

# CLIN

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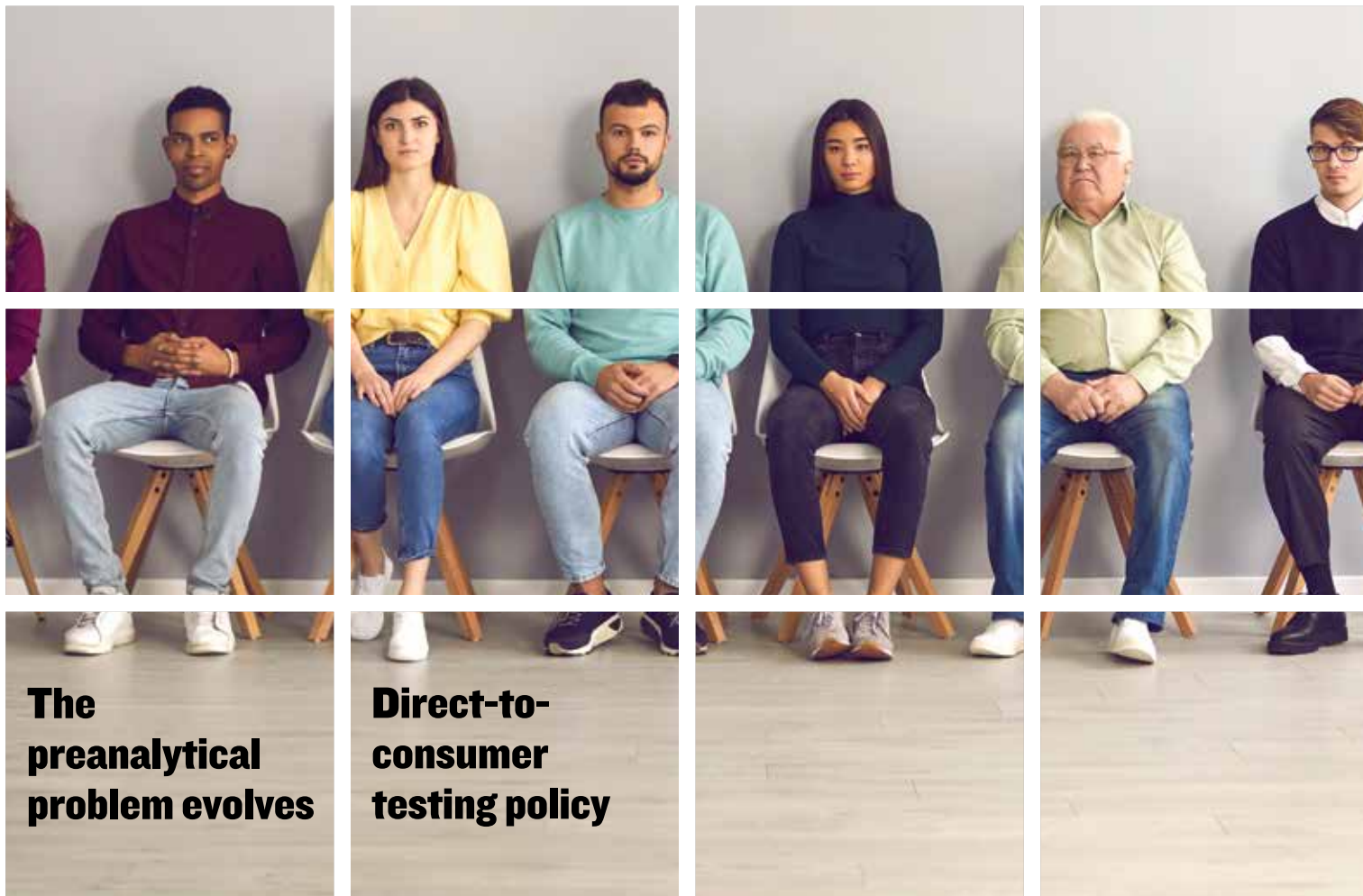
COAGULATION TESTS  
REMAIN ACCURATE  
FOR NEW DRUGS

# 10%

Analytical variation for  
prothrombin time tests in  
patients on dabigatran

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# Hit or miss for cancer biomarker tests



**The  
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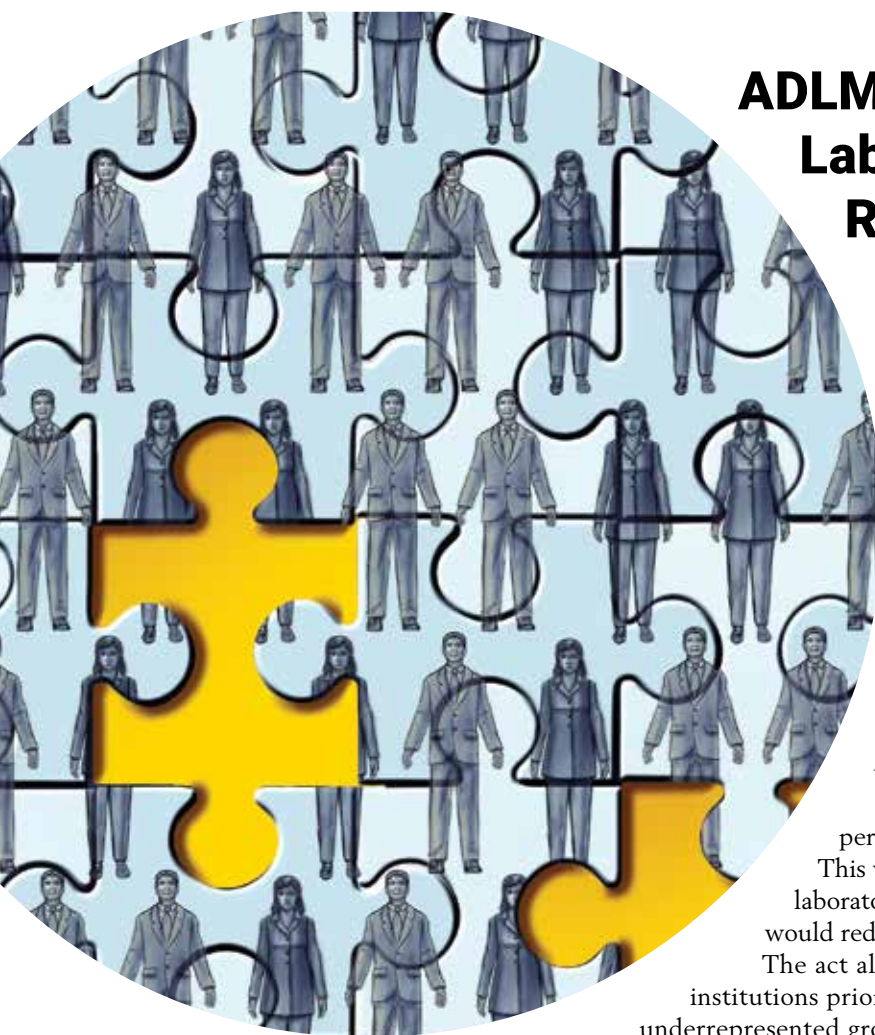


If the new administration revokes the FDA rule or the courts decide against the FDA, then the issue of LDT oversight will go back to Congress.

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## ADLM endorses the Medical Laboratory Personnel Shortage Relief Act of 2024

In a letter addressed to United States Rep. Deborah Ross, the Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) endorsed the Medical Laboratory Personnel Shortage Relief Act of 2024. The act would direct federal funding to grapple with the national shortage of medical laboratory professionals that is affecting healthcare delivery.

The shortage has led to increased workloads and stress for staff, raising risks of errors and delays in test results, ADLM emphasized in the letter.

In rural and underserved areas, some laboratories face temporary closures because of a lack of personnel, limiting patient access to timely and essential diagnostic care. ADLM supports the inclusion of medical laboratory professionals in the National Health Service Corps (NHSC), which will prioritize placement in shortage areas.

Under the bill, loan repayment incentives for medical laboratory personnel would alleviate financial burdens for new professionals.

This would encourage recent graduates to enter and remain in laboratory professions. Longer term, ADLM believes this initiative also would reduce diagnostic delays and support better patient outcomes.

The act also provides funding for educational programs, particularly for institutions prioritizing culturally competent care. By supporting underrepresented groups, this legislation promotes a diverse, well-prepared laboratory workforce capable of meeting the evolving demands of modern healthcare.

### ● ADLM WRITES TO PRESIDENTIAL TRANSITION TEAM ON LDT FINAL RULE

In a letter to President Trump's transition team, ADLM called for the new administration to revoke the Food and Drug Administration (FDA) final rule on laboratory-developed tests (LDTs). This rule, if implemented, would regulate laboratories that develop LDTs as if they were medical device manufacturers. The rule fails to recognize

the difference between the two sectors: Manufacturers develop and sell their devices to anyone, whereas laboratories develop LDTs for their patients only at the request of an ordering physician.

ADLM is concerned that if this rule is implemented, it will hinder the development of new LDTs, which were critical to advancing care, and significantly increase the costs associated with LDT testing, thus forcing laboratories to reduce

or eliminate LDTs. Revoking this rule would preserve patient access to these tests while giving Congress the opportunity to modernize the existing structure if needed under the Clinical Laboratory Improvement Amendments.

The letter also noted that during the first Trump administration, ADLM worked closely with White House staff during the COVID pandemic by serving on the National Testing Implementation

Forum and offering insights and guidance on how to deal with SARS-Cov-2 testing issues.

● **OFFICE OF THE INSPECTOR GENERAL: HIPAA AUDITS MUST DO MORE TO PROTECT AGAINST CYBER THREATS**

In recent years, cyberattacks have become an increasing concern for healthcare providers and patients alike. In its report to Congress for 2022, the Department of Health and Human Services (HHS), Office for Civil Rights (OCR), stated that it received 64,592 reported breaches affecting 42 million individuals and that most of the associated security incidents were related to the hacking of healthcare providers. These cyberattacks raise the question of whether OCR's audits for ensuring the protection of electronic protected health information have been effective.

Now a new HHS Office of Inspector General (OIG) audit has found that OCR's audits only assessed 8 of 180 HIPAA rules requirements. Only 2 of those 8 requirements were related to security rule administrative safeguards and none were related to physical and technical security safeguards.

The OIG provided recommendations aimed at enhancing the OCR's HIPAA audit program, including that it expand its HIPAA audits to assess compliance with physical and technical safeguards from the HIPAA Security Rule; document and implement standards and guidance for ensuring that deficiencies identified during the HIPAA audits are corrected in a timely manner; and define metrics for monitoring the effectiveness of OCR's HIPAA audits.

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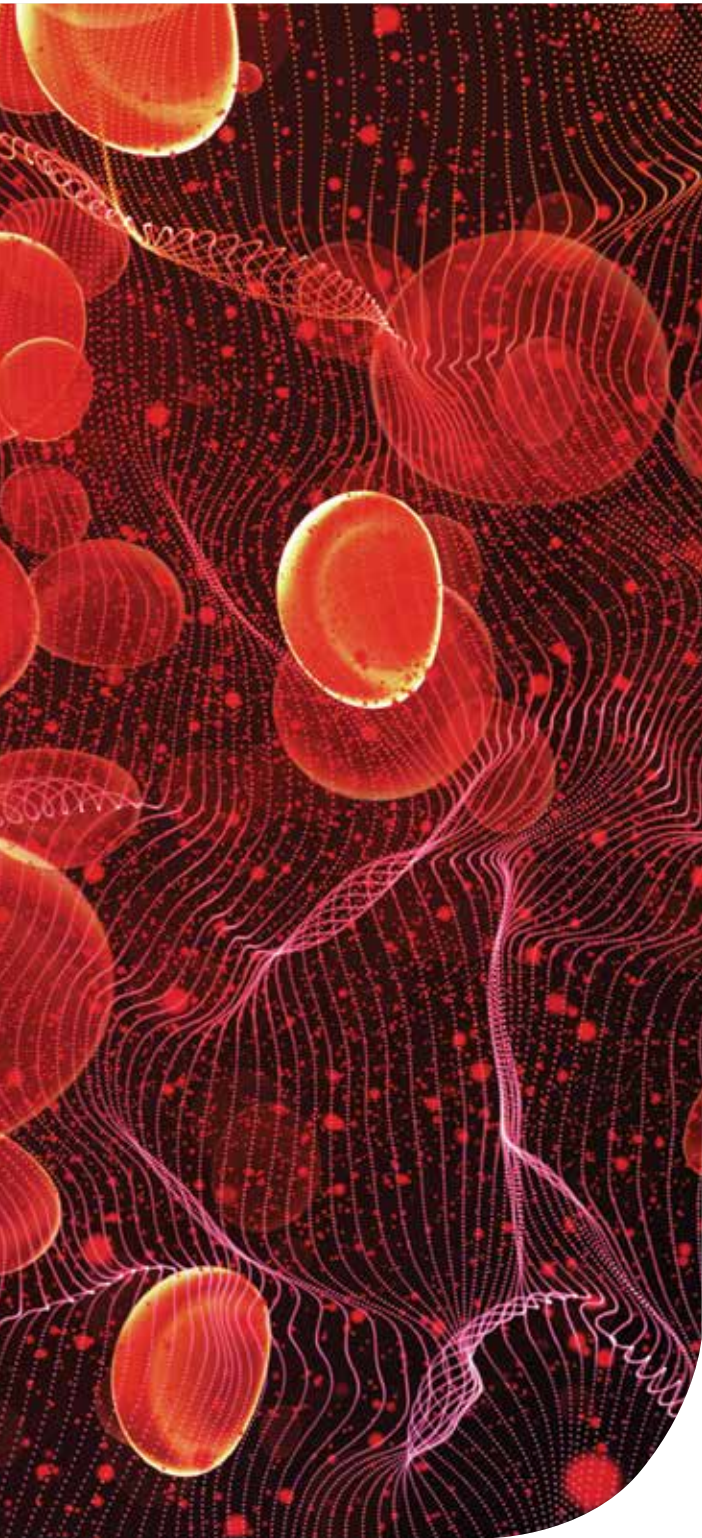
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## Dabigatran does not affect performance of coagulation tests

The analytical performances of laboratory coagulation tests in patients treated with the direct oral anticoagulant (DOAC) dabigatran are comparable to those in a healthy population, according to a recent study (*J Appl Lab Med* 2024; doi: 10.1093/jalm/jfae116).

DOACs are preferred treatments for venous thrombosis and atrial fibrillation (AF). In recent years, their use has soared in patients with these diagnoses, despite unclear biological variation of hemostatic markers among them. Ideally, biological variance should be measured in patient populations for whom these tests are ordered, but underlying data are mostly from healthy individuals.

To fill in this gap, researchers determined the biological variance of activated partial thromboplastin time (APTT), prothrombin time (PT), fibrinogen, and trough dabigatran levels in AF patients treated with dabigatran long-term.

In a prospective cohort study, the researchers followed 18 patients with AF treated with dabigatran for more than 3 months. The researchers determined the biological variation of APTT, PT, fibrinogen, and dabigatran levels during a follow-up of more than 1 year and calculated within-subject, between-subject, and analytical variation. In up to 10 monthly blood collections, the researchers measured APTT, PT, fibrinogen, and trough dabigatran levels and calculated between-subject variance (CV<sub>G</sub>), within-subject variance (CV<sub>I</sub>), and analytical variance (CVA). In all, they measured and made calculations using 130 samples. Ten patients (55.6%) completed the full follow-up of 10 samples. Eight participants did not complete the follow-up protocol.

For APTT, CV<sub>G</sub> was 11.5%, the CV<sub>I</sub> 8.8%, and the CVA 1.1%. For PT, these values were 5.2%, 4.0%, and 1.0%; and for fibrinogen, 13.6%, 11.8%, and 1.6%, respectively. For dabigatran levels, the values were 37.9%, 33.0%, and 3.4%, respectively.

In healthy individuals, previous research had shown CV<sub>G</sub> of 7.2% and CV<sub>I</sub> of 2.8% for APTT. For PT, these previously recorded values in healthy individuals were 5.1% and 2.6%. For fibrinogen, they were 17.1% and 10.2%, respectively, according to the paper.

Study limitations include the small sample size and the use of reagents and instruments that differ from those in related previous research, the researchers noted.

### ● NEW COLORECTAL CANCER SCREENING TESTS FAIL TO MEASURE UP

**N**ew blood screening tests for colorectal cancer (CRC) are more expensive and less effective than colonoscopy and stool tests, according to recent research (*Ann*

*Intern Med* 2024; doi:10.7326/ANNALS-24-00910).

About 40% of people ages 50 to 75 are not up to date with U.S. Preventive Services Task Force colorectal cancer screening recommendations, which call for stool tests,

colonoscopy, CT colonography, or flexible sigmoidoscopy. Medicare covers CRC screening every 3 years with Food and Drug Administration-approved blood-based tests with sufficient sensitivity and specificity. An approved cell-free DNA (cf-DNA) blood test, Guardant Shield, costs \$1,495, and has high sensitivity for CRC stages II to IV but not stage I nor CRC precursors, the study said.

In this changing landscape, tradeoffs have emerged between tests' abilities to detect CRC and CRC precursors, their specificity, their uptake, and their cost. The researchers aimed to estimate the clinical and economic costs of new CRC blood screening tests, compared with commercially available, established alternatives, in average-risk adults aged 45 and older.

Those established tests were colonoscopy, a fecal immunochemical test (FIT), and a multitarget stool DNA test (MT-sDNA, Exact Sciences' Cologuard). The four emerging screening methods were the cf-DNA tests Guardant Shield and Freenome, as well as the next-generation multitarget stool test (ngMT-sDNA) and a new FIT-RNA test, Geneoscopy ColoSense.

The researchers modeled the relative rate of colorectal cancer and deaths among 100,000 average-risk people using various screening approaches. They found that colonoscopy and FIT would reduce incidence of CRC by 70% and mortality by 75%, versus no screening. The MT-sDNA test

## Placental growth factor levels less than 100 pg/mL were associated with 79.4 - fold increased likelihood of early preterm birth.

would reduce CRC incidence by 68% and mortality by 73%, with similar rates for the ngMT-sDNA and FIT-RNA tests, versus no screening. The cf-DNA tests yielded CRC incidence and mortality reductions of only 42% and 56%, respectively, the researchers wrote.

They also found that colonoscopy and FIT were more effective and less expensive than the cf-DNA and MT-sDNA tests. Meanwhile, the MT-sDNA test was more effective and less expensive than the cf-bDNA test.

The blood tests were better than no screening at all. Otherwise, substituting blood tests would lead to worse outcomes on a population level, the researchers commented.

### ● PIGF MAY SPOT HIGH RISK OF PRETERM BIRTH

**M**id-pregnancy placental growth factor (PIGF) testing may be a potential tool for identifying pregnancies at highest risk of early preterm birth, researchers reported (JAMA Netw Open 2024; doi: 10.1001/jamanetworkopen.2024.44454).

Preterm birth is defined as prior to 37 weeks of gestation. One-quarter of these births occur before 34 weeks, constituting early preterm birth. These are associated with the greatest risk of adverse infant

and childhood outcomes, at tremendous societal cost.

To determine whether PIGF testing at the time of gestational diabetes screening finds pregnancies at higher risk for early preterm birth, the researchers conducted a prospective cohort study at a tertiary care center. The study involved 9,037 singleton pregnancies. Unselected participants had PIGF tests at 24 to 28 weeks' gestation. The primary outcome was all early preterm birth, while secondary outcomes included iatrogenic preterm birth, spontaneous preterm birth, preeclampsia, stillbirth, and small-for-gestational-age birth weight.

PIGF levels less than 100 pg/mL were associated with a 79.4-fold increased likelihood of early preterm birth. Low PIGF level was present in more than half of iatrogenic early preterm births and about one-third of all antepartum stillbirths.

These findings suggest that PIGF screening timed with routine gestational diabetes screening may be a powerful clinical tool to identify pregnancies at risk of early preterm birth, especially iatrogenic birth. Strategically redirecting health-care resources to this high-risk group could improve maternal and perinatal outcomes, the researchers said.

As the direct-to-consumer testing market booms, a new ADLM position statement gives recommendations to regulators and lab professionals to ensure that the public benefits from reliable, accessible testing.

# Balancing patient empowerment and quality care in direct-to-consumer testing

BY GRACE BROWNE

**T**he Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) recently released a position statement on direct-to-consumer (DTC) tests, which are tests that individuals can order themselves without going through a provider. DTC tests offer information on health-related matters such as allergies, sexually transmitted diseases, and even a person's genetic makeup. In ADLM's statement, which overhauls one that the association put out in 2019, the organization supports the use of these tests as a way of enabling consumers to gain access to their own health information and manage their healthcare.

Since the 2019 statement, the DTC test market has continued to grow, and it's set to keep expanding. ADLM's new statement estimates that the market could be worth more than \$20 billion by 2030. This growth is in part attributable to the COVID-19 pandemic, during which many people needed to be tested for the virus but couldn't always visit their medical providers. This collectively had the effect of normalizing nontraditional modes of testing such as DTC.



Now, the DTC testing market is here to stay, said Julie Shaw, PhD, FCACB, the head of the division of biochemistry at The Ottawa Hospital and associate professor at the University of Ottawa. “Direct-to-consumer testing is here,” she said. “It’s not going anywhere. So I think as lab professionals, we can either stick our head in the sand and pretend it doesn’t exist, or we can get ahead of it.”

### A STAKE IN UNCERTAIN GROUND

The rapid growth of the DTC test market means that ADLM’s original position on the industry had to shift accordingly. “We blew the old one up, and we started over again,

the industry. “This position statement puts a stake in the ground that says: ‘These are the things that we need here,’ he said. “But we’re in no position to make any of these happen.”

It’s a tricky industry to provide an unqualified endorsement of. Sometimes described as a “Wild West,” DTC testing has not gone without criticism. Various offerings on the market have caught flack for a lack of proven efficacy or making misleading claims, the dubious qualifications of those analyzing the test, taking advantage of patients’ fears, and generating ethical quandaries. Some providers have tried to escape these criticisms by stating that they merely provide health

would love to see the threshold for people to use these get lower,” he said, “because frankly, access to such testing — particularly in socioeconomically disadvantaged environments — is a huge problem.” And the strongest sentiment in ADLM’s position statement is that DTC tests give people more autonomy over their health.

### A DIFFICULT OUTLOOK FOR REGULATING DTC TESTS

That being said, there always will be fraudulent or misleading activity in this space that takes advantage of the consumer, according to Dietzen. ADLM’s statement makes numerous recommendations to U.S. regulatory bodies to try to keep this to a minimum. For one, the Centers for Medicare & Medicaid Services should ensure that all laboratories engaged in commercial testing are CLIA certified. The Federal Trade Commission (FTC) also should vigorously prosecute providers that engage in fraudulent or misleading activity. But the sprawling nature of the market leads Dietzen to think that it’s “unreasonable to expect the FTC to keep up with the number of scams that might flourish in the marketplace.”

According to Katie Stoll, MS, CGC, a genetic counselor and executive director of the nonprofit organization Genetic Support Foundation, one of the biggest issues with DTC testing lies with the subset of these tests that are consumer-initiated but still require an order from a qualified medical provider. The loophole that is often exploited by labs that wish to increase sales through direct access to testing is to work with physician networks that will sign off on test orders “for just about anything” for a fee, she said.

**"We think this is a good idea -  
under very restricted circumstances."  
— Dennis Dietzen**

because so much had changed,” said Dennis Dietzen, PhD, DABCC, FADLM, the division chief of pathology and laboratory medicine at Phoenix Children’s Hospital and chair of ADLM’s Policy and External Affairs Core Committee. Dietzen led the working group that wrote the 2024 position statement.

“The main take home message is that we think this is a good idea — under very restricted circumstances,” he said.

Indeed, the statement offers a number of recommendations for keeping checks and balances on

information as opposed to medical advice, but they cannot control how consumers interpret and use these tests.

But DTC services do have benefits. For instance, those who live in remote or underserved areas can greatly benefit from being able to order and perform tests at home. People can get results more quickly from DTC tests compared to traditional methods. Consumers now can order tests for which they may prefer privacy, such as sexual health tests. Cost is also a factor; Dietzen sees these tests as a way of democratizing access to testing. “We

She also echoed Dietzen's concern that regulatory bodies will not be able to monitor the industry sufficiently to prevent harm to the public. The FTC, for instance, does not review marketing claims before a product is promoted to consumers, she pointed out; the organization can go after companies when they learn of false advertising, but it suffers from "a very limited bandwidth in the area of health and usually would only learn of a bad-actor lab after harm has been caused," she said.

"In my mind, the regulators are not equipped to do this," Dietzen said. "So it's sort of an empty feeling when you make these recommendations, and you know that they're not really realistic at this point."

Outside of the United States, the rise of this industry has other repercussions. In countries with universal healthcare, such as Canada, where Shaw is based, or in the United Kingdom, there are concerns that the growth of DTC testing may be at risk of putting undue burden on these already-stretched public services. "Inevitably, the more testing you do, the more abnormal results you'll find, just statistically," Shaw said. "Is that going to end up costing the healthcare system even more money?"

## HOW LAB PROFESSIONALS CAN TAKE THE LEAD

With all of these potential drawbacks to DTC testing, laboratory professionals have a opportunities to ensure that these tests are used as appropriately as possible and to help consumers to navigate the rocky terrain ahead. ADLM's statement calls on labs performing DTC tests to explain the purpose of each test in an accessible and easily understandable


## ADLM's positions on direct-to-consumer laboratory testing

The Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) has released a position statement supporting consumers' efforts to play active roles in their healthcare by ordering their own laboratory tests. The statement emphasizes that such direct-to-consumer (DTC) testing should be performed only by reputable laboratories that are CLIA certified and that are committed to providing clear information and guidance to help consumers interpret the results.

- Labs should provide prominent instructions for consumers to contact a qualified healthcare provider with any questions or concerns.
- Labs must also ensure customers' data is handled safely and confidentially, while validating all sample collection, sample processing, and testing practices in accordance with CLIA regulations or guidance from the Food and Drug Administration.
- Healthcare providers, regulators, and policymakers should consult with laboratory medicine experts on DTC testing-related issues.
- The Federal Trade Commission should vigorously prosecute DTC testing providers that engage in misleading or fraudulent marketing and testing practices.
- The Agency for Healthcare Research and Quality should encourage further research on outcomes associated with consumer-initiated versus conventional testing practices.

way, detailing appropriate use, specimen-collection methods, risks, results interpretation, and cost to consumers. The statement goes on to say that labs should provide prominent instructions for consumers to contact a qualified healthcare provider with any questions or concerns. Labs must also validate all sample collection, sample processing, and testing practices in accordance with CLIA regulations or guidance from the Food and Drug Administration.

Another issue that DTC testing raises and that lab experts can help answer is the perennial question of how much information is too much information. Although DTC tests may give consumers the opportunity to learn more about their health, they may not always be equipped to interpret the results of their tests. And clinicians also may lack the training or education needed to evaluate the results, or to incorporate the results into clinical care in any meaningful way.

This is where lab professionals can come in, said Hoda Hagrass, MD, PhD, FCAP, FADLM, who worked on ADLM's position statement and is the medical director of clinical chemistry and immunology laboratories at the University of Arkansas for Medical Sciences. At present, lab professionals mostly interact only with the medical community, but according to Hagrass, they will now need to be retrained to communicate directly with the consumer — and to be equipped to educate consumers accordingly. "We need to make sure that we are all built for any question that comes to us from the healthcare provider — or from consumers themselves," she said. 

**Grace Browne** is a freelance journalist who lives in London. She currently has a fellowship funded by the International Center for Journalists through the Health Innovation call.

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# Overlooked and patients missed for cancer



# underserved, biomarker testing risk worse outcomes



Despite decades of research and clear clinical guidelines, many cancer patients miss out on critical biomarker tests, leading to inappropriate or suboptimal treatments. From educational gaps to logistical hurdles, the barriers are high — but the stakes are even higher.

**BY KAREN BLUM**

It's been known for about 20 years that people who have the slow-growing disease chronic lymphocytic leukemia (CLL) and a mutation called 17p deletion do not respond well to chemotherapy and should only be treated with novel targeted agents, said oncologist Jacqueline Barrientos, MD, MS. Since 2018, guidelines from the International Workshop on CLL have recommended laboratory testing for additional biomarkers, such as *TP53* mutations and immunoglobulin heavy chain variable (*IGHV*) status, to help oncologists risk-stratify patients and identify appropriate therapies.

So Barrientos, chief of hematologic malignancies and director of oncology research at Mount Sinai Medical Center in Miami Beach, Fla., said she was surprised to see — in a multisite, 1,462-patient registry she helped create — that biomarker testing occurred in less than one-third of patients, especially as the tests can be run on easy-to-obtain blood samples.

Fluorescence in situ hybridization (FISH) to detect chromosomal abnormalities was performed in just 28% of patients, *TP53* mutation testing in 11%, and *IGHV* mutation testing in 12% (Blood Adv 2023 Sep 12;7(17):4760-4764). What's worse, a third of patients continued to receive chemoimmunotherapy, including those with *del(17p)/TP53* mutation — a high-risk population known to experience poor outcomes with the therapy — which highlights the need for greater awareness of the guidelines among oncologists.

CLL is a heterogeneous disease for which biomarker testing is crucial to pinpointing the right treatment, Barrientos said. "There are

**"Cancer is kind of like playing chess. You're always thinking about your next move."  
— Jacqueline Barrientos**



people that have no issues when they're diagnosed, and they can live a long life without the need for therapy, and there are other people whose disease progresses very quickly," she said. "It's the same disease. The same cancer. The difference is the prognostic markers that they have, and that's why we have to do the testing, to help us identify how to optimize their management and their care."

"Cancer is kind of like playing chess," Barrientos added. "You are always thinking about your next move, because at some point, the original therapy may stop responding." Biomarker testing can identify future therapies to use in those cases. Those recommended for CLL besides 17p/*TP53* include 13q, trisomy 12 and 11q, according to the International Workshop on Chronic Lymphocytic Leukemia guidelines.

CLL is one of several cancers, along with lung and colorectal cancers, where biomarker testing is underutilized. Lung cancer has seen a surge in biomarkers identified over the past 10–15 years to help direct therapy, said Benjamin Levy, MD, a thoracic medical oncologist and clinical director of medical oncology for the Johns Hopkins Sidney Kimmel Cancer Center at Sibley Memorial Hospital in Washington, D.C. Yet only 45% of patients seen in community oncology practices get next-generation testing, he said.

It started with one or two genes discovered that could affect patient response to therapy, he said. Now, "It just blossomed into multiple genetic alterations that we can now wed to particular targeted therapies ... The diagnostic capabilities have been advancing much more quickly than what

we can do with the drugs, but the bottom line is this: We now have the capability to do next-generation sequencing to unearth the genomic alterations that are relevant.”

Guidelines from the National Comprehensive Cancer Network (NCCN) recommend testing for 10 genetic mutations: *EGFR* exon19, *EGFR* exon 20, *HER2* exon 20, *KRAS G12C*, *BRAF* V600E, *MET* exon 14 skipping alteration, *ALK* fusions, *RET* fusions, *ROS1* fusions and *NTRK* fusions, along with immunohistochemistry to study PD-L1 and, more recently, *HER2* overexpression.

While it seems like all oncologists should be doing this, there have been multiple challenges, said Levy. One is an educational gap. The science evolves so quickly that some oncologists can't keep up, and not all commercial testing platforms offer the latest next-generation sequencing techniques. Additionally, he said, the tissue collected from a lung or lymph node biopsy is imperfect and may not be substantive enough for study or sending off to a third-party testing company, a problem known as tissue insufficiency. This could result from the collection itself or because a pathologist aiming for correct diagnosis performs too many immunostains, leading to tissue exhaustion.

Some busy physicians order testing and forget to follow up about results, Levy said. Or even when they do, with next generation testing returning results for 500 genes, the reports are too complicated to interpret.

A study Levy co-authored (*Oncologist* 2015 Oct;20(10):1175-1181) for oncologists on

## Low biomarker testing rates for colorectal cancers also contribute to disparities in care.



how to implement evidence-based recommendations for molecular testing for non-small cell lung cancer remains applicable today, he said. First, understand that next-generation sequencing platforms that include both DNA and RNA testing is most important to unearth a particular genetic alteration. Get help from specialists in interpreting reports and appoint a physician champion within a health system to make sure these tests are ordered.

Good communication between the oncologist and pathologist or other staff procuring tissue also holds importance, said Levy, to make sure they use the optimal procedure and sample the best location, as well as ongoing education about testing, and reminders to conduct both tissue and blood-based testing to best detect a genetic target.

“There’s a new biomarker test that comes out every few months now in lung cancer,” he said. “The complexity of this is no doubt a turning point and an inflection point. It’s a testament to the science that we’re getting a lot better and we’re advancing patient care. We’re developing these new drugs that are better tolerated that lead to better outcomes, which are specifically tailored to the patient, but at the same time, it’s confusing.”

Low testing rates for colorectal cancers also contribute to disparities in care, according to one recent report (*JAMA Netw Open.* 2024;7(7):e2419142). In this retrospective cohort study of 41,061 patients from the National Cancer Database who had metastatic colorectal cancer, just 28.8% underwent recommended biomarker testing for

*KRAS* and 43.7% received testing for microsatellite instability (MSI). Factors associated with a lower likelihood of MSI testing included being age 70–79, receiving treatment at a community cancer program, living in a rural location, living in an area where the percentage of adults with no high school diploma was 17.6% or higher, and receiving treatment at facilities in the East South Central portion of the country including Alabama, Mississippi, Kentucky and Tennessee. Similar patterns were observed for *KRAS* testing.

Genetic biomarkers such as MSI and alterations in the *BRAF* and *RAS* genes have been the mainstay of precision medicine for colorectal cancers, said Arun Nagarajan, MD, senior author of the study and section head of gastrointestinal medical oncology at the Cleveland Clinic Weston Hospital in Florida. *KRAS*-positive alterations alone are reported to be present in 35–45% of cases. NCCN also recommends looking at biomarker targets such as *NRAS*, *HER2*, *POLE/POLD1*, *RET*, and *NTRK*.

“It’s really important to have the biomarker information,” Nagarajan said. “If a patient is microsatellite-unstable or microsatellite-high, you would not use systemic chemotherapy as the backbone, you would start immunotherapy with FDA-approved agents such as pembrolizumab, nivolumab, or ipilimumab.”

Life expectancy also can vary based on biomarkers, he said. “Patients who are MSI-unstable and who don’t have liver metastasis have a much better outcome than patients who have the *KRAS* mutation and who are MSI-stable. You can really counsel

## Patient advocacy groups are making a difference in pushing for testing.



families about their life expectancy, prognosis, and the choice of treatment.”

Additional barriers to testing may stem from Medicare rules or insurance companies declining to pay for next-generation sequencing, Nagarajan said. To cut costs, Nagarajan said that in-house laboratories could test for the following key biomarkers for colorectal cancer: *MSI*, *KRAS*, *NRAS*, *HER2* and *BRAF*. “If you can include these five tests, that solves 99% of all the questions.”

When testing does occur, it is often patient-driven, Nagarajan said. The more educated patients are, and the higher their socioeconomic status, the more likely they are to ask about testing. “It’s the same adage that nobody manages your money like yourself: Nobody manages your health like yourself,” he said.

Patient advocacy groups also are making a difference in pushing for testing. Through COLONTOWN, a community of more than 100 Facebook groups for colorectal cancer patients, individuals share information about biomarkers to test for and clinical trials linked to those biomarkers, Nagarajan said. The CLL Society also pushes biomarker testing, with the motto “Test Before Treat.”

“I think in the future, cancer [treatment] is not going to be [based on] where your cancer is but driven by your mutation,” Barrientos said. “The mutation is what is driving the disease, so you try to attack that mutation with targeted agents.”

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# Closing gaps in preanalytics:

## How technology is driving smarter lab solutions

From automation to sensors to artificial intelligence, technological advancements show progress against persistent preanalytical errors, empowering clinical laboratories to enhance patient care while reducing costs and staff workload.

**BY JEN A. MILLER**

**A** lot can go awry along the pathway from a test order to analysis, and it's long been known that most errors in testing can be traced back to a preanalytical problem. Undetected, these issues cost laboratories time, money, and — most importantly — compromise the quality of patient care.

Like many of the problems clinical laboratories face, a lot of hope is placed on better technology to vanquish one of the most painful weak points in laboratory medicine. Fortunately, both academic and industry research scientists are showing progress that promises to offer relief.

“We’ve made good progress in the last decade in safety and cutting down on preanalytical errors,” said Mario Plebani, MD, FRCPA, FADLM, professor of clinical biochemistry and clinical molecular biology at the University of Padova School of Medicine in Italy, and chief of the department of laboratory medicine at the University-Hospital of Padova, where he was also the dean of the medical school. “But we still have more we can do, especially when it comes to incorporating automation, new technology, and artificial intelligence.”

## A recent survey found that 57% of laboratory professionals were performing sample collection, regardless of their roles.

### DETECTING AND AVOIDING STUBBORN ERRORS

For most clinical laboratories, electronic solutions that replace hand writing and affixing labels have largely taken care of many kinds of mundane errors, according to Plebani. “We are much better now at accurately identifying patients and properly labeling tubes,” he said.

One of the more pressing problems that still plagues clinical laboratories, though, has been hemolysis. This is the case across different countries with different automation systems, he said, especially when analyzing potassium and lactate dehydrogenase in serum plasma. “This interference is problematic because elevated levels of these markers can lead to diagnostic errors.”

It’s a problem companies like Werfen have been working to tackle, said Annie Winkler, MD, the company’s chief medical officer. In 2023, Werfen gained FDA regulatory clearance for the GEM Premier 7000 with iQM3, a new blood gas analyzer that integrates whole blood hemolysis detection into the device. It enables clinical laboratories to assess whole blood samples for hemolysis “without adding sample value or time,” she

said. For patients, that means not having to get a sample recollected and not having to wait in the emergency department for additional time for another potassium result.

The technological key was Werfen’s ability to integrate the separation of whole blood with optical sensors that detect the degree of hemolysis and flag problematic results.

Werfen has also been looking at how their digital solutions can bring value not only to preanalyticals but post-analytical support, which Winkler calls lab or clinical decision support depending on the intended user. Technology could interpret data to uncover findings not possible today by looking at data on a clot curve, for example. “We recognize that there are more and more data getting added to clinical care, and we have the opportunity to potentially provide some digital solutions.”

### HUMAN ERRORS IN FOCUS

An overworked and understaffed workforce can also lead to mistakes, an alarm bell that the Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) has been ringing for some time.

Issues with preanalytical errors aren’t new, but they started to come into sharper focus as a “byproduct of all the staffing challenges” that laboratories have been experiencing, said Paavana Sainath, head of core lab solutions R&D engineering, diagnostics at Siemens Healthineers. A recent survey conducted by Siemens Healthineers and The Harris Poll, which surveyed 408 U.S. laboratory professionals in the healthcare industry in June, found that 57% of laboratory professionals were performing sample collection, regardless of their

role. “We know from our conversations with customers that this isn’t necessarily a choice,” she said.

The report found that 39% of laboratory professionals rank limited staff to support laboratory operations as their greatest challenge, and that 5% percent of laboratory professionals reported that their lab had closed temporarily because of understaffing.

Most concerning, the study found that 22% of laboratory professionals reported personally having made a lower-risk error due to feeling overworked or burned out; and that 14% have made a high risk error due to the same circumstances.

Automation and the introduction of workstations can help by reducing sample management tasks, Plebani said. It can eliminate mundane preanalytical duties, freeing staff to focus on other responsibilities or simply easing their workload to prevent overwork.

Sainath emphasized how Siemens Healthineers has enabled its Atellica Solution (high volume) and Atellica CI Analyzer (low to mid-volume) machines with its Atellica Integrated Automation functionality, which has been able to consolidate more than 25 manual tasks in preanalytics, analytics, and post analytics into a single analyzer. “The capabilities you typically find in these high volume or mega labs are now accessible to the lab around the corner,” Sainath said.

### GETTING SAMPLES TO THEIR DESTINATIONS FASTER

Another possible source of preanalytical errors is in transportation. Pneumatic tubes, which are common in large healthcare facilities to get samples from the bedside to the laboratory, are another opportunity for things to go awry, as is walking

samples from point A to point B.

Samples can be lost or sent to the wrong location, answers sent back to the wrong department, which can mean errors in care, and lengthy patient treatment delays, said Beau Fulbright, national sales and service manager at the laboratory automation division for Sarstedt.

To tackle these challenges, Sarstedt developed the Tempus600, a direct transport system that doesn't require packaging or bagging. It also can send samples directly into a lab automation system, so samples are processed immediately. The system is compatible with the major IVD automation lines, for example Roche and Abbott.

This will also lead to better patient care and lower costs, he added. "If you cut down the time that it takes to get samples to the lab, hospitals can make better decisions on treatment," he said. "Of course, we all know how expensive emergency room visits are, so even from a financial standpoint and not just patient care standpoint, if you free up that emergency bed 30 minutes faster, that's somebody else that can get into that bed faster."

### CAN ARTIFICIAL INTELLIGENCE MAKE A DIFFERENCE?

Artificial intelligence (AI) might be seen as an angel or devil in the room, depending on which person is looking at it on a given day. But its potential for detecting preanalytic error is becoming clear, experts said.

The Siemens Healthineers-Harris Poll report found that 52% of lab professionals strongly or somewhat agree that laboratory automation is a threat to their job — but at the same time, 95% said that the adoption of automated technologies will help them

improve patient care.

"They have that tension, but also feel they could do their job better if they actually adopted the technology," Sainath said.

Plebani is enthusiastic about the potential of AI, and he believes it can revolutionize the detection of preanalytical errors. Plebani pointed to papers published in *Clinical Chemistry* (doi: 10.1093/clinchem/hvad100), *International Journal of Laboratory Hematology* (10.1111/ijlh.13820), and *American Journal of Clinical Pathology* (doi: 10.1093/ajcp/aqy085) showing how machine learning was able to detect interferences.

Another recent study in *Clinical Chemistry* showed that machine learning can help accurately detect intravenous fluid contamination in blood samples even without exhaustive pre-labeled data from experts to train the algorithm (doi: 10.1093/clinchem/hvad207).

As always, further research and data will need to validate and refine such protocols — but the benefit to patients adds urgency to the effort. "The auto-verification of results thought to be erroneous represents a stark departure from the current paradigm and would require extensive observation and validation prior to deployment," the authors wrote. "However, with the recent advances in machine learning development and deployment and [laboratory information systems], combined with the nearly universal staffing shortages for laboratories and the fallibility of human adjudicators, the potential benefits to clinical operations and patient safety indicate the need for further investigation." 🍷

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BY SAMANTHA SANDY, MS LCGC, CPC, CPCO

## Understanding the complexities of molecular pathology coding

**M**olecular diagnostics have emerged as powerful tools for precise disease detection and personalized treatment. While the science is evolving at a rapid pace, the complexity of billing and coding lag behind.

One of the foremost challenges in molecular billing and coding lies in the accuracy and specificity of codes. Unlike more straightforward medical services, molecular tests require codes that account for a wide range of variables, including type of test, specific genes or analytes analyzed, specimens used, methodology, and the purpose of the test, such as diagnostic, screening, or therapeutic.

With around 20,000 genes in the human genome and 160,000 genetic tests, the availability of unique procedural coding is bleak in comparison (1, 2). Without precise coding, payers are left guessing about what occurred on the bench. Incorrect or vague coding can lead to claim denials, delayed reimbursements, compliance issues — and financial toxicity for patients.

Healthcare professionals across medical, laboratory, and payer industries must stay abreast of constantly evolving code sets, such as Current Procedural Terminology (CPT) codes, Healthcare Common Procedure Coding System (HCPCS) codes, and International Classification of Diseases (ICD) codes, some of which publish new code sets quarterly. Each molecular test may require multiple CPT

codes to accurately capture the procedure, while others may be more correctly billed as a single code.

Often tests rely on nonspecific codes, further complicating billing.

### Challenges in interpretation and implementation

Although the testing market continues to expand, available code sets have advanced little (2). Three key areas are ripe for innovation and collaboration: technology, standardization, and administration.

Under technological advances, next-generation sequencing (NGS), for example, has revolutionized the field by allowing the simultaneous analysis of multiple genes. It has also introduced new complexities in coding. Coders must differentiate among types of tests (DNA sequencing, RNA sequencing, copy number analyses, methylation), a task complicated by the continuous emergence of new tests and methodologies.

When a new test materializes, yet no specific coding is available, billers rely on the ambiguous 81479 unlisted procedural code. With so many tests billed as 81479, ambiguity leads to lower or no reimbursement as payers navigate the conundrum of enforcing medical necessity. PLA codes are highly specific, but many are obtained prior to clinical utility studies, leading to a lack of reimbursement (See box). As technology advances, PLA codes lack fluidity for modifications

in gene content and methodology, hastening obsolescence.

A lack of standardization compounds the problem. There is often inconsistency in how different payers interpret and implement coding guidelines. This lack of standardization burdens laboratories and health-care providers, who must navigate a maze of payer-specific rules.

Furthermore, federal and state health programs can differ dramatically from commercial and employer-funded health plans in their enforcement of correct coding. As an adjunct to relying on nonspecific coding, organizations develop CPT identifiers to describe each unique test. These are managed by an independent organization and are only made available to payers or laboratories for whom they contract. Without all the layers of the industry adopting a standard system, the CPT identifiers lack context and challenge consistency.

Once claims for molecular testing are submitted to payers, administrative challenges begin. Coders may rely on laboratory details, test menus, and diagnosis codes to piece together the specifics of a test. The same code may be used for different assays, such as performing sequencing of *BRCA1* in germline and somatic clinical scenarios. The resultant coding of a claim may be unreliable in providing necessary details for enforcement of medical policy.

The administrative burden

extends outward as laboratories and clinics identify documentation within patient charting to justify the service billed as they navigate distinctive payer policies. Claim adjudication is a resource-intensive process for all. Traversing these complexities requires proactive communication, ongoing education, and a keen understanding of regulatory and policy updates.

#### **Case illustration: From clinic to claim**

Consider the journey of Whitney, a 45-year-old patient with breast cancer. Whitney's genetic counselor orders a multigene panel to identify hereditary cancer risks. The laboratory secures prior authorization for a hereditary breast cancer panel, performs the test, and submits the claim. Despite meeting all preauthorization requirements of medical necessity, the claim is denied due to discrepancies in coding interpretations between the lab (billing 81162) and the payer (policy directs billing 81432).

Resolving such issues involves appeals and resubmissions, consuming time and resources. Without resolution, Whitney may be left financially responsible, or the laboratory may not receive any reimbursement. Effective communication between labs, payers, and clinics is essential to streamline this process and minimize delays in patient care.

#### **Moving forward: Collaboration and standardization**

To overcome these challenges, stakeholders must continue to collaborate on standardizing coding practices and guidelines, including:

### **Types of molecular codes**

Molecular pathology coding can be broken into subgroups that define the type of molecular testing being performed.

- Tier 1 codes often are single-gene tests whose descriptors may specify gene content, methodology, sample type, and/or clinical use.
- Tier 2 codes are arranged by level of complexity and have descriptors providing suggestions of applicable genes/genetic content.
- Genomic sequencing procedures provide a single code to encompass simultaneously assayed genes or regions.
- Multianalyte assays with algorithmic analyses offer combinatorial information of biomarker/genetic tests with biological details of the patient as an algorithmic score or probability.
- Proprietary Laboratory Analysis (PLA) codes introduce the opportunity for specificity by providing a unique alphanumeric code for a laboratory or manufacturers' test; however, they do not reflect an assessment of clinical utility.

Policy alignment: Harmonizing coding guidelines and policies across different payers can help ensure uniformity in coding practices, reduce administrative burdens, and improve reimbursement processes.

Expanded expertise and training resources: Increasing the number of professionals with expertise in both genetics and coding can lead to more accurate, efficient, and consistent coding. Identify easy and streamlined methods to provide education and training on correct coding to all stakeholders.

Technological adaptation: Keeping coding systems updated with the latest advancements in genetic testing technology is crucial for maintaining relevance and accuracy. Determining a path forward in coding that allows both fluidity and specificity is integral to reducing burdens on the healthcare system and barriers to patient care.

#### **Conclusion**

Molecular pathology coding is undeniably complex, but understanding the reasons behind these complexities is the first step toward a better system for all involved, including patients. By fostering collaboration among labs, clinics, and payers, and by continuously updating and standardizing coding practices, the healthcare industry can improve the efficiency and accuracy of molecular pathology coding. This effort is essential to providing high quality care and ensuring that the benefits of genetic testing are fully realized for all patients.

**Samantha Sandy, MS LCGC, CPC, CPCO**, is a genetic counselor and certified coder currently working in the payer industry.

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BY SANJAI NAGENDRA, MD, MMM

## Discontinuing clinician-ordered peripheral smear reviews by pathologists: A story of change management

Clinicians order peripheral smear reviews (CPSR) by pathologists for a variety of reasons, including CBC abnormalities or signs and symptoms of hematologic disease (1). For decades, this practice has been deeply embedded in the minds of many physicians, reinforced by textbooks and decision-support tools. In a CPSR, the pathologist reviews the morphology of erythrocytes, leukocytes, and platelets along with the CBC and renders an interpretation.

More than 20 years ago, I first came across the CPSR as a freshly graduated hematopathologist in a 500-bed tertiary hospital. Every day, I would interpret 10–20 CPSRs on nonspecific abnormalities, such as macrocytosis without anemia and neutrophilia not otherwise specified. I also would review peripheral smears that met laboratory criteria for pathologist review (laboratory-derived smear review or LDSR). The LDSR would include abnormalities such as hemolysis, myelodysplastic syndrome, and acute leukemia, among others.

I soon questioned the utility of the CPSR. In the last several decades, advances in automated analyzers coupled with middleware software programs have significantly improved the detection of hematologic abnormalities, including blast identification, with near 100% sensitivity (2). It was time to examine this practice systematically.

### Change management in a hospital setting

In 2016, I assessed 106 CPSRs at a 500-bed tertiary care hospital in the Midwest, including inpatient and outpatient clinics. The findings showed that CPSR was unnecessary more than 99% of the time; LDSR captured virtually all significant hematologic abnormalities, including hemolysis, chronic myeloproliferative disorders, and acute leukemia. These findings and the literature confirmed that pathologists' CPSR were of low clinical utility.

A committee of pathologists, oncologists, and primary care physicians reviewed the data and unanimously agreed that CPSR was unnecessary. This led to an educational campaign and smooth discontinuation. However, despite having an oncologist on the committee, one oncology group resisted. We collected 2 months of additional data on their patients ( $n=212$ ) and showed that 99.5% of cases were caught with LDSR criteria. The LDSR criteria were further improved to catch the one false negative case.

Additional data did not influence the oncologists' opinion. With the intervention of the facility's chief medical officer and additional education, the oncologists reluctantly agreed to the discontinuation. Based upon this discontinuation, a significant amount of pathologists' time was reallocated to more clinically relevant activities.

### Change management in a reference lab setting

Upon arriving at Labcorp, I saw the same pattern of nonspecific findings in the nearly 300,000 CPSRs/year ordered across the enterprise. Our teams wondered whether discontinuation of CPSR could be accomplished in a reference laboratory with thousands of physicians spanning the country.

To accomplish this gargantuan task, we realized we needed a systematic approach to change management. Our strategy would include 1) reviewing peer-reviewed literature, 2) performing an internal study to validate the literature, 3) educating and obtaining feedback from internal stakeholders and key external clients, 4) obtaining internal stakeholder buy-in, and 5) planning ongoing educational support.

Published studies suggested that CPSRs have limited clinical utility, but the literature was sparse. Beckman et al. found that CPSRs infrequently provide clinical value (13% of the time) in reviews for anemia and thrombocytopenia (the most common indication for CPSR) (3). Mangold et al. found that CPSRs were clinically useful only 1% of the time in a large tertiary care hospital (4).

We performed our internal study at the Burlington Labcorp location. In early 2023, we reviewed 200 consecutive CPSRs and asked whether standard processes with

CBC and LDSR capture significant hematologic abnormalities seen in CPSR. We also established whether LDSR missed any significant hematologic abnormalities.

Our findings confirmed that CPSR had limited value and that significant hematologic abnormalities would have been detected by LDSR. The discrepancy rate between CPSR and LDSR was negligible (0.6%) because of a minor discrepancy between platelet counts (5).

### **Securing stakeholder buy-in, addressing dissent, and offering education**

Obtaining buy-in from internal stakeholders and quelling internal dissent was another challenge that required carefully crafted conversations with leaders in affected areas. We presented our study findings to the internal laboratory stewardship committee and recommended test discontinuation. The committee approved our request and recommended discontinuation after an extensive educational effort.

Next, we embarked on an externally facing educational campaign that covered the scientific basis of discontinuation, a CBC guide describing how to interpret nonspecific abnormalities that don't meet the criteria for LDSR, and a webinar. All materials were published on Labcorp's webpage. Hematology directors also had meetings with field team members.

Before discontinuation, we encountered pockets of dissent with several internal stakeholders. A few sales executives believed that clinicians should be able to order whatever they want based on the patient's clinical picture.

Pathologists also had concerns. How would they effectively

communicate the discontinuation to their clinician partners who have utilized this test for decades? We reassured them that physicians should be directed to the educational materials, and if they were not satisfied, the hematology directors would consult with them.

### **Managing physician concerns and resistance**

On July 29, 2024, we discontinued CPSR. Although educational materials were provided several months before the discontinuation, many physicians were unaware of the change. The number of calls from providers and field executives increased logarithmically. We held additional educational meetings with field executives as well as many one-on-one meetings with physicians.

Despite educational materials, some physicians, especially oncologists, resisted the change. They were upset that some patient's CBC abnormalities did not reflex in a pathologist review. We reviewed the peripheral smears on these patients and reassured the physicians that the findings were nonspecific.

Yet a handful of oncology providers continued to resist. They felt they needed a CPSR regardless of reflex criteria and threatened to use another laboratory. Based on their concerns, we realized they needed more time to accept this change. We allowed these select providers to continue ordering CPSR for a limited time while additional educational material was offered.

Our experience with this project has highlighted a pearl in lab stewardship: Changing deeply-seated clinician beliefs takes time and patience. We are

confident that physicians will embrace these changes through education and become confident of our LDSR processes. We hope that these changes can be adopted by other best practice committees, such as ASCP's Choosing Wisely, so that there can be a broad recommendation to discontinue CPSR ordering for all laboratories.

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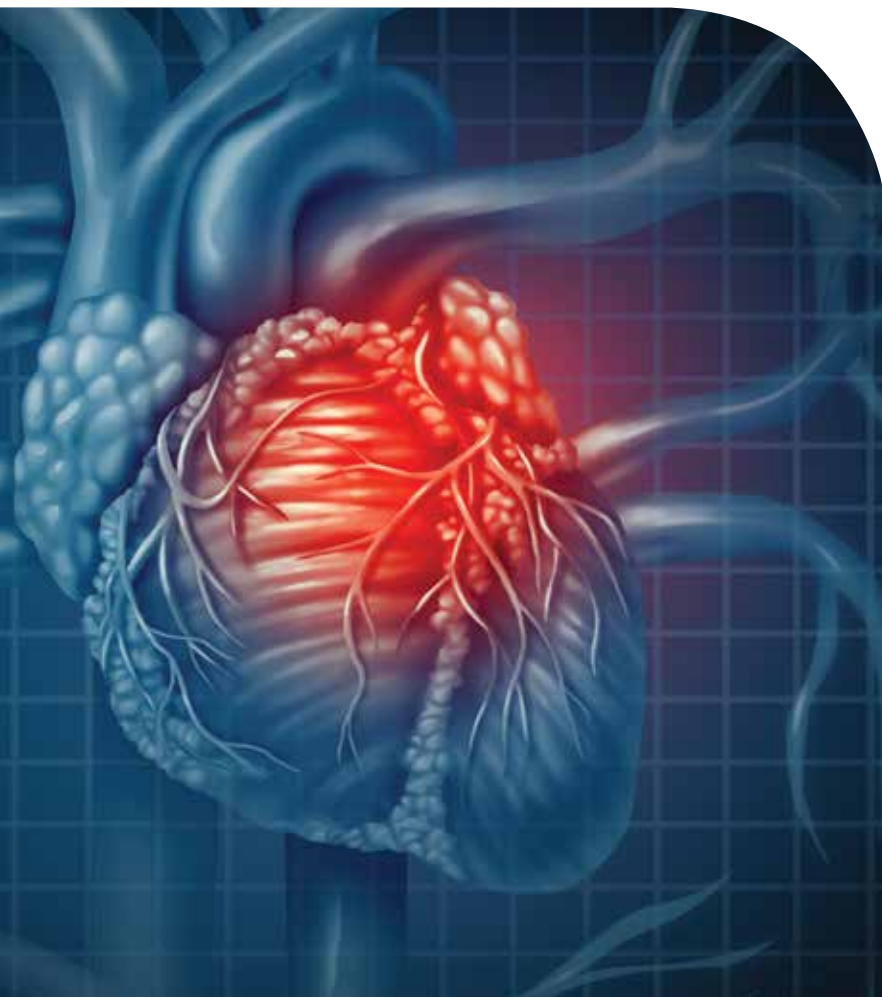
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**LABORATORY  
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# Regulatory Roundup



## Troponin test gets FDA claim for predicting likelihood of future cardiac events and death

Siemens Healthineers recently announced that its Atellica IM High-Sensitivity Troponin I blood test has received Food and Drug Administration clearance for helping identify patients at risk of major cardiac events and death for up to 1 year, a new claim for a test previously cleared only for detecting acute myocardial infarction.

Many U.S. hospitals use the test to measure cardiac troponin I. Now, for chest pain patients without a heart attack diagnosis, the Siemens Healthineers Atellica IM TnIH test may give information about their impending risk after presenting to the emergency department with signs and symptoms of acute coronary syndrome.

The test runs on the Atellica Solution, Atellica CI Analyzer, and ADVIA Centaur platforms. With a 10-minute time to first result, the Atellica IM TnIH test now can be used as an aid in prognosis for 30-, 90-, 182-, and 365-day all-cause mortality and major adverse cardiac events (MACE) in patients presenting with signs and symptoms suggestive of acute coronary syndrome.

MACE consists of myocardial infarction, urgent revascularization, cardiac death, or heart failure hospitalization, according to Siemens Healthineers.

### ● QIAGEN RECEIVES FDA CLEARANCE FOR NEUROLOGICAL AND RESPIRATORY DIAGNOSTICS

Qiagen recently announced Food and Drug Administration clearance for its QIAstat-Dx Meningitis/Encephalitis Panel for use in various clinical settings to help diagnose central nervous system infections and QIAstat-Dx Respiratory Panel Mini to support clinical diagnosis of upper respiratory infections in outpatient settings.

The QIAstat-Dx Meningitis/Encephalitis Panel simultaneously

analyzes several of the most common viral, bacterial, and fungal pathogens responsible for community-acquired meningitis and encephalitis.

The QIAstat-Dx Respiratory Panel Mini is designed to support clinical decision making in diagnosing upper respiratory infections in outpatient settings. It covers five common viral causes of illness: influenza A, influenza B, human rhinovirus, respiratory syncytial virus, and SARS-CoV-2.

The panel uses the QIAstat-Dx system to quickly amplify many

genetic targets at the same time using real-time PCR technology, according to Qiagen.

### ● CANADA APPROVES HPV TEST FOR SELF-COLLECTED SPECIMENS

BD has announced Health Canada approval of its BD Onclarity HPV Assay for human papillomavirus (HPV) testing with vaginal specimens patients collect at home.

According to the company, its assay is less invasive, more cost-effective, and requires less frequent

use than the traditional Pap test. BD says the test makes cervical cancer prevention more accessible, especially to remote, rural, and vulnerable populations. Cervical cancer incidence is three times higher in underserved populations in remote communities who have limited access to screening when compared with the general population, the company added.

In addition to advancing more equitable access to care, the BD Onclarity HPV Assay is the only Health Canada-licensed test that supports self-collection with HPV extended genotyping to measure a woman's true risk for cervical precancer and cancer more precisely, according to BD.

#### ● BIOTIA INFECTIOUS DISEASE URINE GENOMIC TEST GETS NEW YORK STATE REGULATORY APPROVAL

The New York State Department of Health Clinical Laboratory Evaluation Program has approved the BIOTIA-ID Urine NGS assay as a laboratory developed test, Biotia announced.

According to the company, BIOTIA-ID is the first genomics-based urine assay using artificial intelligence approved by the state. It offers 97% sensitivity and 99% specificity for identifying urogenital pathogens, including those often missed by traditional culture methods.

Researchers recently reported that BIOTIA-ID identifies pathogens in 60% of urine samples for which traditional culture-based techniques fail. Seventy percent of patients who gave the samples had been prescribed antimicrobials

## Cervical cancer incidence is three times higher ... in remote communities who have limited access to screening.

that were ineffective for the pathogens BIOTIA-ID identified, according to Biotia.

The company said BIOTIA-ID is particularly valuable for patients with complicated and recurrent urinary tract infection or immunocompromised patients, who often face diagnostic challenges and delays in appropriate treatment.

#### ● CARIS LIFE SCIENCES RECEIVES FDA APPROVAL FOR MI CANCER SEEK AS A COMPANION DIAGNOSTIC

Caris Life Science has announced Food and Drug Administration (FDA) approval for its MI Cancer Seek as a companion diagnostic (CDx) to identify cancer patients who may benefit from treatment with targeted therapies.

The assay includes one pan-cancer and five tumor-specific indications for various FDA-approved therapies. MI Cancer Seek is the first and only simultaneous whole exome sequencing and whole transcriptome sequencing-based assay with FDA-approved CDx indications for molecular profiling of solid tumors.

MI Cancer Seek uses total nucleic acid isolated from formalin-fixed paraffin-embedded tumor tissue specimens to detect single nucleotide variants, insertions, and deletions in 228 genes. It also detects microsatellite instability and determines tumor mutational burden.

The tests have several companion diagnostic indications encompassing various biomarkers and drugs.

#### ● NGS CANCER TESTS RECEIVE NEW YORK STATE APPROVAL

NeoGenomics recently announced New York State Department of Health conditional approval for its Neo Comprehensive Solid Tumor assay and NeoTYPE DNA & RNA Lung test.

The approvals allow immediate commercial access to these next-generation sequencing tests (NGS) in New York state. The company says they offer better diagnostic value and cost-effectiveness than single gene testing and direct the first-line treatment of diverse solid tumors, including non-small cell lung cancer.

The tests analyze a broad panel of genes, including less common genetic markers that cancer-specific profiles or single-gene tests may miss. Neo Comprehensive offers physicians a pancancer genomic profiling solution that aligns with National Comprehensive Cancer Network guidelines for diverse cancers.

NeoTYPE DNA & RNA Lung uses the same technology as Neo Comprehensive Solid Tumor, but in the context of a more focused NGS panel that focuses on what the company says is an unmet need in lung cancer testing across the state.



## Cardio diagnostics holdings gets preliminary medicare pricing for AI-powered cardiovascular tests

Cardio Diagnostics Holdings has announced that its PrecisionCHD and Epi+Gen coronary heart disease (CHD) tests have preliminary pricing determinations from the Centers for Medicare and Medicaid Services (CMS).

PrecisionCHD, a blood test powered by artificial intelligence (AI), aids diagnosis of coronary heart disease (CHD) by evaluating genetic and epigenetic markers. Epi+Gen CHD assesses the three-year risk for a CHD event, including heart attack, using a similar AI-driven integrated genetic-epigenetic approach.

The company developed and validated the test using machine learning techniques that rely on datasets from the Framingham Heart Study and Intermountain Healthcare. It incorporates several single nucleotide polymorphisms and methylation markers.

CMS recently issued preliminary determinations to price both PrecisionCHD and Epi+Gen CHD on a gapfill basis because the tests have no fee scheduling pricing history. The determinations serve as crucial steps toward securing Medicare reimbursement. If finalized, the determinations will be effective for claims with dates of service on or after Jan. 1, 2025, and will allow Medicare contractors to determine pricing for PrecisionCHD and Epi+Gen CHD based on actual cost data from Cardio Diagnostics, the company said.

### ● AMPRION GETS FINANCING FOR NEW NEUROLOGIC DIAGNOSTICS

**A**mprion has announced an initial \$6 million close of \$15 million in Series B financing to drive development of what it calls disruptive new assays for Parkinson's disease, Alzheimer's disease, Lewy body dementia, and other neurological disorders.

The financing from Formation Venture Engineering (FVE) with participation by Eli Lilly and Company and Amprion's Series A

investors will expand Amprion's commercial reach and increase research and development investment.

Through Amprion, seed amplification testing — which enables detection of small amounts of misfolded proteins in cerebrospinal fluid and other biological samples — has evolved. Amprion's SA Amplify-αSYN biomarker test is the only validated seed amplification assay available to aid diagnosis of synucleinopathies associated with Parkinson's disease, Lewy body dementia, and

Alzheimer's disease with neocortical Lewy body copathology.

FVE officials said they believe “the shift to diagnosis based on biology, rather than symptomology, will be transformative for patients and clinicians.”

### ● PARTNERSHIP AIMS TO DEVELOP NEXT-GENERATION TAU BLOOD TEST FOR ALZHEIMER'S

**V**eravas, Inc. and Phanes Biotech recently announced a collaboration to develop a blood-based

Alzheimer's disease (AD) tau pathology test.

The test will leverage Veravas' proprietary VeraBIND technology and Phanes' biological intellectual property on tau pathology to detect active disease through measurable binding activity between hyperphosphorylated tau (HPT) and normal tau (nTau), a hallmark of AD.

The partnership will focus on measuring disease pathology. The goal is to combine Veravas' VeraBIND platform with Phanes' proprietary tau pathology insights to give clinicians a positive or negative answer about whether a patient has AD early in disease progression, when treatment is most likely to be effective.

● **CARDINAL HEALTH TO SELL T2 BIOSYSTEMS RAPID BLOOD TEST FOR SEPSIS PATHOGENS**

**A** recent multiyear exclusive U.S. agreement gives Cardinal Health exclusive rights to sell T2 Biosystems' FDA-cleared direct-from-blood diagnostics for the rapid detection of sepsis-causing pathogens.

The deal includes the T2Dx Instrument, the T2Bacteria Panel, and the T2Candida Panel. The T2Bacteria Panel detects *E. faecium*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, and *E. coli*, which account for nearly 75% of U.S. bacterial bloodstream infections, with 90% sensitivity and 98% specificity.

The T2Candida Panel detects the *Candida* species *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata*, which account for up to 95% of U.S. *Candida* blood stream infections, with 91% sensitivity and 99% specificity. The panels are not affected by prior antimicrobial treatment.

T2 Biosystems says its diagnostics can detect sepsis-causing bacterial and fungal pathogens directly from blood in just 3-5 hours, without the need to wait days for a positive blood culture. Blood culture, the most common means of identifying sepsis, is beset by low sensitivity, slow time to result, vulnerability to contamination, reduced effectiveness in patients who have received antibiotics, and a labor-intensive process requiring skilled technicians, the company said.

● **SAPIO SCIENCES AND WATERS DEAL AIMS AT BETTER LABORATORY EFFICIENCY**

**S**apio Sciences has entered a comarketing agreement with the Waters Corporation to improve data integrity, workflow efficiency, and laboratory productivity, Sapio announced recently.

The data processing and review capabilities of Waters Connect software, when combined with Sapio LIMS, can help laboratories make their workflows more efficient, enabling laboratories to handle larger volumes of samples with greater speed and precision. This connectivity not only streamlines operations but also enhances collaboration among laboratory personnel by providing a unified solution for data sharing and analysis, Sapio said.

Integrating liquid chromatography mass spectrometry software with a laboratory information management system (LIMS) can make laboratory operations more efficient as laboratory-based organizations expand and handle more samples. Improvements can include streamlining workflows, reducing data silos, enhancing compliance with regulatory

standards, and eliminating manual data entry and transcription errors.

● **EUROFINS BUYS SYNLAB'S DIAGNOSTICS OPERATIONS IN SPAIN**

**E**urofins has reached an agreement with SYNLAB to acquire its clinical diagnostics operations in Spain, Eurofins recently announced.

The transaction, expected to close in 2025, will cover laboratory services provided to public and private clients in all regions of the country. The combined company will have a highly specialized workforce of more than 2,000 employees and a large portfolio of clinical diagnostic laboratory tests.

SYNLAB's clinical diagnostics operations in Spain include genetics and anatomical pathology services. Eurofins Megalab will provide all types of clinical diagnostics testing and manage intrahospital laboratories in Spain.

Eurofins officials said the company aims to provide high quality and accessible testing services to both the private and public sector, including regional healthcare services, private hospital groups and insurance companies.

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## How could the 2024 election affect clinical laboratories?

### How will the election affect laboratory developed test (LDT) oversight?

**A:** The election alters the political environment in which decisions affecting laboratory developed test (LDT) oversight will be made. The incoming president is opposed to expansive government regulation. During his first administration, the policy debate largely centered around Congress. An internal Department of Health and Human Services (HHS) memo questioned whether the Food and Drug Administration (FDA) had the authority to regulate LDTs. On this issue, President Trump is likely to be more sympathetic to laboratory concerns than the Biden White House, which has permitted the Food and Drug Administration to advance this policy objective.

### What are the chances that CLIA modernization will get attention in the new Congress?

CLIA modernization, in the near term, is tied to congressional discussions of LDTs. If the new administration revokes the FDA rule or the courts decide against the FDA, then the issue of LDT oversight will go back to Congress. The Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) and many others in the healthcare community have suggested that any changes to LDT oversight should take place within the current CLIA regulatory framework. The issue

may gain traction if legislators, such as Sen. Bill Cassidy, R-La., the incoming chair of the Senate Health, Education, Labor and Pensions Committee, decide to take up the broader issues of device and laboratory testing reform.

### Will AI policy change?

In 2023, the Biden Administration issued an executive order outlining how the federal government would oversee the development of artificial intelligence (AI). HHS stated it would create an AI council to develop strategic priorities involving machine learning and healthcare. President-elect Trump has vowed to repeal this directive but has given little guidance on how he plans to move forward. Congress will continue to be active in this issue as both the House and Senate have created bipartisan task forces to develop blueprints for regulating AI.

### What other topics will ADLM advocate for under the new administration?

ADLM remains committed to improving the quality of pediatric testing. We have succeeded in getting congressional recognition for better pediatric reference intervals (PRIs) but need to obtain the funding to develop and disseminate them. Over the past year, Rep. John Joyce, MD, R-Pa., the co-chair of the House Children's Healthcare Caucus, who recently won re-election, took a leadership



**By Dennis J. Dietzen, PhD, DABCC, FACB**

role in championing this cause. ADLM is hopeful that a new Congress and new administration will provide the necessary funding to begin this long process of advancing pediatric care.

### What are some other issues Congress may tackle?

Medicare and Medicaid reimbursement are always possible issues given their amount of spending and the size of the deficit. Also, new administrations always seek to root out fraud and abuse when looking to curtail spending, so that issue may garner additional interest as well. The Affordable Care Act seems safe, as President-elect Trump has stated he will seek to improve the law rather than replace it. One issue that may get some attention is financial relief for laboratory professionals and others in the healthcare community who agree to work in underserved areas. ADLM supports these efforts.

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