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Jane Pine Wood, JD, on...

Essential Steps for Laboratories to Protect Laboratory Developed Tests

Compliance will be costly, time consuming

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From the Desk of R. Lewis Dark...

THE DARK REPORT

RELIABLE BUSINESS INTELLIGENCE, EXCLUSIVELY FOR MEDICAL LAB CEOs / COOs / CFOs / PATHOLOGISTs

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COMMENTARY & OPINION by...

R. Lewis Dark
Founder & Publisher

What's a Big Headwind for Labs? It's LDT Rule!

EXECUTIVES AT PUBLICLY-TRADED CORPORATIONS AND THE FINANCIAL ANALYSTS WHO COVER THESE COMPANIES like to use the term "headwinds" when describing problems preventing these companies from succeeding. It's the polite euphemism that acknowledges real-world negatives without calling them by their real names, such as high customer turnover, shrinking market share, and poor economic times.

I mention this because several recent events besetting the clinical laboratory industry could aptly be called "headwinds." They are specific developments and forces that make it harder for clinical labs and pathology groups to deliver state-of-the-art diagnostic services to physicians and patients in a way that is financially sustainable.

Of course, one such headwind is the federal **Food and Drug Administration's** (FDA) final rule on laboratory developed tests (LDTs) that was published last May. There is widespread agreement among pathologists and clinical lab scientists that the future of laboratory medicine is the use of customized assays in support of precision medicine and personalized care. These are tests developed as LDTs and commonly run in small batches because—unlike the daily high volumes of chemistry panels, CBCs, and cholesterol tests—only a handful of patients at any one time benefit from these LDTs.

However, the FDA's LDT rule is a solution from another era of medicine and government regulation. It is inappropriate for this era of genomics and precision medicine. The FDA's solution as implemented misses the mark in important ways. In fact, I'm bold enough to say that the FDA's LDT rule throws the academic lab innovation "baby" out with the "bathwater" of some private lab companies that offer LDTs in an unethical manner.

Many lab professionals understand that it would be timely to implement some form of regulatory oversight for LDTs as they are currently performed by labs. The caveat is that regulators must use a framework that accurately reflects current and future technologies and clinical practices.

Until that happens, the FDA's LDT rule is a headwind of hurricane force. Whether the LDT rule proves to be a Category 1 hurricane or a Category 5 has yet to be determined. TDR

Global Computer Outage Shows Risk to Clinical Labs

Along with the move to cloud-based computing comes greater risk of disruption and cyberattacks

CEO SUMMARY: Last Friday's global computer outage was due to a faulty update to a widely used endpoint security software system. The level of disruption worldwide in air travel, commerce, and information processing was unprecedented. This incident highlights that there are risks when a clinical laboratory or hospital puts both data and services in the cloud.

MANY CLINICAL LAB MANAGERS AND PATHOLOGISTS were at work last Friday when major disruptions happened to their cloud-based information technology services. This was particularly true for labs at health systems and hospitals using cloud-based services.

The cause was a global computer outage that had consequences across many industries and businesses. For example, air travel and financial services were disrupted in the United States and several other countries.

In the United Kingdom, *NPR* wrote, "The **U.K.'s National Health Service** has been widely affected. The NHS said Friday that doctors' appointments and patient records had been affected but that there was no known impact on emergency services. The *BBC* reported that two-thirds of doctors' practices in Northern Ireland had been affected, with doctors unable to access patient records, generate prescriptions or see the result of laboratory tests."

ABC News identified that "at least 12 hospitals or hospital systems across the U.S. were affected by the outage with some reporting that they had canceled elective procedures Friday."

According to *ABC News*, "Those affected include **Cleveland Clinic**, **Cincinnati Children's**, **Kaleida Health/Cayuga** in New York, **Harris Health System** in Texas, **Hospital for Special Surgery** in New York City, **Martha's Vineyard Hospital**, **Mass General**, **Memorial Hermann** in Texas, **Mount Sinai** in New York, **Nationwide Children's Hospital** in Ohio, and **Ohio State University Wexner Medical Center**."

Media reports quickly identified a faulty software update issued by Austin, Texas-based **CrowdStrike** as the immediate cause of the computer outages experienced globally. However, during these same hours, **Microsoft** had service disruptions to its Azure Cloud Service, particularly in several Midwest states. These

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issues affected users of Microsoft 365 and other Microsoft services for several hours.

TechCrunch reported that "CrowdStrike said the outage was not caused by a cyberattack, but was the result of a 'defect' in a software update for its flagship security product, Falcon Sensor. The defect caused any Windows computers that Falcon is installed on to crash without fully loading."

Because their systems do not run the CrowdStrike Falcon Sensor software, **Linux** and **Apple** systems were not affected. As the CrowdStrike update would load on computers with Microsoft software, the computer would show the "blue screen of death." CrowdStrike scrambled to issue a fix to this problem.

Road Map for Threat Actors?

One interesting observation emerged from the widespread disruption this problem caused globally. Several experts in cybersecurity pointed out that this incident will be studied by those nation states known to actively hack the computer systems of developed countries to sow discord and steal valuable data.

What caused this disruption to global digital systems and the time required to restore services back to normal should be studied by every clinical laboratory's cybersecurity team. This incident just created a new category of emergency and disaster planning that should motivate both labs and hospitals to develop contingency plans for similar events.

Meanwhile, the extensive disruption to a wide variety of businesses and services in countries throughout the world—even if only for a few hours—is a reminder that there is risk when both a company's data and service systems are hosted in the cloud.

Lab managers should expect this event to stimulate discussion and debate about how critical service providers, be they hospitals, airlines, or communications companies, should have a back-up plan to access company data and deliver services to customers if their organization's primary cloud service provider goes offline for whatever reason.

CrowdStrike Big Player in Digital Cybersecurity

WHAT CROWDSTRIKE SELLS IS AN "ENDPOINT PROTECTION" SOFTWARE. This is the latest name for what is commonly called anti-virus and firewall software. **Norton AntiVirus** and **McAfee Antivirus** are early examples of anti-virus software from the 1990s.

An endpoint protection system uses a backend control center, with agent software installed on the endpoints, such as servers, computers, and even mobile devices.

Until last Friday, CrowdStrike was not a high profile company. And yet, it has grown to $3 billion in revenue. It has more than 20,000 customers globally, including such major players as Microsoft and Amazon.

CNBC quoted CrowdStrike CEO George Kurtz, who said CrowdStrike is "actively working with customers impacted by a defect found in a single content update for Windows hosts. He added that Mac and Linux hosts are not affected."

Market Concentration

Another fact should be considered when clinical labs and pathology groups work to update their strategic plans and emergency responses. Ever-larger corporations are capturing ever-larger shares of the market. Certainly economies of scale for customers can be a positive outcome from this market concentration.

That concentration of market share is happening in cloud services. **Amazon Web Services** (AWS) has 31% market share, followed by Microsoft Azure at 24% and **Google Cloud Platform** with 11% of the market share. Collectively, these three companies control 77% of the global cloud services market! TDR

Legislative Update

Language in Draft House Bill Directs FDA to Suspend LDT Rule

It is a sign that some members in Congress recognize how FDA's actions to regulate LDTs can disrupt care

THERE IS AN INTERESTING NEW DEVELOPMENT associated with the regulation of laboratory developed tests (LDTs) by the **Food and Drug Administration** (FDA). In recent days, a House committee published draft legislation that directs the FDA to suspend its implementation of the LDT rule.

As part of an appropriations bill, the House Appropriations Committee issued a draft published on the House website, written as follows:

> ***Laboratory Developed Tests.***—*The FDA's final rule on Laboratory Developed Tests (LDTs) puts forth a proposed regulatory framework that is a significant shift in the way LDTs are regulated and changes expectations for patients, doctors, and laboratories for the first time since the Clinical Laboratory Improvement Amendments Act was passed in 1988 at the risk of greatly altering the United States' laboratory testing infrastructure and reducing patient access to information that informs their healthcare decision making.* ***The Committee directs the FDA to suspend its efforts to implement the rule and continue working with Congress to modernize the regulatory approach for LDTs.*** *(Boldface by THE DARK REPORT.)*

THE DARK REPORT contacted several Washington insiders working to educate Congress and federal agencies about the significance of this development. Collectively, these sources emphasized that this is language in a draft bill and much has to happen before it is included in a bill that becomes law and requires action by the FDA.

One lobbyist noted, "language like this in draft legislation is more of a messaging effort. It is directionally helpful and the right type of message in support of clinical lab professionals who want revisions in how federal agencies regulate LDTs."

Disagreement with LDT Rule

Although this is a draft bill in the House, there are members in the Senate who don't agree with the FDA's actions to regulate LDTs. For example, on April 29, following the FDA's publication of the final LDT rule, U.S. Senator Bill Cassidy, MD (R-LA), the ranking member of the Senate Health, Education, Labor, and Pensions (HELP) Committee, issued a statement critical of the FDA's actions.

He said, "The FDA does not have the authority to unilaterally increase its regulatory jurisdiction. This rule will undermine access to essential laboratory tests, increase healthcare costs, and ultimately harm patients. During the pandemic, we saw how too much government interference and red tape delays lifesaving care to Americans. Congress needs to take action to clarify the regulatory structure for diagnostic tests."

The language in this draft bill demonstrates that some members of Congress see flaws in the FDA's LDT Rule and have an interest in fixing them. TDR

2023 Ranking of the World's Top 13 IVD Corporations

BASED ON 2023 DIAGNOSTICS-RELATED REVENUE, four *in vitro* diagnostics (IVD) manufacturers continued to lead the global IVD market just as they did in 2022. They are: **Thermo Fisher Scientific, Inc.**, **Roche Holdings**, **Abbott Laboratories**, and **Danaher Corporation**.

The top 13 firms collected $88.7 billion in annual revenue, compared to $99 billion in fiscal 2022 and $85 billion in 2021.

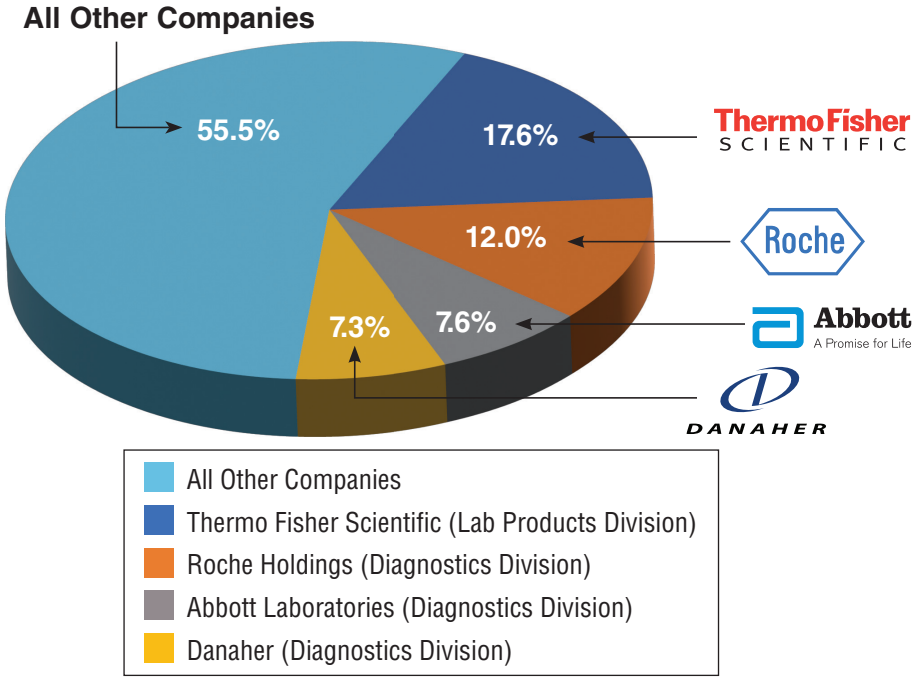
Shifts of note in the 2023 list include **Becton Dickinson** jumping to the fifth spot, as **Siemens Healthineers** settled into the sixth. **Hologic** edged out **QuidelOrtho** for the eighth position. Joining **Bio-Rad** in a tie for the 10th position is **Revvity** (formerly **PerkinElmer**) which during 2023 divested its Applied, Food, and Enterprise Services businesses to **New Mountain Capital**.

Top 13 IVD Companies by Global Revenue in 2023 (in billions)

IVD Corporation	2023 revenue	Cumulative revenue	Percent of market	Cumulative percent of market	2022 prior rank	
1. Thermo Fisher Scientific–Lab Products Div. *Waltham, Mass., founded 1956*	$23.0	$23.0	17.6%	17.6%	1	
2. Roche Holdings–Diagnostics Division *Basel, Switzerland, founded 1896*	$15.7	$38.7	12.0%	29.6%	2	
3. Abbott Laboratories–Diagnostics Division *Abbott Park, Ill., founded 1888*	$9.9	$48.6	7.6%	37.2%	3	
4. Danaher–Diagnostics Division *Washington, D.C., founded 1969*	$9.5	$58.1	7.3%	44.5%	4	
5. Becton Dickinson–Life Sciences Division *Franklin Lakes, N.J., founded 1897*	$5.1	$63.2	3.9%	48.4%	6	▲
6. Siemens Healthineers–Diagnostics Division *Erlangen, Germany, founded 1896*	$4.9	$68.1	3.7%	52.1%	5	▼
7. bioMérieux *Marcy-l'Étoile, France, founded 1963*	$4.0	$72.1	3.0%	55.1%	7	
8. Hologic–Diagnostics Division *Marlborough, Mass., founded 1985*	$3.6	$75.7	2.8%	57.9%	9	▲
9. QuidelOrtho *San Diego, Calif., founded 1979*	$3.0	$81.4	2.3%	60.2%	8	▼
10. (tie) Bio-Rad Laboratories *Hercules, Calif., founded 1952*	$2.7	$84.1	2.0%	62.2%	10	
10. (tie) Revvity *(formerly PerkinElmer)* *Waltham, Mass., founded 1937*	$2.7	$86.7	2.0%	64.2%		
12. Sysmex *Hyogo, Japan, founded 1968*	$2.6	$88.7	2.0%	66.2%	10	▼
13. Qiagen *Venlo, The Netherlands, founded 1984*	$2.0	$88.7	1.5%	67.7%	12	
Total Market Share Top 13 IVD Firms	$88.7	$88.7	67.7%	67.7%		
Market Share, Other IVD Firms	$41.3	$41.3	32.3%	32.3%		
Total Global IVD Revenue in 2023 (est.)	**$130.0**	**$130.0**	**100.0%**	**100.0%**		

Sources: Company documents, news reports.

Four IVD Companies Make up 44.5% of Market



GLOBAL SALES FOR THE *IN VITRO* DIAGNOSTICS (IVD) INDUSTRY were estimated at $130 billion in 2023, compared to $124 billion in 2022, according to reports issued by **Kalorama Information**. This is a growth rate of 4.8% and reflects the progress the IVD industry is making since the falloff of COVID-19 testing in recent years.

The top four companies in THE DARK REPORT'S (TDR) 2023 ranking of Global IVD firms by diagnostics-related revenue continue to hold a substantial market share of 44.5%. However, this is down from 53% in 2022 and probably reflects the impact of acquisitions and organic growth among the other nine of the 13 largest IVD manufacturers in the world.

For the second year in a row, **Thermo Fisher Scientific** posted the largest sales of IVD products and topped the rankings. Its market share was estimated at 17.6%, a gain of 0.3% since 2022. During this same time, **Roche Diagnostics Division's** global market share fell to 12% from 14.8%; **Abbott Laboratories'** decreased to 7.6% from 12.8%; and **Danaher Corporation's** dropped slightly to 7.3% from 8.3%. Some of these shifts were caused by the sustained decline in the volume of COVID-19 test instruments and kits during 2022.

The new addition to THE DARK REPORT'S ranking of the top global IVD companies in 2023 is **Revvitty** (formerly **PerkinElmer**), with global sales of $2.7 billion.

Virchow
Medicine ➤ Money ➤ Managed Care

This column is named after the famous German pathologist Rudolf Virchow (1821-1903), and it presents opinions and intelligence about managed care companies and their laboratory test contracting practices.

Labs, Payers Don't Like Prior Authorization for Genetic Tests

EDITOR'S NOTE: Our column, Virchow, is written by anonymous insiders working within the managed care world. The column aims to help clients of THE DARK REPORT better understand the decisions, policies, and actions of payers as they manage their laboratory networks, establish coverage guidelines, process lab test claims, and audit labs.

PRIOR AUTHORIZATION REQUIREMENTS FOR GENETIC TESTS are among the biggest pet peeves that clinical laboratories have with health plans. Payers impose these requirements to ensure that they are spending healthcare dollars appropriately. They want the right test at the right time for the right patient.

This sounds fine in theory. But in the real world, the process often fails to work as intended, leaving labs on the hook for costly claim denials. For their part, payers recognize that prior authorization creates administrative headaches, yet it is payers who set these rules!

Providers of all types must deal with prior authorization, but the process is especially vexing for laboratories, given their unique position in the healthcare ecosystem.

How Prior Authorization Works

Under prior authorization, health plans require providers to get advance approval for specified services before agreeing to pay for them.

As prior authorization requirements apply to clinical laboratories, they typically address complex—and often costly—genetic tests.

The ordering physician is usually responsible for obtaining prior authorization, but the lab must file the claim if it wants to be paid. Should the doctor make a mistake and the claim is denied, the lab is left holding the bag. This could be for a test that costs $5,000 or more to run.

Each plan has its own prior authorization policies. For example, some plans require prior authorization for noninvasive prenatal testing (NIPT) if the patient is 35 or older. Other plans will cover the test—without a prior authorization requirement—regardless of age.

Plans also need evidence that the patient meets the criteria to have a certain test performed. But they have varying guidelines for what kinds of documentation they require.

In the Real World

Here's a common scenario that often plays out in the real world: A physician decides to prescribe a genetic test, applies for authorization, and submits the required documentation. The doctor thinks, "OK, I'm sure this will go through," and orders the test. The patient goes to a service center, or has the blood drawn in the doctor's office.

The specimen goes to the lab, which is legally required to run the test. It might be a complex test that takes a few days, but the physician gets the results. Then, 30 days later, the lab hears from the payer: "We didn't get all the documentation we needed to authorize the test. Claim denied." Now the lab must contact the doctor's office to get the paperwork it needs to refile the claim, but good luck with that. The doctor is low on staff and already has the results. He or she no longer has skin in the game.

The doctor says, "Yeah, we'll get that to you." The lab waits. They can't appeal the denial until they get the information. But the clock is ticking because they only have so much time to refile. If they don't hear from the doctor, maybe they will refile the claim with the limited information they have and pray that it is not denied a second time. This can go on for six months or longer, and in the meantime, the lab is on the hook for the money it cost to run the test.

This is all assuming that the health plan is clear about the information it needs to approve the claim. That's not always the case. Maybe the plan required a baseline test before it could approve a more advanced $10,000 test, and the doctor forgot to include those earlier results. But the claim denial letter might not specify the information that was missing.

Payers' Perspective

Now, let's look at it from the payer's perspective. Incoming claims are missing required information. Maybe it is a complex oncology test, and the policy requires that the patient had a basic BRCA test within the previous two years. Did that patient have the required test? How long ago and what was the result?

Without that information, the claim is denied. The plan knows that the lab has spent $5,000 to run the test and is going to appeal. That creates an administrative burden. The payer has created a monster.

The plans know this is not working, and many have said they are reducing prior authorization requirements. But from everything I see, they're not reducing prior authorizations for genetic lab tests.

Could help be coming from the government? In January, the **Centers for Medicare and Medicaid Services** (CMS) issued a final rule that mandates prior authorization changes in **Medicare Advantage** and other federally regulated health plans. In addition, the AMA and other physician groups are advocating prior authorization reform legislation in Congress and the states.

What Labs Can Do

How can labs deal with this? In some cases, health plans will allow labs to obtain prior authorizations. That removes physicians from the equation, but now the burden is on the lab. A lab could set up its own prior authorization department, but typically they hire third-party companies that handle prior authorizations for a fee.

It is not clear to me that these third-party vendors have significantly reduced denial rates. I do not have evidence, but I am skeptical. For one thing, much of the information a payer needs for prior authorization is in the patient's medical record and these third-party companies typically do not have those records either. So, they still need to deal with the ordering physician.

Is there a better way? One possible solution lies in artificial intelligence (AI). *The New York Times* reported in July that some doctors are using generative AI software to rapidly draft prior authorization requests for their own claims.

What's clear is that no one is happy with the status quo: The labs, the ordering physicians, the patients, and even the health plans themselves. Whether it's through better technology, more training, policy changes or other measures, something has to give. TDR

Compliance with LDT Rule will be time-consuming and costly for majority of LDTs

What Labs with LDTs Must Do to Comply with FDA's LDT Rule

Jane Pine Wood, J.D.

CEO SUMMARY: Until the recently filed court challenge to the Food and Drug Administration's LDT rule succeeds or Congress intervenes with new legislation, those clinical laboratories performing laboratory developed tests (LDTs) must comply with the requirements of the new rule. This compliance will require substantial staff time and costs that may outweigh the benefit to the lab of continuing to perform one or more of its LDTs.

EDITOR'S NOTE: Attorney Jane Pine Wood, J.D. has been at the forefront of legal issues involving anatomic pathology and clinical laboratories since entering practice in 1988. Nationally recognized for her expertise and insights, she can be appropriately described as the "Doyenne of Regulatory and Compliance Issues involving Laboratory Medicine."

Following the release by the federal ***Food and Drug Administration*** *(FDA) of its final rule regulating Laboratory Developed Tests in early May, Wood prepared a Legal Update for her clients at Cleveland-based* ***McDonald Hopkins****. Because of its clarity and completeness on the complexities of the FDA's Final LDT Rule,* THE DARK REPORT *is reproducing it in full in the following intelligence briefing.*

Wood's explanations of the ramifications of the FDA's final LDT rule will help lab executives and pathologists prioritize the specific elements of the LDT rule that will have the greatest consequences for their respective laboratories.

by Jane Pine Wood, J.D.

On May 6, 2024, the **Food and Drug Administration** (FDA) issued its long-anticipated final rule regulating laboratory developed tests (LDTs). For approximately two decades, the FDA has been signaling its intent to regulate LDTs as a category of medical devices known as *in vitro* diagnostics (IVDs).

During this timeframe, the FDA has taken the position that it has the authority to regulate LDTs as IVDs, but has exercised "enforcement discretion" not to subject LDTs to FDA regulatory controls. On October 3, 2023, the FDA published a proposed rule that would have subjected all LDTs to a phase out of this enforcement discretion so that all LDTs would have been subject to full FDA regulatory control at the end of the phase-out period.

The FDA received over 6,500 comments regarding the proposed rule, many of which expressed significant concerns regarding the adverse impact of the rule upon patient care, as the proposed rule would limit the availability of many medically necessary clinical laboratory tests. In the May 6, 2024, final rule, the FDA appears to have considered the concerns regarding the adverse impact upon patient care. This final rule outlined several categories of full and partial enforcement discretion, as described in more detail below.

➤ No 'Grandfathering' of LDTs

It is critical for laboratories to understand that the FDA's use of enforcement discretion is not the same as an "exception" or "grandfathering" under the final rule. Rather, the FDA's enforcement discretion can be altered or withdrawn at any time unilaterally by the FDA. In addition, the three most significant categories of partial enforcement discretion involve the following, although they remain subject to significant FDA regulation:

- Certain LDTs performed by hospitals and health systems;
- LDTs with New York State Clinical Laboratory Evaluation Program (NYS CLEP) approval; and,
- Currently marketed LDTs.

LDT FINAL RULE

PHASE-OUT PROCESS

Pursuant to the new rule, the FDA will phase out its historic enforcement discretion over a four-year period. All LDTs (with the exception of four very limited categories of LDTs that are eligible for full enforcement discretion) will be subject to the first transition deadlines in the table "FDA's Final Timeline for LDT to IVD Transition" shown on page 13. These three transition items required in the final LDT rule are:

- Medical device reporting system requirements.
- Registration, class-based listing, labeling, investigational use standards.
- At least some of the quality systems requirements.

Those LDTs not eligible for any enforcement discretion will be subject to premarket review requirements, which include premarket application submissions for high-risk tests and premarket review for low and moderate-risk LDTs, as outlined in the fourth and fifth transition deadlines in the table on page 13.

LDT FINAL RULE

LDTS SUBJECT TO FULL ENFORCEMENT DISCRETION

The FDA indicated in the final rule that four categories of tests will be subject to full enforcement discretion—meaning they will not be subject to any of the FDA's regulatory controls (at least for so long as the FDA deems it appropriate to continue its full enforcement discretion).

These four categories of tests are:

- 1976-type LDTs, which are assays that use manual techniques performed by laboratory technicians with specialized expertise and only use components that are legally marketed for clinical purposes. These tests must also otherwise meet the FDA's LDT definition.
- Human leukocyte antigen tests that meet the FDA's LDT definition.
- Tests intended solely for forensic purposes in law enforcement.
- LDTs manufactured and performed in laboratories within the **Veterans Health Administration** or the **Department of Defense**.

LDT FINAL RULE

NYS CLEP-APPROVED TESTS

The FDA indicated that it will exercise partial enforcement discretion for LDTs that have been approved under New York State's Clinical Laboratory Evaluation Program (NYS CLEP) given the FDA's determination of the rigor of the NYS CLEP and the similarities between NYS CLEP and the FDA's premarket review process.

LDTs that are approved under the NYS CLEP will be exempt from the premarket review processes of the FDA *(as described in the fourth and fifth transition deadlines in the sidebar on page 13)*, but will still be subject to the phase-out of the FDA's enforcement discretion for:

- The medical device reporting requirements (effective May 6, 2025).
- Registration class-based listing and labeling (effective May 6, 2026).
- All remaining quality systems requirements not covered in the first two phase-outs (applicable to each laboratory and each LDT), effective Nov. 6, 2027.

LDT FINAL RULE

CERTAIN HEALTH SYSTEM AND HOSPITAL LDTS

A second category for which the FDA has indicated its intent to exercise partial enforcement discretion are LDTs manufactured and performed by a laboratory that is integrated within a health system and designed to address an unmet medical need of patients receiving care within such system.

The FDA will continue to exercise enforcement discretion with respect to the premarket review requirements *(the fourth and fifth transition deadlines in the sidebar on page 13)* as well as the medical records standards of the quality systems requirements *(the third transition deadline in the table on page 13)*.

In addition, the testing must be for an unmet need, which the FDA considers to be a situation where there is no available FDA-authorized test that meets the patient's needs. Importantly, the FDA stated that potential improvements and performance or lower cost in comparison to an FDA-authorized test that meets the patient's needs would not fall within the exemption.

Furthermore, the FDA indicated that its enforcement discretion is only applicable when the laboratory is owned by the health system (it does not include testing performed by a laboratory that is under different corporate ownership), the patient is a patient of the health system, and the ordering physician must be on staff at the health system. This means that LDTs performed by health system laboratories for "outreach" patients would be subject to the full phase out of the FDA's enforcement discretion, unless the LDTs fall within another enforcement discretion exception.

LDT FINAL RULE

CURRENTLY MARKETED LDTS

Perhaps the most important new category of partial enforcement discretion announced by the FDA is for tests that are currently marketed as LDTs.

The FDA announced that it intends to exercise enforcement discretion and not enforce the premarket review *(the fourth and fifth transition deadlines in the sidebar on page 13)* and most of the quality system requirements (except for records require-

FDA's Final Lab Developed Test Rule Includes Multi-year Schedule of Compliance for Labs

IN THE LEGAL UPDATE SHE WROTE ABOUT THE FDA'S FINAL LDT RULE, attorney Jane Pine Wood, J.D. of Cleveland-based McDonald Hopkins described how labs currently offering laboratory developed tests (LDTs) will be required to comply as the FDA phases out its historic enforcement discretion over a four-year period. With the exception of four very limited categories of LDTs that are eligible for full enforcement discretion, all LDTs will be subject to the final rule's transition deadlines, as presented below.

FDA's Final Timeline for LDT to IVD Transition

1 EFFECTIVE DATE: May 6, 2025

Medical device reporting system (adverse event reporting, correction, and removal standards):

- 21 CFR Part 803
- 21 CFR Part 806
- 21 CFR Part §820.198

2 EFFECTIVE DATE: May 6, 2026

Registration and class-based listing, labeling (includes summary of performance data) and investigational use:

- 21 CFR Part 8013
- 21 CFR Part 807
- 21 CFR Part §809.10
- 21 CFR Part 8012

3 EFFECTIVE DATE: May 6, 2027

All remaining quality systems requirements not covered in the first two phase-outs (applicable to each laboratory and each LDT):

- 21 CFR Part 820

4 EFFECTIVE DATE: Nov. 6, 2027

PMA submissions for "high-risk" LDTs (includes mandatory on-site inspections).

5 EFFECTIVE DATE: May 6, 2028

FDA submissions for 'moderate risk" LDTs.

ments) *(the third transition deadline in the sidebar on page 13)* for tests that were first marketed prior to the issuance of the rule (May 6, 2024), and currently are marketed as LDTs.

These tests remain subject to all other FDA requirements under the phase-out policy *(the first and second transition deadlines in the sidebar on page 13)*. As explained in more detail below, these remaining requirements under the phase-out policy are still significant for many laboratories and could present a significant burden.

It is critical to note that these LDTs will only remain eligible for enforcement discretion from premarket review and most of the quality systems requirements as long as they are not modified, individually or in the aggregate, to:

- Change the indications for use,
- Alter the operating principle of the test,
- Include significantly different technology in the test, or,
- Adversely change the performance or safety specifications of the test.

If a currently marketed LDT is modified in such a way, it would then be subject to full FDA controls, including the premarket review and all quality systems requirements.

LDT FINAL RULE

RARE BLOOD CELL ANTIGEN TESTING

The FDA also intends to exercise partial enforcement discretion with respect to rare blood cell antigen testing performed by blood establishments such as transfusion centers and immunohematology laboratories, and when there is no available FDA-authorized test to meet the patient's needs.

These LDTs will be exempt from premarket approval requirements *(fourth and fifth transition deadlines in the sidebar on page 13)* and most of the quality systems requirements *(third transition deadlines in the sidebar on page 13)*.

LDT FINAL RULE

AREAS OF CONCERN FOR LABORATORIES

Although the final May 6, 2024 rule is not as onerous as the proposed October 3, 2023 rule, most clinical laboratories that perform LDTs will still face significant challenges and burdens in complying with the final rule. This is because the existing systems and protocols they have in place for compliance with federal and state laboratory regulations—such as the Clinical Laboratory Improvement Amendments of 1988 (CLIA)—are not adequate for compliance with the FDA's controls.

For example, all laboratories covered under the partial enforcement discretion will need to comply with the requirements for medical device reporting *(first transition deadline in the sidebar on page 13)*. This means laboratories must develop and/or refine policies and protocols to identify, track, and report defects or errors in their LDTs and, as applicable, correct or withdraw the LDTs.

One or more responsible parties in the laboratory organization will need to be designated (and trained) to oversee compliance with these requirements. In many laboratories, the sales representatives are often the first to hear of complaints from ordering physicians and therefore they will need to be trained to immediately report such complaints to the responsible parties within the laboratory.

As part of the labeling requirements *(second transition deadline in the sidebar on page 13)*, laboratories will first need to determine the class into which their LDTs fall, and, second, prepare the labeling to reflect the characteristics and performance data related to their LDTs. The labeling will be available to the public on the FDA's website. In the commentary to the final rule, the FDA alluded to the review of this publicly available labeling data by laboratory competitors as a way to ensure compliance with the labeling standards.

The labeling requirements will require strict adherence to FDA guidelines by all sales and marketing functions in the laboratory. Sales representatives will need to be trained to stay "on script" with the laboratory's labeling in all conversations with ordering clinicians regarding the ordering and use of the LDT. Going "off script" could be viewed as promoting off-label use of the LDT.

Similarly, all of the laboratory's marketing materials, whether digital or hard copy, must align completely with the laboratory's labeling of the LDT. Protocols must be developed and monitored to ensure that the sales and marketing personnel comply with these requirements and the laboratory must maintain documentation of the same.

Depending upon which quality systems requirements are applicable *(the third transition deadline in the sidebar on page 13)*, a laboratory may discover that its existing laboratory information system or document control system is inadequate to meet the quality systems requirements. Laboratories will need to make this determination and, if necessary, budget for, acquire, and install adequate systems to meet the FDA requirements.

As noted above, the enforcement discretion for currently marketed LDTs will be lost if the LDT is modified in a manner that individually or in the aggregate:

- Changes the indications for use,
- Alters the operating principle of the test,
- Includes significantly different technology in the test, or,
- Adversely changes the performance or safety specifications of the test.

Laboratories frequently "tweak" their LDTs to improve performance, address vendor modifications to reagents, deal with vendor shortages, etc. Prior to making such modifications in the future, laboratories will need to determine if the modifications are such that the LDT would no longer be eligible for enforcement discretion.

Steps Labs Should Take Now

Laboratories should assemble an internal team (with outside consultant assistance if needed) and map out a timeline for compliance with the FDA's four year phase-out process. After this team is assembled, the laboratory should assess whether any of the categories of enforcement discretion are applicable to its LDTs. If so, the next step will be to determine the FDA standards to which each LDT will be subject, along with the deadlines for compliance with the applicable standards.

Following these determinations, it is advisable for the laboratory's team to estimate the costs of compliance with the FDA standards for each LDT, including not only actual dollars invested, but also personnel time and effort. Most laboratories do not have extra personnel sitting around with time on their hands, so personnel who already are busy with other tasks may need to be partially or fully redirected to the FDA project, or new personnel hired to work on the project.

Once the laboratory has estimated the costs of compliance for each LDT, the laboratory should consider a "make vs. buy" analysis. In other words, does it make financial business sense for the laboratory to continue to perform the LDT at issue? Or can a similar test be performed with an existing FDA approved test kit, or purchased from a reference laboratory?

Finally, the FDA will issue additional guidance in coming months and years with respect to compliance with the final rule. Given that much of the final rule rests upon "enforcement discretion," the FDA can modify this enforcement discretion at any time. Therefore, the lab's internal team should regularly monitor the FDA's website and other applicable publications and resources for important developments. TDR

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Lab Market Update

Quest Diagnostics Moves to Acquire LifeLabs of Canada

Following deal, U.S.-based Quest, like Labcorp, will own a major national Canadian lab company

QUEST DIAGNOSTICS, ALREADY A CLINICAL LABORATORY BEHEMOTH IN THE U.S., is expanding its North American footprint by acquiring Canada's largest independent laboratory company.

Quest Diagnostics announced on July 3 that it had a "definitive agreement" to acquire **LifeLabs** from the **Ontario Municipal Employees Retirement System** (OMERS) in a deal valued at approximately $1.35 billion in Canadian dollars (US$985 million).

Should the deal close, the two dominant clinical laboratory companies in the U.S. will own counterparts north of the border. **Labcorp**, the other U.S. laboratory giant, acquired Canada-based **Dynacare** in 2002. Dynacare is LifeLabs' largest rival in Canada.

Accelerating Growth

Canada's *The Globe and Mail* described LifeLabs as "Canada's leading laboratory testing company and a household name for many people who have needed a blood test or a range of other screening, genetic, and diagnostic procedures."

The company operates 16 laboratories and 382 collection centers in British Columbia, Ontario, and Saskatchewan, according to the website. It currently has more than 6,500 employees, according to a Quest press release about the deal.

"This transaction is predicated on our strong belief that we can help LifeLabs accelerate growth and improve healthcare," said Quest CEO Jim Davis.

LifeLabs will continue to operate from its Canadian headquarters under its current brand and management, Quest stated, adding that as the new owner, it will offer "new expertise, innovations, and resources."

More specifically, Quest promised "improved online appointment scheduling and faster patient service center processing," as well as enhanced data security. Patient data will remain in Canada, Quest said.

Advanced Testing

The press release noted that Quest recently introduced advanced tests in Alzheimer's disease, women's health, oncology, and cardiometabolic health, suggesting that the deal will allow LifeLabs to offer these tests as well. The deal is expected to close by the end of the year.

The press release also noted that Quest and LifeLabs have worked together in recent years, including a "reference relationship" in which Quest provides access to advanced diagnostic tests. LifeLabs is also part of Quest's Global Diagnostics Network, formed in 2018 to share expertise about clinical laboratory testing. That group currently consists of 12 laboratories around the world.

Quest Diagnostics was one of two companies in the running to acquire LifeLabs, according to media reports. The other was **Andlauer Healthcare Group**, a medical logistics company headquartered in Vaughan, Ontario. Quest outbid Andlauer by CAN$100 million. TDR

Lab Market Update

Invitae's Troubled Journey: Rise, Fall, and Bankruptcy

Investors poured billions into the genetic testing firm, but the outcome was billions in losses and liquidation

On May 7, the remnants of genetic testing giant **Invitae** (NYSE: NVTA) were scooped up by **Labcorp** when the **United States Bankruptcy Court** approved Labcorp's bid to acquire Invitae's assets.

Labcorp will receive "select assets of Invitae on a going concern basis for $239 million in cash consideration, plus other non-cash consideration," *PR Newswire* noted. The sale completion is slated to be wrapped up by the third quarter of 2024.

With this outcome, one of the nation's largest genetic testing companies has come to an ignominious end. It started fast and attracted plenty of capital from investors. But Invitae proved unable to address the challenges of succeeding in the genetic testing market. It filed for bankruptcy with the specific goal of selling its assets. *(See TDR, "Genetic Testing Firm Invitae Files Chapter 11 Bankruptcy, Pursues Sale," Feb. 26, 2024.).*

High-Flying Genetic Test Firm

Invitae was a high-flying genetic testing company that was highly-regarded by professional investors.

Founded in 2010 by Randy Scott, PhD, the San Francisco-based medical testing company was at the forefront of genetics and worked hard to create a sense that such testing was the new norm. In its marketing, the company described genetic testing as "part of your routine healthcare," and gave the feeling of household familiarity.

Invitae's first product came in 2013. It was "an assay of 216 genes covering 85 genetic disorders," *Workweek* reported. The lab company focused on hereditary cancers such as colon, pancreatic, and breast. Initial tests cost consumers $1,500, and strong investor backing aided the company's rapid growth.

Quick Start in 2014

"In the first nine months of 2014, the company had $729K in revenue and 1,189 tests completed. Fast forward to 2021 and the company had generated over $460.4 million in revenue and completed over 1.1 million billable tests," *Workweek* added.

"The company's vision and early scientific success enabled it—six different times—to raise over $200 million in capital from the private markets. Invitae then successfully IPO'd in February 2015 at a $492 million post-money valuation. The company raised $101.6 million and started trading at $16/share," *Workweek* noted.

But all of that growth in genetic test volume never reached a level where the company could breakeven or show a profit on operations. In assessing the woes at Invitae, *Fierce Biotech* wrote, "As *The Wall Street Journal* noted in its report, the company has never turned a profit in its decade of existence. In its last full-year earnings report, covering 2022, it reported a net loss of more than $3.1 billion, a massive increase over 2021's $379 million loss. As of the third quarter of 2023, Invitae had already tallied a net loss of more than

$1.3 billion for the year, with cash burn of $311 million as of Sept. 30, 2023, and just under $265 million left in cash on hand."

Some Wall Street analysts commented about the weakness in the current genetic testing market. One example is **23andMe**. On Feb. 24, 2024, *Wired* wrote how "23andMe is facing more than 30 lawsuits after a data breach last year exposed personal information from nearly seven million customers' profiles. Valued at $6 billion in 2021 when it went public, 23andMe now risks being delisted from the **Nasdaq** as its stock continues to trade below $1 a share."

Why Did Invitae Fail?

Pathologists and clinical lab executives should understand the reasons behind Invitae's appeal to investors in its early years versus its financial collapse and sale of remaining assets to Labcorp. Some of Invitae's troubles were of its own making. But the troubles genetic testing labs are having with getting reimbursed for tests claims is also a contributing factor.

As financial analysts work to unravel the true reasons behind Invitae's failure to reach a profitable level of operations, several ideas are circulating and were discussed in recent years as Invitae's downward spiral became obvious.

Invitae excecutives themselves described the company's downfall as a result of having "taken on too much debt to fund its expansion from 2019 to 2021," *Reuters* noted.

13 Acquisitions

During the time referenced, the company acquired 13 companies which upped debt at Invitae by an additional $1.5 billion. It's challenging to effectively integrate just one laboratory testing company while keeping referring physicians and patients happy. Invitae had to do this 13 times in recent years.

In its analysis of the problems at Invitae, *Reuters* described the company as buffeted by a perfect storm of additional competition, decreased demand for discretionary genetic tests, and climbing interest rates.

Another factor may have been a revolving door for senior management. *The Wall Street Journal* added more insight on this point, noting that a "turnover in its top ranks" also may have contributed to the company's situation turning sideways given that the company's situation was already tenuous.

Invitae's revenue growth in its early years is evidence that its sales team was producing year-over-year growth in the number of genetic tests. However, it also was incurring substantial expenses—both the sales cost to acquire a new client and the cost to support the genetic testing—such that it posted large operating losses in recent years. This is evidence that Invitae's new referring physicians were not referring enough genetic tests to offset the sales cost to acquire their business.

Unpaid Genetic Test Claims

Another factor that was generally unrecognized by many financial commentators in the wake of Invitae's bankruptcy filing last February is the challenge all genetic testing companies are having when they submit claims to health plans, but do not receive reimbursement.

Onerous prior authorization requirements and difficulties in becoming an in-network provider were probably issues at Invitae, as they are for many other lab testing companies. In fact, because of Labcorp's contracts with most of the nation's health insurers, it may end up getting paid much more frequently for those genetic test claims generated by former Invitae customers.

Additionally, the rapid rise in interest rates during the current administration meant that Invitae's interest costs increased substantially. And it came at the same time that the country's recent inflation drove up operational costs at the genetic testing company. TDR

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

Some hospitals failing to comply with the federal price transparency regulation have been fined. The website of CMS.gov lists 15 hospitals and the amount each was fined. On June 6, 2022, the first fines were levied against **Northside Hospital of Atlanta** ($883,130) and **Northside Hospital Cherokee** of Canton, Ga. ($214,320). On Feb. 27, 2023, **UF Health North** of Jacksonville, Fla., was fined $979,000, the largest amount of fines assessed to date. **Jackson Memorial Hospital** of Miami was the most recent hospital to have been fined, on July 3, 2024, for a total of $871,122.

MORE ON: *Federal Price Transparency Rule*

Since the price transparency rule took effect, hospitals operating in the United States are required to provide clear, accessible pricing information online about the items and services they offer. In 2022, the federal **Centers for Medicare and Medicaid Services** (CMS) increased the maximum yearly fine to more than $2 million for larger hospitals that do not comply, up from a maximum of $110,000 a year. Hospital laboratories are covered by this federal rule and their prices should be easily accessible to patients in advance of service. With some regularity, local news outlets will investigate hospitals in their community, then publish stories about whether or not the hospital was in compliance.

SYSMEX AMERICA HAS NEW CEO

Sysmex America announced that Dan Zortman is the company's new CEO. He takes over for Andy Hay, who served as the company's CEO since 2021. Hay will continue as the Chairman and President of Sysmex America. Zortman is a multi-decade veteran of the IVD industry. He came to Sysmex from **Roche Diagnostics**, where he was Vice President of Commercial Operations.

TRANSITIONS

• Theresa Heath is the new Vice President, U.S. Business Development and Marketing at **MLM Medical Labs** of Memphis. Health's previous positions were at **LabConnect**, **Cerba Research**, **Exact Sciences**, **Ventana Medical Systems**, and **Quest Diagnostics**.

• **Beckman Coulter** of Brea, Calif., selected Ashley Autin for the role of Health System Executive. Her prior positions were with **Qiagen** and **Ortho Clinical Diagnostics**.

• **PreciseMDX** of Los Angeles, announced the selection of Jack Redding as Vice President, Sales. Redding's previous positions were with **Drugscan**, **BioReference Laboratories**, **Montefiore St. Luke's**, and **Halfpenny Technologies**.

Anne Beall joined **Thermo Fisher Scientific** as Lab Optimization Consultant. She served for 19 years at **bioMérieux** and before that with **Sarasota Memorial Hospital**, and **Integrated Reference Labs**.

That's all the insider intelligence for this report. Look for the next briefing on Monday, August 12, 2024.

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