2	Compliance Within 2 Years (April 6, 2026)	Beginning on May 6, 2026, which is 2 years after the publication date of the final LDT rule, FDA will expect compliance with requirements not covered during other stages of the phaseout policy, including registration and listing requirements, labeling requirements, and investigational use requirements.	Laboratories must ensure that all their devices are properly registered and listed with the FDA, which involves accurate cataloging and ongoing updates to the FDA. Additionally, labeling must meet FDA standards, which may require revisions to current labeling practices to include necessary warnings, usage instructions, and regulatory markings. For investigational devices, compliance involves adhering to regulations governing their use, including obtaining necessary approvals for clinical trials if warranted.	*Registration and Listing:* Laboratories must ensure that all medical devices are properly registered with the FDA. This includes submitting accurate and timely information about the devices they manufacture or distribute to ensure transparency and regulatory oversight. Maintaining up-to-date listings is crucial for compliance and must be reviewed and renewed annually. *Labeling Requirements:* Compliance with labeling requirements involves ensuring that all labels on medical devices provide adequate directions for use, including safety and warning information. Labels must be designed to remain intact and legible under the conditions of use and throughout the device's lifetime. Laboratories need to establish controls to verify that labels meet all specifications and regulatory requirements before devices are released for distribution. *Investigational Use Requirements:* For devices intended for investigational use, laboratories must comply with regulations that include obtaining an investigational device exemption (IDE) where necessary. This involves submitting detailed information about the device's design, manufacture, and intended use to the FDA, along with assurances regarding the protection of human subjects during clinical studies. These efforts align with the FDA's aim to harmonize its regulations with international standards, notably ISO 13485:2016, which focuses on maintaining effective quality management systems across the lifecycle of medical devices. The alignment with these international standards is intended to simplify global regulatory obligations and enhance the quality assurance processes of medical device manufacturers.

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Table 1 (*continued*)

Stage	Compliance Time Frame	Requirements	Operations Impact	Strategic Actions
Stage 3	Compliance Within 3 Years (April 6, 2027)	Beginning on May 6, 2027, which is 3 years after the publication date of the final LDT rule, FDA will expect compliance with QS requirements (full compliance with QS regulations under 21 CFR Part 820, except for the complaint files already addressed).	This stage requires comprehensive compliance with QS regulations, which will necessitate a thorough review and possibly a redesign of all quality control and manufacturing processes. Laboratories will need to document and implement standard operating procedures (SOPs) for design controls, production, process controls, and quality checks to ensure consistent device quality and safety.	*Documented Quality Management System (QMS):* Laboratories must have a fully documented QMS that covers all aspects of their operations. This includes detailed procedures for design controls, production and process controls, corrective and preventive actions (CAPA), and other critical QMS elements. The emphasis is on ensuring that the QMS is comprehensive and covers all regulatory requirements. *Design Controls:* Implement design controls that are crucial for ensuring that medical devices meet user needs and intended uses. These controls should include planning, design input, design output, design review, design verification, design validation, and design changes. *Production and Process Controls:* Establish and maintain methods and procedures for controlling production processes that ensure the medical device conforms to its specifications. Control activities must include monitoring and control of process parameters and component and device characteristics during production. *Corrective and Preventive Actions (CAPA)*: Develop a CAPA system that is capable of identifying problems, correcting them, and preventing their recurrence. This system must be able to handle feedback, complaints, nonconformities, defective products, and other problems. *Training:* Ensure that all personnel are trained and qualified to perform their assigned responsibilities. This includes training specific to the use, maintenance, and application of the QMS and associated regulatory requirements. *Supplier Management*: Establish and maintain a supplier management system that ensures external providers meet all specified requirements and quality standards. *Device History Records:* Maintain device history records that demonstrate the device was manufactured in accordance with the design specifications and QMS requirements. By the end of Stage 3, the laboratory should have a robust, fully operational QMS that aligns with both FDA expectations and international standards like ISO 13485:2016, further preparing them for any future regulatory audits or inspections.
Stage 4	Compliance Within 3.5 Years (November 6, 2027)	Beginning on November 6, 2027, which is 3.5 years after the publication date of the final LDT rule, FDA will expect compliance with premarket review requirements for high-risk IVDs offered as LDTs (IVDs that may be classified into class III or that are subject to licensure under section 351 of the Public Health Service Act), unless a premarket submission has been received by the beginning of this stage in which case FDA intends to continue to exercise enforcement discretion for the pendency of its review.	High-risk IVDs will need to have been completed or be very close to completing the premarket approval (PMA) process. This involves preparing and submitting a substantial amount of data on device safety and efficacy, conducting clinical trials, and undergoing rigorous FDA review. Laboratories must allocate significant resources towards compliance documentation and regulatory strategy.	*Submission of Premarket Approval (PMA):* Laboratories must prepare and submit a PMA for each high-risk IVD. This involves compiling comprehensive data on the device's safety, effectiveness, and manufacturing processes. The PMA must include clinical trial data that demonstrates the device's safety and effectiveness. *Risk Assessment:* Conduct a thorough risk assessment as part of the PMA process. This includes identifying and evaluating potential risks associated with the device. The assessment should align with FDA guidance and consider both the likelihood of harm occurring and the severity of the harm. *Quality Data and Manufacturing Information:* Provide detailed information about the device's design, manufacturing process, and quality control measures. This is critical to ensure the device consistently meets safety and performance standards. *Regulatory Compliance:* Ensure that all regulatory requirements are met, including labeling, reporting of adverse events, and post- market surveillance. Compliance with these regulations must be maintained and documented. *FDA Review and Feedback*: Once submitted, the PMA undergoes a rigorous review process by the FDA. Laboratories should be prepared to provide additional information and participate in discussions with the FDA to address any questions or concerns regarding the application. *Timeline and Resource Allocation:* Understand and plan for the time- intensive nature of the PMA process, which often extends beyond the initial submission. Allocate sufficient resources, including expert regulatory advice and support, to navigate this phase effectively. *Engagement with FDA:* Engage proactively with the FDA through pre-submission meetings and other regulatory interactions to clarify expectations and requirements for the PMA submission. This can help in anticipating potential challenges and aligning the submission with FDA expectations.

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Table 1 (*continued*)

Stage	Compliance Time Frame	Requirements	Operations Impact	Strategic Actions
Stage 5	Compliance Within 4 Years (April 6, 2028)	Beginning on May 6, 2028, which is 4 years after the publication date of the final LDT rule, FDA will expect compliance with premarket review requirements for moderate-risk and low-risk IVDs offered as LDTs (that require premarket submissions), unless a premarket submission has been received by the beginning of this stage in which case FDA intends to continue to exercise enforcement discretion for the pendency of its review.	For moderate and low-risk devices, the necessary 510(k) submissions or De Novo requests must be prepared and submitted, demonstrating that these IVDs are safe and effective. This may involve comparative studies, performance testing, and additional documentation to prove substantial equivalence or support a classification request. Laboratories need to prepare for possible FDA feedback and additional data requests.	*Premarket Notification (510(k)) for Class II Devices:* Laboratories must submit a 510(k) notification to the FDA demonstrating that the moderate-risk IVD is substantially equivalent to another legally marketed device in the U.S. This involves a comparative analysis demonstrating that the new device is as safe and effective as the existing one. *De Novo Classification Request for Novel Class I and II Devices:* If no predicate exists, laboratories may need to submit a De Novo classification request to obtain FDA approval for a new classification for low or moderate-risk devices that do not have a legally marketed predicate. *Documentation and Evidence:* Comprehensive documentation must be prepared, including data from clinical or analytical studies that support the safety and efficacy of the device. The documentation should also detail the device's intended use, technical characteristics, and manufacturing process. *Quality System (QS) Regulation Compliance:* Ensure that the device manufacturing process is compliant with QS regulations, particularly focusing on areas such as design controls, production and process controls, and corrective and preventive actions. *Regulatory Strategy and Communication:* Develop a clear regulatory strategy for each device, including timelines for submissions and potential FDA interactions. Engage with the FDA through pre-submission meetings or early feasibility studies to clarify requirements and streamline the review process. *Risk Management and Post-Market Surveillance:* Implement robust risk management practices and plan for ongoing post-market surveillance to monitor the safety and effectiveness of the device after it has entered the market. *Resource Allocation and Planning:* Allocate appropriate resources for the potentially lengthy and resource-intensive process of preparing and supporting premarket submissions. This includes technical, clinical, and regulatory expertise. *Stakeholder Engagement:* Engage with key stakeholders, including clinical experts and potential users, to gather supportive evidence and endorsements that reinforce the clinical utility and safety of the device.

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that can continue to offer their LDTs with minimal modification also enjoy a competitive advantage. As they are not bogged down by new compliance costs and processes, they can respond more agilely to market needs and opportunities, potentially expanding their business more effectively than competitors who might be new entrants or are still adjusting to comply with the full breadth of the new regulations.

Adapting to new FDA compliance challenges

The overarching implication of the new FDA rule for laboratories is related to compliance challenges that laboratories will face, the resources required to meet compliance, and strategies to overcome potential bottlenecks in the compliance processes. The implementation of these regulations will potentially increase the demand for resources in several areas. Laboratories will likely require additional financial resources to update or implement quality management systems and processes that meet the FDA's compliance standards. This includes investment in new technology and software for tracking and reporting, as well as in personnel training and development to ensure that staff are well-versed in new regulatory requirements. More sophisticated quality management systems will need to be adopted, and laboratories may need to hire additional quality assurance specialists or regulatory affairs professionals to manage these systems effectively.

The regulations could introduce several bottlenecks, particularly in areas such as the PMA process for high-risk IVDs, and the increased documentation and reporting requirements. For instance, the process of gathering and submitting the necessary documentation for FDA review can be time-consuming and complex, potentially delaying product launches or the introduction of new diagnostic tests. Laboratories will need to streamline these processes, possibly through the adoption of advanced data management systems that can handle large volumes of information efficiently and securely.

To address these challenges, laboratories can adopt several strategic actions. First, early engagement with the FDA through presubmission meetings and other forms of communication can help clarify expectations and reduce the likelihood of submission rejections or delays. Second, investing in training programs to enhance employee understanding of regulatory requirements will be crucial. This not only ensures compliance but also helps in identifying potential compliance issues before they escalate. Furthermore, laboratories might consider implementing scalable solutions that can grow with their operations to prevent future bottlenecks. For instance, adopting modular quality management systems that can be expanded as laboratory operations grow can be a proactive measure. Additionally, forming dedicated teams to handle different aspects of the compliance process—such as documentation, reporting, and internal audits—can help distribute the workload and improve efficiency.

Beyond the immediate challenges, these regulatory changes will also have long-term implications for laboratory operations. They will likely drive improvements in the quality and reliability of diagnostic tests, enhancing patient safety and confidence in medical diagnostics. However, laboratories that fail to adapt effectively may face operational disruptions, increased costs, and potential legal and regulatory penalties. In sum, while the new FDA regulations for LDTs present compliance challenges, they also offer an opportunity for laboratories to enhance their operational standards and improve overall performance. By understanding and planning for these impacts, laboratories can position themselves to meet regulatory demands successfully and maintain a competitive edge in the evolving healthcare landscape.

Concluding thoughts

The FDA's final rule on LDTs represents a significant regulatory shift that directly impacts reference laboratories currently utilizing LDTs. As outlined above, these laboratories are granted a transitional period that will allow them to adapt to new regulations gradually, effective from April 6, 2024. The phased enforcement strategy allows laboratories time to adapt to new regulations while maintaining their essential role in providing diagnostic information critical to clinical decision-making and patient care.

Importantly, the FDA provides provisions for laboratories that have validated LDTs prior to April 6, 2024. Accordingly, these laboratories may continue operation under a relaxed regulatory regime that fundamentally delivers a competitive advantage to this segment of laboratories, and potentially increases their market stability, value, and attractiveness to investors.

For stakeholders in the health services, especially those focused on the integration and management of healthcare delivery systems, understanding these regulatory changes is important. Ensuring that laboratory information systems and operational protocols align with new regulatory standards will be essential for maintaining the efficacy and safety of LDTs. The implications of this regulatory update may necessitate a reevaluation of existing systems and the adoption of enhanced compliance measures to meet the new standards.

The developments discussed here should stimulate further research and discussion within the health services community. This dialogue is essential for navigating the challenges and opportunities presented by the FDA's new rule, fostering a deeper understanding of its impact on healthcare delivery. As the laboratory medicine field continues to evolve, continuous engagement with these regulatory changes will be crucial in shaping the future of diagnostic medicine, ensuring that it not only meets clinical needs but also adheres to the highest standards of patient safety and care.

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References

[1] U.S. Food and Drug Administration. Medical devices; Laboratory developed tests (Docket No. FDA-2023-N-2177; RIN 0910-AI85 *Federal Register*. 2024; https://federalregister.gov/d/2024-08935

[2] Javitt GH. In search of a coherent framework: Options for FDA oversight of genetic tests. Food Drug Law J 2007;62:617–52. https://heinonline.org/HOL/LandingPage?handle=hein.journals/foodlj62&div=46&id=&page=.

[3] Kelly S. As FDA's LDT rule looms, experts warn patients may lose access to critical tests. MedTech Dive 2024. March 22 https://www.medtechdive.com/news/fda-lab-developed-test-rule-congress-access/711084/ .

[4] Maxwell K. Easing medical device regulatory oversight: The FDA and testing amidst the COVID-19 pandemic. American J of Law & Med 2021;47(2-3):291–326. doi:10.1017/amj.2021.18.

[5] Kelly S. FDA defends LDT final rule, while critics fear it upends lab industry. MedTech Dive 2024. April 30 https://www.medtechdive.com/news/ldt-final-rule-shuren-lab-test-access/714714/ .

[6] U.S. House of Representatives. "Committee Approves FY25 Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill." House Appropriations Committee, July 10, 2024. https://appropriations.house.gov/news/press-releases/committee-approves-fy25-agriculture-rural-development-food-and-drug.

[7] Lepage R, Albert C. Fifty years of development in the endocrinology laboratory. Clin Biochem 2006;39:542–57. doi:10.1016/j.clinbiochem.2006.03.007.

[8] U.S. Food and Drug Administration. Laboratory Developed Tests. https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests. Accessed May 3, 2024.

[9] Rehrauer WM, Yang DT. Laboratory-Developed Tests: A critical bridge during the COVID-19 pandemic. WMJ 2023;122:432–3. https://wmjonline.org/122no5/rehrauer/.

[10] Carpenter RE, Tamrakar VK, Almas S, Brown E, Sharma R. COVIDSeq as laboratory developed test (LDT) for diagnosis of SARS-CoV-2 variants of concern (VOC). Arch of Clin and Biomed Res 2022;6:954 *2022*. doi:10.26502/2Facbr.50170309.

[11] Carpenter RE, Tamrakar VK, Almas S, Sharma A, Rowan C, Sharma R. Optimization of the Illumina COVIDSeq™ protocol for decentralized, cost-effective genomic surveillance. Pract Lab Med 2023;34:e00311. doi:10.1016/j.plabm.2023.e00311.

[12] Carpenter RE, Tamrakar V, Chahar H, Vine T, Sharma R. Confirming multiplex RT-qPCR use in COVID-19 with next-generation sequencing: strategies for epidemiological advantage. Glob Health, Epi and Gen 2022 e4. doi:10.1155/2022/2270965.

[13] Carpenter RE, Tamrakar VK, Almas S, Sharma A, Sharma R. SARS-CoV-2 Next Generation Sequencing (NGS) data from clinical isolates from the East Texas Region of the United States. Data in Brief 2023;49:109312. doi:10.1016/j.dib.2023.109312.

[14] Graden KC, Bennett SA, Delaney SR, Gill HE, Willrich MA. A high-level overview of the regulations surrounding a clinical laboratory and upcoming regulatory challenges for laboratory developed tests. Lab Med 2021;52:315–28. doi:10.1093/labmed/lmaa086.

[15] College of American Pathologists. Laboratory Accreditation Program. https://www.cap.org/laboratory-improvement/accreditation/laboratory-accreditation-program. Accessed May 3, 2024.

[16] Genzen JR. Regulation of laboratory-developed tests: A clinical laboratory perspective. Amer J of Clin Path 2019;152:122–31. doi:10.1093/ajcp/aqz096.

[17] Luo Y, Wang J, Zhang M, Wang Q, Chen R, Wang X, Wang H. COVID-19-another influential event impacts on laboratory medicine management. J of Clin Lab Anal 2021;35:e23804. doi:10.1002/jcla.23804.

[18] U.S. Food and Drug Administration. *Laboratory developed tests*. n.d. Retrieved from https://www.fda.gov/medical-devices/in-vitro-diagnostics/laboratory-developed-tests

[19] U.S. Food and drug administration. Webinar - Final rule: Medical devices; Laboratory Developed Tests 2024. May 14 https://www.fda.gov/medical-devices/medical-devices-news-and-events/webinar-final-rule-medical-devices-laboratory-developed-tests-05142024 .

[20] Aboy M, Crespo C, Stern A. Beyond the 510 (k): The regulation of novel moderate-risk medical devices, intellectual property considerations, and innovation incentives in the FDA's De Novo pathway. Digital Med 2024;7:29. doi:10.1038/s41746-024-01021-y.

[21] Zhuang J, Zhuang J. Medical devices. In *Fundamentals of Drug Development* 2022;353-363. ISBN: 978-1-119-69173-0

[22] Ashter SA. Classification of medical devices. In *Applications of Polymers and Plastics in Medical Devices: Design, Manufacture, and Performance* William Andrew. 2022; 27-44. 10.1016/C2019-0-02846-4

[23] Pathology in Practice. US FDA to Reclassify High-Risk IVDs. February 2, 2024. https://www.pathologyinpractice.com/story/43839/us-fda-to-reclassify-high-risk-ivds. Accessed May 3, 2024.

Rob E. Carpenter is a healthcare executive and educator. He is founder and current CEO of Advanta Genetics, a highly complex clinical and research laboratory accredited by the College of American Pathologists with concentration in infectious disease molecular genomics and co-founder of Scienetix, a bioscientific company centered around products to optimize molecular genomic workflows. He holds an M.B.A. in Healthcare Administration and a Ph.D. in Human Resource Development from the University of Texas at Tyler Soules College of Business.