May/June 2026

CLN Clinical Laboratory News

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CONNECTING GUM DISEASE AND DIABETES

36%

of dental patients had previously undiagnosed, abnormal blood sugar levels

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How to improve health outcomes for American Indian communities

Extracting essential info from lab documents

Inborn errors of immunity

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Laboratorians find inhalants challenging to detect because many are highly volatile, rapidly absorbed, and quickly eliminated from the body.
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CMS publishes new resources for 2026 PAMA reporting window

Under the Protecting Access to Medicare Act (PAMA), from May 1-July 31, all applicable labs must report their private payer data collected from January 1, 2025, through June 30, 2025, to the Centers for Medicare and Medicaid Services (CMS).

To aid labs with this requirement, CMS has updated its Clinical Laboratory Fee Schedule (CLFS) and PAMA reporting webpage with several operational resources, including new FAQs, the applicable Healthcare Common Procedure Coding System code list, the CLFS Submitter and Certifier user guides, and the CLFS data reporting template.

The 2026 PAMA reporting requirement applies to all labs that have more than $25,000 in annual Medicare CLFS payments, including hospital, independent, and physician office laboratories.

Approximately 2,600 hospitals fit this category, according to *Laboratory Economics*. Yet only 46% of lab directors and executives say they will fulfill PAMA's data reporting requirements, according to a March survey from *Laboratory Economics*. Without overall reporting from hospitals, the CLFS rate calculations for 2027 will be skewed by lower commercial insurance rates offered by Quest and Labcorp.

Based on CMS' CLFS and PAMA reporting webpage, the Association for Diagnostics & Laboratory Medicine (ADLM) recommends that labs focus on a few immediate steps:

- Labs should complete CLFS Submitter and Certifier registration as soon as possible.
- Labs should also review whether their organization meets the applicable laboratory definition and reporting thresholds.
- Finally, labs should validate the data that must be reported.

Although Congress delayed the next scheduled round of PAMA cuts until 2027, the 2026 reporting cycle is moving forward, and timely preparation will be critical to compliance. ADLM aims to continue to keep members informed as implementation moves forward. The association is also actively working alongside allied stakeholders to fix longstanding flaws in PAMA and advocate for reforms that better support patient access and the clinical laboratory community.

ADLM ADVOCATES FOR PUBLIC HEALTH DATA MODERNIZATION

The Association for Diagnostics & Laboratory Medicine (ADLM), along with several other organizations, encouraged Congress to advance a Labor, Health and Human Services, Education, and Related Agencies (LHHS) appropriations bill that supports the modernization and long-term sustainability of public health data infrastructure.

In a letter addressed to Subcommittee on LHHS chairs Shelley Moore Capito (R-W.Va.) and Robert Aderholt (R-Ala.) and ranking members Tammy Baldwin (D-Wis.) and Rosa DeLauro (D-Conn.), ADLM explained that data systems are the foundation of a strong, responsive, and resilient public health system. Updating and integrating data infrastructure is a core function of public health. Whether preventing overdoses, tracking disease trends, responding to outbreaks, or monitoring chronic disease, maternal and child health, and environmental exposures, public health leaders depend on timely, accurate, and

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complete data. Without reliable, interoperable systems, agencies are forced to rely on fragmented, manual processes that slow responses and create gaps in critical information, leaving communities exposed.

Equally important is maintaining the Centers for Disease Control and Prevention (CDC) and state, tribal, local, and territorial (STLT) public health workforce of highly trained experts to keep these systems operational, ADLM said. Without these professionals, agencies risk delayed responses, gaps in disease surveillance, and diminished capacity to protect communities. Sustaining CDC's infrastructure, its expert workforce, and the STLT public health workforce is essential to a resilient, effective national public health system.

To support these critical initiatives, ADLM requested $340 million for Public Health Data Modernization at the CDC, as well as $55 million for Response Ready Enterprise Data Integration and $100 million for the CDC's Center for Forecasting and Outbreak Analytics as Congress finalizes the fiscal year 2027 LHHS bill.

Sustaining CDC's infrastructure, its expert workforce, and the STLT public health workforce is essential to a resilient, effective national public health system.

● AUSTRALIA'S BAN ON GENETIC DISCRIMINATION BY LIFE INSURERS MAY BOOST DNA SCREENING

The Australian Parliament passed legislation banning life insurance companies from discriminating against applicants based on their genetic testing results. The bill, which was made law through Royal Assent from Governor-General Samantha Mostyn on April 8, will take effect on October 8, giving insurers time to comply with the new law.

Experts are saying that the bill will strengthen public confidence in genetic testing and may even provide additional incentive for the Australian government to invest more in a nationwide preventive genomic screening program.

"It paves the way for government investment in preventive genomic screening for adults … knowing people won't have to weigh up preventive health against financial fears," said Jane Tiller, PhD, in a statement. Tiller is a genomics and legal expert at Monash University in Melbourne, Australia, and co-leader of a pilot nationwide genetic screening program called DNA Screen.

In the United States, the Genetic Information Nondiscrimination Act of 2008 offers federal protection against health insurers' and employers' discrimination regarding genetic information. However, this law does not include life, long-term care, and disability insurance. Thus, these areas of coverage depend on state law and lack uniform protection against discrimination.

While Australia's new legislation was being pushed for, Tiller's research group at Monash University explored the feasibility of implementing DNA Screen. She and her colleagues published a report in 2023 titled the A-GLIMMER (Australian Genetics & Life Insurance Moratorium: Monitoring the Effectiveness and Response) Project.

"The most common reason people who had initially registered interest in the DNA Screen study ultimately declined was because of life insurance fears," Tiller said. "We conducted a survey of thousands of decliners, and more than 50% cited insurance concerns as their reason for declining." A peer-reviewed paper on these results is currently in the final stages of review.

When minutes matter: The laboratory's role in rapid hemostasis assessment

BY CRISTINA FIGUEROA VILLALBA, MD

Cristina Figueroa Villalba, MD

Hemorrhage remains one of the leading causes of preventable death in trauma and critical illness, underscoring the need for immediate laboratory guidance for intervention. The challenge for today's laboratories is to not only generate accurate results, but also deliver the right information quickly enough to guide care in real time. When a patient is actively bleeding, the clock is not just ticking — it's accelerating. Yet many laboratories still operate within frameworks optimized for accuracy over speed, which leaves a critical gap in the care of actively bleeding patients.

To bridge this gap, we must change the mindset around coagulation testing in these scenarios, shifting our focus from precision to speed with a result "accurate enough" to guide management and change outcomes. Labs should also keep in mind that some of the most effective approaches are also the simplest — targeted testing strategies that employ outside-of-the-box approaches to prioritize speed, clinical relevance, and changes in sample workflow.

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Utilizing common tests

The emergency hemorrhage panel at our institution provides information about hemostasis using four widely available tests: prothrombin time, hematocrit, fibrinogen, and platelet count.

This panel provides swift answers to clinicians who are caring for actively bleeding patients and need to know promptly whether the hemostasis parameter is above or below the threshold for replacing the required component.

When implementing this panel, the lab should collaborate with clinicians to ensure that testing is limited to patients who are actively bleeding and that samples are delivered to the central laboratory in a timely manner. Evidence suggests that such streamlined approaches can achieve turnaround times well under 20 minutes when workflows are optimized and testing is prioritized appropriately (*1*).

Another evolving area is the assessment of anticoagulant status in urgent scenarios. Direct oral anticoagulants (DOACs) are increasingly encountered in emergency settings, where their presence can dramatically influence clinical decisions. Although these medications do not require routine monitoring, the ability to rapidly detect them in urgent situations — such as active bleeding or emergency surgery — can be critical.

However, traditional quantitative assays for DOACs are not yet widely available. As an alternative, laboratories can use widely available tests such as thrombin time and anti-Xa to provide qualitative assessment of anticoagulant presence with a faster turnaround time (*2*).

Striking a balance

It is critical that coagulation tests remain within the central laboratory, where trained staff can identify preanalytical issues, such as hemolysis or inadequate tube filling, that could falsely skew results. To that end, achieving a balance between accuracy and speed requires the laboratory director to serve as a key liaison between the clinical frontline and the laboratory bench. The director must ensure that laboratory staff understand the clinical context: that in an emergency, the goal is not a perfect analytical value, but a rapid, reliable result centered on the thresholds that drive immediate management changes.

Together, these challenges highlight a broader shift in laboratory medicine: moving toward testing strategies that are not only accurate, but also timely, targeted, and aligned with clinical need. This shift involves reexamining established workflows, challenging assumptions about testing priorities, and engaging more directly with clinical teams. It also calls for practical solutions — approaches that labs can implement in real-world settings without needing entirely new technologies and resources.

Innovation in laboratory medicine does not always require new tools. Sometimes, it just means using the available tools and reconfiguring their use while balancing speed, accuracy, and workflows. In the end, when minutes matter, strategy matters just as much.

Interested in learning more? Attend the ADLM 2026 roundtable, "All you need is blood: Strategic laboratory solutions to rapid assessment of hemostasis in emergency situations," on Monday, July 27 in Anaheim, California. Find out more at meeting.myadlm.org.

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The Sample

Experience matters in pipetting

Experience level and task sensitivity significantly influence pipetting performance, recent research shows (J Appl Lab Med 2026; doi.org/10.1093/jalm/jfag006).

The researchers call for ongoing training and performance assessment for all laboratory staff, because even experienced personnel involved in the study occasionally failed to meet International Organization for Standardization (ISO) standards.

Accurate and precise pipetting is crucial for reliable laboratory results, especially when small volumes or sensitive analytical techniques are involved. Despite common use of piston-operated pipettes, operator-dependent variability remains a major source of error.

To assess the effect of experience level on pipetting, the researchers conducted what they describe as the first study to comprehensively assess manual pipetting performance using both gravimetric and photometric methods across a large and diverse cohort of participants.

The researchers evaluated pipetting performance among laboratory personnel with varying levels of experience. The study had 108 participants, including laboratory school students, PhD students, clinical chemists, and laboratory technicians. They were stratified into three groups: those with minimal experience, moderate experience, and high-level experience. The researchers evaluated pipetting performance using gravimetric replicates at 10 µL and 100 µL volumes and a dilution task involving serial dilutions of 1 M copper sulfate. Then they compared accuracy and precision metrics across the groups.

The median coefficient of variation was lower for 100 µL replicates (0.3–0.8%) than for 10 µL replicates (1.4–5.9%). Laboratory students showed the greatest variability and longest task completion times, suggesting that inexperience and limited hands-on practice are key contributors to low reproducibility and accuracy. However, students' performance improved the longer they'd been in school. Ten percent of participants exceeded ISO-defined accuracy limits for 10 µL pipetting, and 22% for 100 µL. Additionally, 36% and 20% of participants surpassed imprecision limits for 10 µL and 100 µL, respectively. The group with high-level experience achieved optimal dilution performance, while students showed the highest deviation.

Training programs should emphasize techniques for low-volume pipetting, regular proficiency evaluations, and refresher training that incorporates gravimetric and dilution-based assessments for all laboratory personnel, the researchers suggested.

DENTAL VISIT SCREENINGS REVEAL HIGH GLUCOSE FOR ONE IN THREE PATIENTS

Thirty-six percent of dental patients who had chairside HbA1c tests had previously undiagnosed, abnormal blood sugar levels, a recent study found (J Dent 2026; doi.org/10.1016/j.jdent.2026.106563).

Diabetes and prediabetes cases are steadily increasing worldwide. Screening and early detection help reduce complications and treatment costs. Previous research established that the inflammatory process in gum disease can change the metabolic system, and the metabolic system affects inflammation further.

In response, researchers performed a cross-sectional study to investigate the potential associations between periodontitis and HbA1c concentration and to assess the usefulness of a chairside test for diabetes screening in a dental setting.

The researchers studied 911 patients from an oral, dental, and

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craniofacial biobank at King's College London in the United Kingdom. Six percent of patients were periodontally healthy, and the remainder had gingivitis or periodontitis. Just over 11% of patients self-reported a type 2 diabetes diagnosis. Based on patients' self-reported medical and dental history and periodontal clinical data, they underwent chairside HbA1c screening via a fast fingerprick blood test.

The patients' mean HbA1c value was 5.71. Excluding self-reported diabetics, 28.7% of the patients had blood sugar levels indicating prediabetes, and about 7% had full-blown diabetes, the researchers found. The HbA1c levels increased from diagnosis of periodontal health (5.43 ± 0.51%), gingivitis (5.51 ± 0.91%), and periodontitis (5.76 ± 0.97 %). Adjusted linear regression showed a significant association between age and HbA1c and a borderline association with periodontal diagnosis. Analysis by age showed similar findings after excluding self-reported diabetics. Logistic regression confirmed significant associations with age and body mass index (BMI), while periodontal diagnosis was not statistically significant. Periodontitis showed a borderline association with higher levels of HbA1c after adjusted analysis.

Dental visits could be important opportunities for early detection of undiagnosed hyperglycemia, especially for older people, those with higher BMI, and patients with gum disease, the researchers concluded.

Knowing whether an individual's M1 status can help guide kidney disease diagnosis and other clinical scenarios remains underexplored.

APOL1 TESTING IN BLACK PATIENTS MAY AID KIDNEY DISEASE DIAGNOSIS

A closer examination of the *APOL1* gene in patients with chronic kidney disease (CKD) can determine the cause of their kidney disease more effectively and potentially alter diagnosis, risk stratification, transplant evaluation, and treatment, recent research shows (JAMA Netw Open 2026; doi:10.1001/jamanetworkopen.2026.1452).

The *APOL1* M1 variant protects against focal segmental glomerulosclerosis (FSGS) and CKD associated with the G2 variant of *APOL1*. However, knowing whether an individual's M1 status can help guide kidney disease diagnosis and other clinical scenarios remains underexplored.

The researchers aimed to determine whether that status could help identify the true cause of a patient's kidney disease. They examined the health records of approximately 107,696 individuals with a diagnosis of FSGS or CKD from two large academic medical centers, the UK Biobank, and the National Institutes of Health's All of Us Research Program. Of the total, 8.2% had African ancestry, 72.9% had European ancestry, and 15% had multiethnic ancestry. The study included 3,460 participants with FSGS or steroid-resistant nephrotic syndrome (SRNS), 24,382 with non-FSGS CKD, and 79,854 controls enrolled in the discovery cohort.

After reviewing medical records and available biopsy data, the researchers found that nearly all patients with CKD who carried both an *APOL1* high-risk (HR) genotype and M1 did not have *APOL1* kidney disease. In the *APOL1*-HR group, M1 demonstrated an inverse association with FSGS or SRNS cases, compared with controls without kidney disease. Among individuals with CKD and *APOL1*-HR genotypes, M1 was four times more frequent in those whose CKD was not FSGS or SRNS.

Electronic health record and biopsy review identified an alternative, non-*APOL1* cause for CKD in nearly all *APOL1*-HR-M1 cases. The study found no association between individuals with *APOL1* low-risk genotypes with M1 and protection against CKD or FSGS.

The research also showed that the *APOL1*-HR-M1 genotype was significantly associated with protection against kidney disease. The finding suggests that it may have a role as a genetic modifier.

Patients with CKD with an *APOL1*-HR genotype and M1 should be evaluated for an alternative and potentially treatable cause of their CKD, the researchers said.

How laboratory medicine can support

healthy American Indian communities

Ongoing studies and initiatives aim to reduce barriers to care.

American Indian and Alaska Native (AI/AN) communities experience some of the worst racial and ethnic healthcare disparities in the United States. From 2008 to 2019, self-identified AI/AN individuals had an average life expectancy of 72.7 years, 6.5 years shorter than the national average. Though each population faces unique health needs and challenges, AI/AN individuals are, on average, more likely to die from diabetes, heart disease, chronic liver disease, cancer, and suicide than white Americans.

BY YAAKOV ZINBERG

Fortunately, there have been some highly successful interventions. For example, the Special Diabetes Program for Indians, which Congress established in 1997 to fund diabetes treatment and prevention services in American Indian communities, has been credited with reducing end-stage diabetic renal disease by more than half in this population.

Although sometimes overlooked, laboratory medicine is emerging as an avenue for improving health outcomes in these communities. Partnerships between laboratorians, researchers, and tribes are shedding light on specific gaps in healthcare and the ways that diagnostic testing could help fill them.

COLONOSCOPIES AND COLOGUARD IN RURAL ALASKA

Alaska Natives — the Indigenous people of Alaska who make up over 15% of the state's population — experience the highest rates of colorectal cancer (CRC) of any population globally. The reason why remains unclear. Factors associated with CRC risk in other populations, such as diet, tobacco use, and a sedentary lifestyle, might be at play. Researchers are also studying whether unique genetic determinants might be involved.

There's no doubt, however, that timely screening serves as the single most effective way to mitigate these cancers. Screening rates have improved dramatically in Alaska Native communities, up from less than 40% in 1999 to 69% in 2024.

"Alaska Native people actually have higher screening rates than non-Alaska Native people in our state," said Diana Redwood, PhD, MPH, a senior epidemiologist at the Alaska Native Tribal Health Consortium (ANTHC). As an expert on CRC screening methods and prevention for Alaska Native people, Redwood noted that these high screening rates are particularly impressive given the logistical challenges Alaskans living in remote areas face when it comes to accessing care.

"Imagine you have to fly from New York to Miami to get your colonoscopy." That's a rough approximation of the distance some Alaska Native people need to travel to receive a screening.

"Imagine you have to fly from New York to Miami to get your colonoscopy," she said. That's a rough approximation of the distance some Alaska Native people need to travel to receive a screening — and driving usually isn't an option since roads don't connect to most rural areas. The timing often isn't in people's control, either: Only one regional hospital within the Alaska Tribal Health System offers colonoscopies year-round, while some others set up week-long screening clinics throughout the year.

Redwood credits several factors for the extraordinary increase in CRC screenings. "It's a multicomponent approach," she said. "We do a lot of provider training, making sure that family history is checked and that those with a history get screened earlier and more frequently, in addition to using local Alaska Native patient navigators to help guide people through the screening process."

Additionally, ANTHC places strong emphasis on engaging with tribal leaders to understand how to best communicate the importance of CRC screening. "We've been told by Alaska Native elders that having more humor in the message is really important," Redwood said. That advice has led to the introduction of an 8-foot-tall, walkthrough inflatable replica of a human colon at community screening awareness events.

The introduction of Cologuard, a multitarget, stool-based DNA test, is currently being experimented with for CRC screening expansion, since the test is noninvasive and patients collect samples at home.

However, there are still logistical hurdles. All Cologuard samples are processed at the lab for Exact Sciences (the test manufacturer) in Madison, Wisconsin, and must arrive within 96 hours of collection. As part of a recent study, Redwood and colleagues set up a preprocessing facility in Anchorage, Alaska, for samples that otherwise would not have made the 96-hour deadline. Although that facility was only in operation for the duration of the study, it's a proof of concept for the establishment of future sites, Redwood said.

Earlier surveys conducted by Redwood and her colleagues show

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that Alaska Native people view stool-based testing quite favorably, at least when compared with the inconvenience and discomfort associated with colonoscopy. Another study she conducted showed that multitarget stool testing in a cohort of Alaska Native people resulted in fewer false negative results compared with fecal immunochemical testing, which detects blood in stool.

A colonoscopy remains the recommended screening test at the Alaska Native Medical Center, because it's more accurate than Cologuard and allows for precancerous polyps to be removed during the procedure, but the center encourages multiple testing options.

"I fully subscribe to the idea that the best test is the one that gets done," Redwood said.

HBA1C AWARENESS IN THE LUMBEE TRIBE

The HbA1c test plays a crucial role in diagnosing prediabetes and diabetes. However, Ryan Dial, MCLS, a citizen of the Lumbee Tribe of North Carolina, found that many of his community members were either unfamiliar with the test or didn't understand the significance of their results. Dial manages the Southeastern American Indian Cancer Health Equity Partnership at the University of North Carolina (UNC) Lineberger Cancer Center. With a background in laboratory science, he was motivated to collect data on the HbA1c testing experiences and health history of Lumbee people.

At the ADLM 2025 Annual Meeting, Dial shared the results of his research project, which surveyed 173 Lumbee adults in North Carolina. The key finding: 36% had never received an HbA1c test.

"In a completely perfect world, if everyone was following the United States Preventive Services Task Force recommendations, that number would be zero," Dial said during the presentation. That's because high-risk individuals, such as members of the Lumbee Tribe, should be screened in adolescence according to those recommendations. Other results from the survey underscore the importance of timely HbA1c screening: 72% of respondents had a family history of diabetes, while a little over 20% were diagnosed with the disease.

Dial also found that younger people were the least likely to have been screened or be familiar with HbA1c testing. "Diabetes is seen as a disease that you get when you're

Dial also found that younger people were the least likely to have been screened or be familiar with HbA1c testing.

"Unfortunately ... we don't have the privilege of waiting until we're 40 to worry about this."

40 or 50, but unfortunately, I have to break it to our youth that we don't have the privilege of waiting until we're 40 to worry about this."

Dial continues to analyze data from the survey and improve understanding in the Lumbee community about the importance of laboratory testing.

LESSONS FROM COVID-19

The COVID-19 pandemic, and the unique diagnostic testing requirements it created, shined a light on strategies that could improve access to testing for AI/AN communities. One survey of 679 American Indian individuals living in the Great Plains found that people who were unable to isolate if they tested positive were only half as likely to be tested. Additionally, testing uptake was greater among those who worked full-time, possibly because negative test results were required to return to work after showing symptoms, or because those with full-time jobs are more likely to have health insurance.

Another study, which surveyed 778 AI/AN patients and 77 providers from urban areas in the U.S., found that patients' concern about contracting the virus during an in-person appointment was the most commonly reported barrier to COVID-19 testing. Although difficulty finding transportation to a clinic was the barrier least often reported by patients, it was the one most frequently cited by healthcare providers — an indication that providers may sometimes misunderstand the reasons why their patients hesitate to receive diagnostic testing.

During the early days of the pandemic, First Nations organizations in Manitoba, Canada, partnered with public health and government officials to ensure access to testing and treatment for First Nations people. Although they experienced disproportionate rates of COVID-19 infection, testing rates among First Nations were twice as high as those of other residents of Manitoba."[This shows that] First Nations' sovereignty over their data and health priorities can support First Nations health and well-being during a public health emergency," the authors of a study on First Nations-led COVID-19 interventions wrote in a 2024 publication.

OPEN COMMUNICATION AND CULTURAL SENSITIVITY

Laboratorians and researchers seeking to work with AI/AN communities should be mindful of cultural sensitivities and the history of misconduct in this area, according to Ronny Bell, PhD, MS, chair of the division of pharmaceutical outcomes and policy in the Eshelman School of Pharmacy at UNC and a member of the Lumbee Tribe.

"There might be hesitancy [among tribes to participate] because of some of these past exploitations," he said, the most famous case being that of the Havasupai Tribe of Arizona and researchers at Arizona State University. In the 1990s, tribe members donated blood samples to the researchers with the understanding that they'd be used only for genetic studies on diabetes. In reality, the samples were also used for studies on schizophrenia, the tribe's origin, and their degree of inbreeding — topics considered taboo in the Havasupai community.

It was an egregious violation of informed consent, especially considering that many AI/AN communities, including the Havasupai, view blood as sacred. The case was taken to court and eventually settled in 2010; one of the terms of the settlement was the return of the samples to the Havasupai Tribe so the blood could be buried.

The case serves as a striking reminder that laboratory medicine professionals should carry out their research and initiatives in full partnership with the communities they seek to support.

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- Fentanyl Plus
- High Sensitivity Opiates
- Zolpidem
- Zopiclone

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AI-driven search tool retrieves results from technical documents in seconds.

Jonathan Montgomery was intrigued when his manager told him about the Association for Diagnostics & Laboratory Medicine's (ADLM's) latest data science challenge. Called LabDocs Unlocked, the 2025 contest asked participants to build an artificial intelligence (AI)-powered tool that could accurately extract information from complex laboratory documentation stores.

Montgomery, a systems specialist with Indigo BioAutomation and master's student in data science and AI at the University of Denver, thought that sounded like a fun project. So he dedicated his free time over the next several months toward building his program, ensuring the tool could retrieve information accurately and quickly, whittling down the time between a query entry and response to just 4.5 seconds.

His efforts paid off. Montgomery's tool, "Contextual Retrieval for Intelligent Chatbots," was voted the winner of the fourth annual ADLM challenge during a live demonstration webinar in February that was viewed by more than 200 people, including laboratory directors and other data analytics and informatics experts.

BY KAREN BLUM

"I am excited about the opportunity to leverage AI to extract value from internal documents not in the public domain," Montgomery said. "These AI tools and concepts open a new frontier to improve business efficiency, quality of life, and human-computer interactions, and I'm excited by the success of my design as a reusable tool for knowledge retrieval."

HOW THE TOOL WORKS

Montgomery developed a retrieval-augmented generation (RAG) system based on Anthropic's contextual retrieval framework, a system for easily and accurately accessing specific information from a large set of documents, Montgomery explained. It uses a combination of keyword matching and semantic embeddings, which are numerical representations of text trained to represent the meaning of the text as a whole rather than specific keywords. "If you merge the two techniques, they fill in the holes that each of them has," he said.

Montgomery made retrieval his first priority as he organized his project: "I wanted to ensure that I had accurate retrieval, and I could find the information in the documents reliably. Then I used a large language model to summarize the facts found in the documents." A user can interact with the tool through a chat interface. "The idea is that a user can quickly ask their question, see the summary version [of the answer], and then trace to the actual source document if needed," he said.

SELECTING THE FINALISTS

The competition was tough, said challenge organizers Mark Zaydman, MD, PhD, an associate professor of pathology and immunology at Washington University in St. Louis, and Dustin Bunch, PhD, DABCC, FADLM, director of laboratory informatics and data analytics at Nationwide Children's Hospital in Columbus, Ohio.

The competition required entrants to pose 15 trial questions to their interfaces and record the responses after searching for information among 13,600 PDF documents of different sizes and formats, such as standard operating procedures or Food and Drug Administration 510(k) submissions. The tools they created had to not only answer the questions correctly, but also provide a link or access to the primary source.

Montgomery's program was one of nine submitted. Zaydman and Bunch evaluated each program independently using a scoring rubric they developed with other members of ADLM's Data Analytics Steering Committee; Andrea Hobby, ADLM's director of data science; and Matt Boyle, ADLM's senior director of publishing and scientific content.

They reviewed each entry with four criteria:

- Accuracy: Did the tool's responses deliver the correct answers?
- User experience: Was it easy to navigate and aesthetically pleasing?
- Explainability: Could it provide references or links to the relevant sections of documents?
- Best practices (including coding reusability): Can it ingest new document stores?

Zaydman and Bunch also took into consideration the entrants' comments and their use of version control software to track development. Then, the two organizers met with Hobby to discuss their results and select two finalists: Montgomery and a group from Baylor College of Medicine in Houston.

THE FINAL STEP

Next came a live webinar, in which Montgomery and pediatric neurologist Mikael Guzman Karlsson, MD, PhD, a clinical informatics fellow at Baylor College of Medicine and Texas Children's Hospital, described their tools and what inspired them to enter the contest. Karlsson and his colleagues developed PathFinder, a generative AI tool that also uses RAG to help laboratory teams quickly find and interpret essential information buried in complex diagnostic and regulatory documents.

During the program, Zaydman and Bunch gave the finalists three new challenge prompts, such as, "What specimens are acceptable for the quetiapine assay?" Audience members watched as each tool gave its responses live and then voted on their favorite. While the finalists answered audience questions, ADLM staff tallied the votes so that the winner could be announced.

Montgomery said he was more excited than nervous leading up to the event.

"I ran through my slides a ton of times just to make sure the timing was right, because 10 minutes is not a long time," he said. Montgomery tried to find a balance between explaining what he did on the engineering side and providing information that could be useful to audience members who were considering similar solutions. "There are some fundamental concepts that I wanted to bring people up to speed on, so if they're looking to purchase something, they can have some idea what's 'in the box.'"

WINNING QUALITIES

Although Zaydman and Bunch were impressed by all of the contest entries, Montgomery's was a clear standout.

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"Even just finding where the information is stored out of the thousands of documents can take an excruciating amount of time … It's a pain that's felt across every laboratory."

"First of all, it was extremely accurate," Zaydman said. "The quality of responses it gave was exceptional. It was complete, but it was also very concise. It gave you exactly what you needed, and then it didn't drone on and waste your time with extraneous detail. That was really appreciated."

Montgomery put a tremendous amount of engineering into the program, Zaydman added. In the documentation he provided, he described experiments he ran to optimize the quality, speed, and accuracy with which the tool retrieved documents. "You can clearly see that he's a professional software developer in the quality of his code," Zaydman said. "He hit all the best practices as well, so he really knocked it out of the park across all our scoring domains."

The submitted tools varied in approach to information retrieval, programming languages, and large language models, said Zaydman and Bunch. Even among the two finalists, the Baylor team made use of enterprise tools out of the box, while Montgomery's platform was mostly developed from scratch. "It illustrates that both approaches can produce a really well-performing tool," Zaydman said.

WHY AI?

Zaydman and Bunch selected AI retrieval of documentation as the focus of this year's contest because it's a relatable problem that all labs struggle with, they said.

"We're at a point where AI and data science might radically change this process in the near future," Zaydman said. "We wanted a challenge that would incorporate large language models and generative AI. This is a technology that has really evolved rapidly in recent years, and there's a lot of excitement around the potential, but at the same time, there are safety concerns."

Humans face many challenging tasks in the lab that they either don't have sufficient time for or find mundane and unenjoyable, Zaydman added.

"We have so much documentation, protocols, regulatory documents, and checklists. They change and it's hard to keep up to date," he said. "Even just finding where the information is stored out of the thousands of documents can take an excruciating amount of time. Our current manual process is terrible, to say the least. It's a pain that's felt across every laboratory."

For example, a person might click on a document and wait 20 seconds for it to load, only to realize it's not the one they want, he said. So they click on one in a different folder and repeat the process. Being able to access correct information quickly is essential. "If there's friction, [people are] going to rely more on their memory than going and verifying, and that's not the safest or best way to proceed," Zaydman said.

Montgomery's company is evaluating the tool's business utility, including safety, security, and effectiveness. "What I hoped to demonstrate in the ADLM challenge is that you can leverage some of the tools that come out of AI semantic embeddings, and merging those with traditional search functions can result in better retrieval," Montgomery said. "AI and systems like this can … help people turn their ideas into real solutions backed up with real information."

"We wanted to educate and build community in ADLM around data science, and I think it's a really effective way to do that," said Zaydman, who noted that the contests also help engage professionals across disciplines in trying to solve a shared problem.

The source code for all nine submissions is available for download from the LabDocs Unlocked GitHub page at https://github.com/myADLM/ADLM-2025-Data-Challenge. Zaydman and Bunch are planning the association's next data science challenge, to be announced July 30 at the ADLM Data Science Symposium in Anaheim, California.

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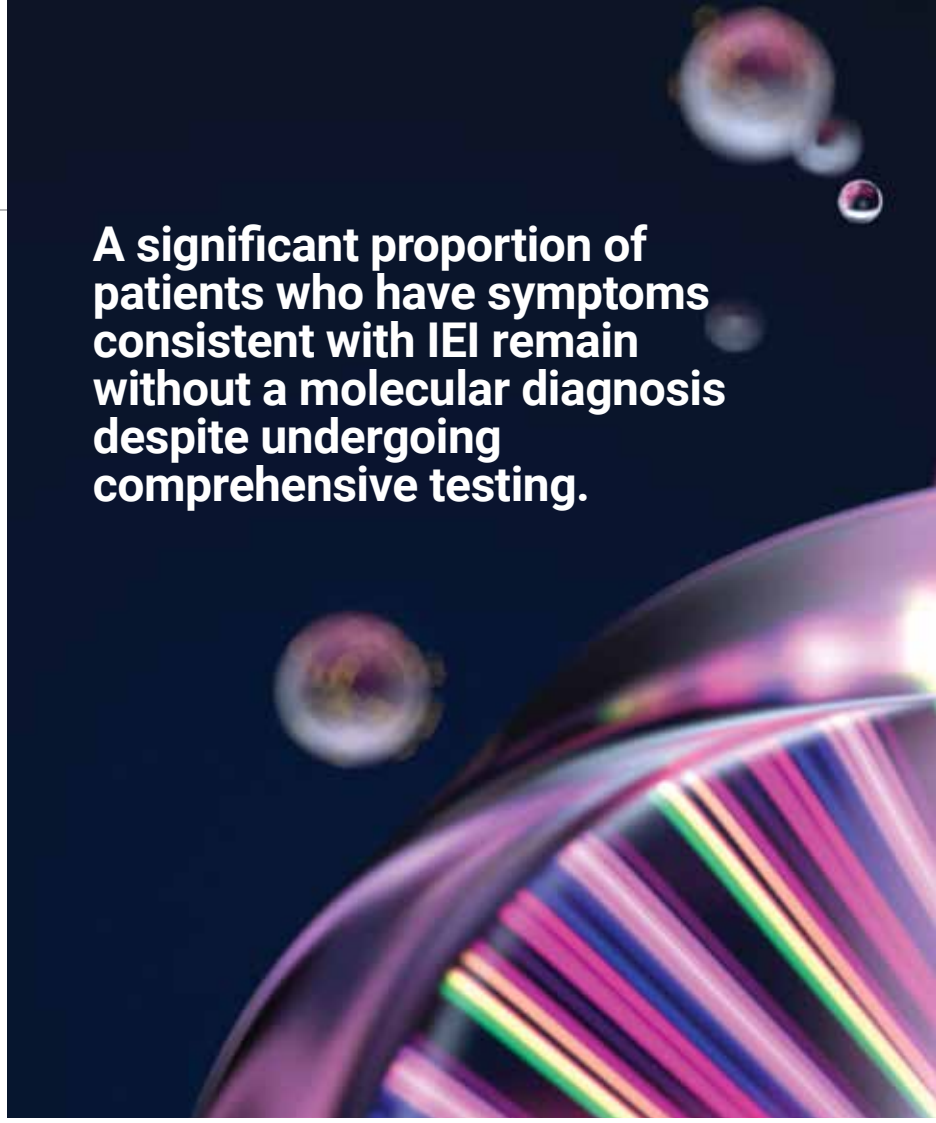
Genomic complexities in inborn errors of immunity

Are your diagnostic approaches keeping pace with the evolving genetic landscape?

BY JAHNAVI ALURI, PHD

Twenty years ago, the diagnosis of a rare immunological disease often meant years of uncertainty for patients and their families. Since then, the advent of next-generation sequencing (NGS) technology has revolutionized the identification and treatment of rare genetic disorders, particularly inborn errors of immunity (IEI).

IEI are a heterogeneous group of disorders characterized by immune dysfunction. Formerly known as primary immunodeficiency disorders (PID), they were initially associated with an increased susceptibility to infection. However, the application of NGS revealed that they actually span a diverse clinical spectrum, including autoimmunity, autoinflammation, atopy, and malignancy. This led experts to adopt the term IEI. The most recent International Union of Immunological Societies (IUIS) classification, a key diagnostic reference guide for these disorders, lists nearly 600 gene defects associated with IEI (*1*,*2*).



At the same time, NGS also revealed that the underlying genetic etiology is far more complex than previously believed. As more patients undergo sequencing, the classical model of genetic diseases — in which mutations to a single gene result in an inborn disorder — is being challenged. In fact, the growing recognition that autoantibodies or somatic gene variants developed after birth cause some forms of IEI has prompted some in the field to advocate for returning to the use of the term "PID" (*3*,*4*).

Further complicating matters, the same genetic variant can cause a variable degree of clinical manifestation, or even the absence of symptoms, sometimes among patients within the same family. This occurs due to two distinct but related phenomena: incomplete penetrance and variable expressivity. Together, they suggest that the clinical picture for IEI not only depends on the variant, but also on additional regulatory mechanisms. Moreover, a significant proportion of patients who have symptoms consistent with IEI remain without a molecular diagnosis despite undergoing comprehensive testing.

These diagnostic challenges may result from both the limitations of the current sequencing platforms and the inherent biological complexity of IEI. Addressing them requires clinical laboratory professionals and clinicians to work together, moving beyond a narrow genetic lens and refining their diagnostic practices accordingly.

This article reviews some of the increasingly recognized genetic mechanisms that complicate the diagnosis of IEI and discusses their implications for laboratory professionals.

WHEN TARGETING ONE GENE IS NOT ENOUGH

Traditionally, IEIs were considered monogenic disorders. They were thought to be linked to a single gene that followed standard Mendelian patterns of inheritance, including X-linked, autosomal dominant, or autosomal recessive inheritance.

However, recent studies reveal that far more complex genetic mechanisms are at play. In some cases, clinical disease development requires pathogenic variants in two genes (digenic inheritance) or three or more genes (oligogenic inheritance), challenging the "one gene, one disease" paradigm. This has been well described in some IEIs, such as hemophagocytic lymphohistiocytosis and certain subsets of combined variable immunodeficiency.

These mechanisms affect laboratory and clinical diagnosis in multiple ways. First, they necessitate the development of bioinformatics pipelines capable of finding multiple gene variants, because existing pipelines are largely optimized for single-variant analysis. Second, they underscore the need to perform validation studies to determine the functional consequence of each variant.

Third, they illustrate that the combined effect of multiple variants may lead to an atypical clinical presentation. Thus, standard treatment protocols may not be applicable, and clinicians may need to personalize

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therapeutic decisions. This complexity highlights the importance of multi-disciplinary collaboration between laboratorians, immunologists, and other clinicians for accurate diagnosis and improved patient care.

BEYOND GERMLINE VARIANTS: SOMATIC MOSAICISM IN IEI

IEIs have long been considered to result from germline variants, or gene changes that get incorporated into the DNA of every cell of a person's offspring. However, recently there has been growing recognition that this may not always be the case, because IEI sometimes shows somatic mosaicism.

Somatic mosaicism results from a postzygotic mutation that leads to the presence of a pathogenic variant in only a subset of a person's cells. The timing of the postzygotic mutation determines the variant allele frequency (VAF) and tissue distribution of the variant. Somatic variants with high VAFs can be detected relatively easily, compared with clinically relevant somatic variants with low VAFs (below 10–15%), because standard sequencing pipelines filter out low VAFs as background noise.

Tissue restriction of these variants further affects their detection. For instance, a variant may be missed if the only bodily substance analyzed is a patient's blood. Finding the variant may require the testing of additional tissues such as hair, nail, buccal swab, or fibroblast samples.

Experts recognized the role of somatic mosaicism in IEI in the 2000s, and the concept gained renewed interest in recent years. This has been largely driven by the application of deep sequencing (200–500x) and amplicon-based

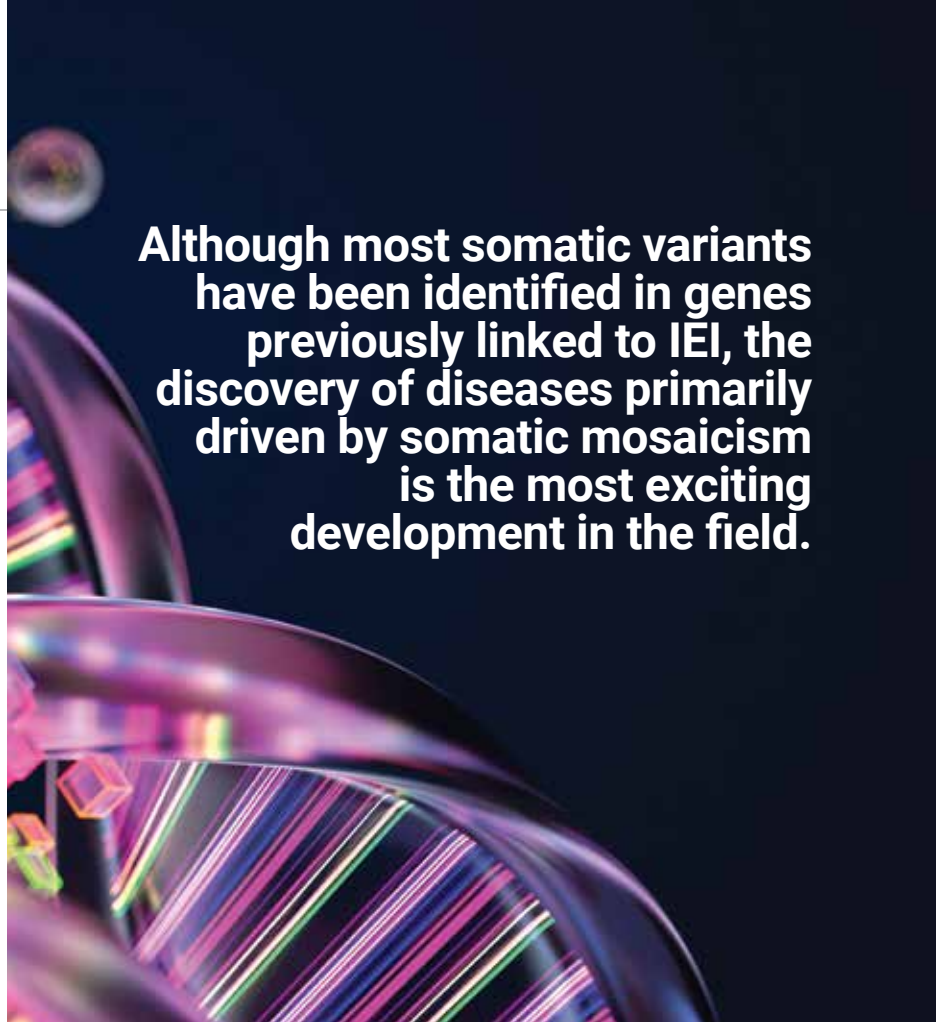
sequencing methods with high sensitivity and specificity for detecting variants with low VAFs (*5*). Although most somatic variants have been identified in genes previously linked to IEI, the discovery of diseases primarily driven by somatic mosaicism is the most exciting development in the field. For example, the discovery of somatic mosaicism in the gene *UBA1* explains the cause of a previously uncharacterized adult-onset autoinflammatory disease (*6*).

Unfortunately, the application of high-depth sequencing technology and the integration of multitissue testing remains limited in routine diagnostics because of the cost and logistical challenges. However, it is worth considering a targeted approach that involves deep sequencing in IEI patients, particularly those with sporadic symptoms that remain genetically uncharacterized. Along with functional validation studies, these tools might uncover the underlying cause of IEI in patients who would otherwise remain undiagnosed.

HIDDEN REGULATORS OF PHENOTYPIC VARIABILITY IN IEI

Identifying a pathogenic variant might not always equate to finding disease or predicting clinical severity in affected individuals. Multiple factors may significantly influence the penetrance and expressivity of a genetic variant, including epigenetic silencing, modifier genes, and environmental triggers such as microbiome composition or infection. These dynamic changes work at the level of gene regulation or involve environmental interactions invisible to DNA sequencing.

The process of skewed X-inactivation in female carriers of X-linked disorders offers a classic example of epigenetic silencing that influences disease presentation. These disorders include X-linked chronic granulomatous disease, Wiskott-Aldrich syndrome, or X-linked agammaglobulinemia. The mechanism for X-inactivation is random, with around 50% of cells expressing a wild type (healthy) copy of the gene and the other 50% expressing a defective copy. Skewed inactivation of the X-chromosome that leads to a preferential inactivation of the wild type gene can also lead to clinical symptoms even among female carriers. The severity of symptoms varies depending on the degree of skewing, with some showing minor symptoms and others demonstrating a full-blown manifestation of the disease.



Autosomal random monoallelic expression is a more recently recognized cause that contributes to phenotypic variability, or variability in how IEI manifests in different patients (*7*). In this process, experts believe that cell type–specific bias in expression due to random inactivation of an allele influences the phenotype.

An interesting example is the study of a *JAK1* variant that showed varying patterns of expression in multiple members of a family with different clinical presentations. Although the affected carrier expressed both the healthy and defective *JAK1* allele, the unaffected carrier expressed only the healthy *JAK1* allele, suggesting that both the genotype (gene makeup) and transcriptotype (pattern of RNA transcription) are required to understand the molecular basis of a few IEIs.

These findings emphasize the need to integrate genomic data with assays such as X-inactivation analysis and RNA sequencing

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studies to aid diagnosis, particularly in patients with an uncharacterized or atypical presentation.

NAVIGATING DIAGNOSTIC CHALLENGES

Diagnosing an IEI is not a straightforward process. It requires a strategic approach that integrates data from multiple teams. Although genetic sequencing is essential, it represents only one piece of the clinical puzzle. Determining the pathogenicity of the variant is equally crucial.

Further, the diagnostic yield of genetic testing depends on both the testing methodology and the patient cohort. For example, whole exome sequencing or whole genome sequencing typically yield a molecular diagnosis in approximately 40% of cases (*8*), with higher yields observed in early-onset or familial presentations and lower yields in adult sporadic cohorts.

That leaves a significant percentage of patients who have either variants of uncertain significance or who remain genetically uncharacterized despite a strong clinical suspicion of IEI. Addressing this diagnostic gap requires labs to embrace the genetic complexities outlined in this article.

Increasingly, this may involve deploying additional tools such as high-depth sequencing, RNA studies, single-cell sequencing, protein studies, machine learning algorithms, and artificial intelligence (*9*). Additionally, functional characterization, including flow cytometry, cytokine studies, and animal models, remain critical for validating uncertain findings and translating the genetic information into clinically actionable insights (*10*). Diagnosing IEI should involve a team-based approach, since these disorders sit at the intersection of immunology, genomics, and functional biology.

CONCLUDING THOUGHTS

Just as white light passing through a prism reveals a spectrum of colors, the study of IEI reflects a spectrum of biological and clinical diversity. And as an inverted prism can blend those colors back into clear white light, a collaborative analysis of clinical, functional, and genetic data can yield precise diagnosis.

Clinical laboratorians are tasked with recombining these scattered pieces of data — which often requires recognizing the "gray" areas in immunogenetics, including outliers and unexpected patterns. This demands questioning our standard genetic pipelines and, in some instances, adopting a completely different strategy tailored to the patient. Only through an integrated approach can the diagnostic ambiguity of IEI be addressed to provide meaningful answers to patients.

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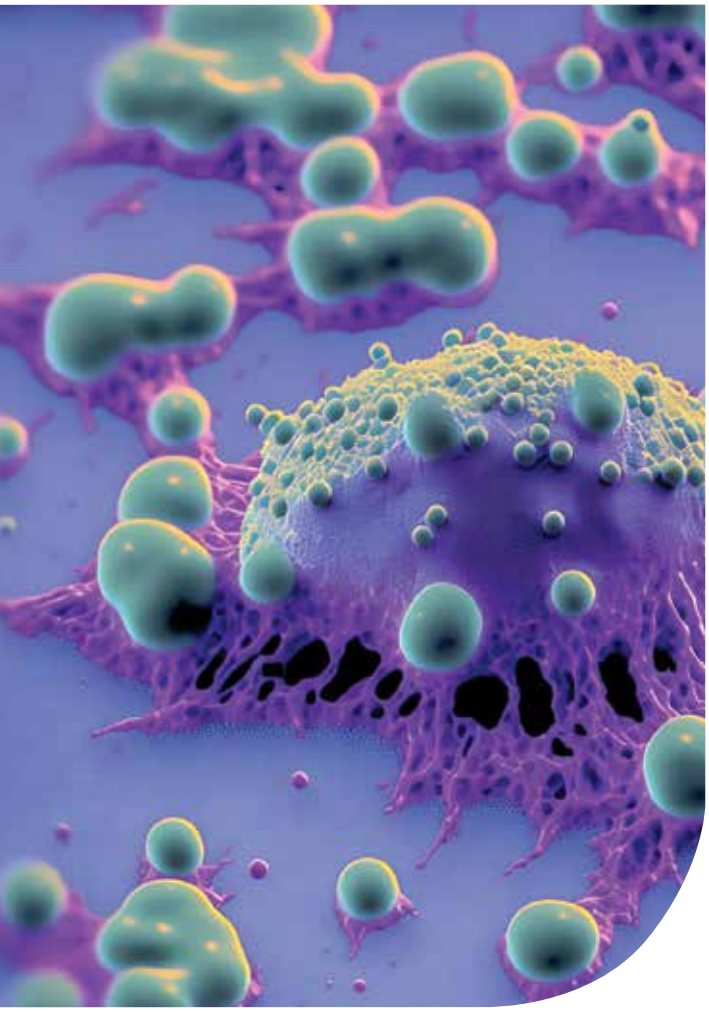
Regulatory Roundup



FDA approves Myriad Genetics companion diagnostic for ovarian cancer

Myriad Genetics' My Choice CDx Test received Food and Drug Administration (FDA) approval as the companion diagnostic (CDx) for GSK's polymerase (PARP) inhibitor Zejula (niraparib), which is intended for patients with advanced ovarian cancer.

The approval is based on final data from the PRIMA trial, which used the MyChoice CDx Test to determine homologous recombination deficiency (HRD) status and stratify advanced ovarian cancer patients. The test determines HRD status by leveraging next-generation sequencing technology to conduct a comprehensive assessment of *BRCA1* and *BRCA2* genes. The assessment offers information about large rearrangements and a tumor genomic instability score that includes loss of heterozygosity, telomeric allelic imbalance, and large-scale state transitions.

The MyChoice CDx is the only FDA-approved companion diagnostic test in the United States to identify patients with HRD-positive status (HRD+) who are eligible for treatment with Zejula.

Healthcare providers prescribe Zejula for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer that is associated with HRD+ status. That status is defined by a deleterious or suspected deleterious *BRCA* mutation or genomic instability. Patients receive Zejula after a complete or partial response to treatment with first-line platinum-based chemotherapy.

Nearly 50% of patients with advanced ovarian cancer have HRD+ tumors. Identifying these patients is critical to ensuring appropriate use of PARP inhibitor therapy and improving personalized treatment decisions, Myriad Genetics said.

MEMED AI-POWERED HOST-RESPONSE TEST ON CAPILLARY BLOOD GETS FDA BREAKTHROUGH DEVICE DESIGNATION

MeMed recently announced Food and Drug Administration Breakthrough Device Designation for its investigational device MeMed BV Flex, designed to accurately distinguish between bacterial and viral infections based on the body's immune response.

From just a few drops of capillary blood, the test measures multiple immune proteins and applies machine learning algorithms to generate a clinically actionable score in 15 minutes. Running on the MeMed Key platform, the test is designed for simplicity and intended for use across hospitals and CLIA-waived and decentralized care settings, pending regulatory clearance.

The test also expands accessibility, particularly for children and older people, while delivering accuracy traditionally limited to central laboratory infrastructure, MeMed said.

FDA CLEARANCE GRANTED FOR QIAGEN GASTROINTESTINAL PANELS ON AUTOMATED SYSTEM

Qiagen's QIAstat-Dx Gastrointestinal (GI) Panels on the QIAstat-Dx Rise automated syndromic testing system recently got Food and Drug Administration (FDA) clearance, the company said.

Laboratories now can run both QIAstat-Dx respiratory and QIAstat-Dx GI panels on QIAstat-Dx Rise, the high-throughput version of the QIAstat-Dx system.

Both versions support comprehensive syndromic testing with panels designed to detect multiple pathogens associated with similar symptoms in a single test, and targeted mini panels that focus on a defined group of pathogens.

The FDA clearance includes the QIAstat-Dx GI Panel 2, which detects 16 bacterial, viral, and parasitic pathogens from a single stool sample. The pathogens include clinically relevant Shiga toxin-producing *E. coli* (STEC) subtypes such as stx2f. The clearance also includes QIAstat-Dx GI Panel 2 Mini B and Mini B&V, which provide targeted detection of five GI pathogens, including STEC.

QIAstat-Dx Rise automates cartridge loading and unloading and can process up to 160 tests per day. Laboratories can run 16 samples in a batch while maintaining dedicated urgent slots for high-priority samples.

● MERIDIAN BIOSCIENCE MOLECULAR ASSAY PORTFOLIO GETS IVDR CERTIFICATION

Meridian Bioscience recently announced that a broad portfolio of its Alethia molecular assays achieved CE marking under the European In Vitro Diagnostic Regulation (IVDR).

The certification gives IVDR Class C certification to Alethia Pertussis and Alethia Pertussis External Controls, Alethia GBS and Alethia GBS External Controls, Alethia CMV and Alethia CMV External Controls, Alethia Malaria and Alethia Malaria External Controls, Alethia Chlamydia, Alethia Gonorrhea, and Alethia HSV 1&2 and Alethia HSV 1&2 External Controls.

Both versions support comprehensive syndromic testing with panels designed to detect multiple pathogens associated with similar symptoms in a single test.

The IVDR represents a significant evolution in the European regulatory framework for in vitro diagnostics and introduces more rigorous requirements for clinical evidence, performance evaluation, quality systems, and post-market surveillance. Achieving IVDR certification underscores Meridian Bioscience's commitment to delivering high-quality, compliant diagnostic solutions to laboratories and healthcare providers across Europe, the company said.

● LEX DIAGNOSTICS MOLECULAR DIAGNOSTIC PLATFORM FOR RESPIRATORY PATHOGENS GETS FDA 510(K) CLEARANCE, CLIA-WAIVED STATUS

LEX Diagnostics received Food and Drug Administration (FDA) 510(k) clearance and CLIA-waived status for its VELO system, an ultra-fast point-of-care molecular diagnostics platform designed to deliver highly sensitive PCR results for key respiratory pathogens directly from a swab sample in under 10 minutes.

Among the respiratory pathogens supported by the LEX multiplex system are influenza A, influenza B, and SARS-CoV-2. The system can be integrated into point-of-care clinical workflows across primary care settings, urgent care clinics, pharmacies, physician office laboratories, and decentralized acute settings, the company said. The system's proprietary cartridge-based design eliminates the need for external liquid handling and promotes ease of use and reliability.

LEX completed clinical studies in the United States with the VELO system and the influenza and SARS-CoV-2 assay during the 2024-2025 respiratory season.

● BIOCARTIS COLORECTAL CANCER COMPANION DIAGNOSTIC RECEIVES EUROPEAN IVDR CERTIFICATION

Biocartis recently announced that its Idylla CDx MSI Test received Class C companion diagnostic (CDx) certification under the European Union's In Vitro Diagnostic Regulation as a CDx for colorectal cancer (CRC).

The test is indicated as an aid to identify adult patients with microsatellite instability-high (MSI-H) metastatic CRC who may benefit from treatment with nivolumab in combination with ipilimumab. Designed for use on the Idylla platform, the Idylla CDx MSI Test qualitatively detects MSI-H/microsatellite stable in CRC tissue samples within a single-use cartridge and requires less than 3 minutes of hands-on time. The test and platform deliver results in under 3 hours, Biocartis said.

The test is commercially available in the United States and soon will be available in Europe.

Industry Playbook

Metabolon and Michael J. Fox Foundation partnership supports Parkinson's biomarker discovery

Metabolon and The Michael J. Fox Foundation for Parkinson's Research (MJFF) have established a collaboration for discovery of biomarkers and biological pathways associated with Parkinson's disease through the LRRK2 Investigative Therapeutics Exchange, Metabolon recently announced.

The collaboration aims to unlock new biological insights to improve early diagnosis and treatment of Parkinson's disease. It leverages Metabolon's Global Discovery Platform to power comprehensive multiomic analysis across MJFF's extensive Parkinson's Progression Markers Initiative (PPMI), which is the world's most deeply characterized Parkinson's disease cohort, according to Metabolon.

Through Metabolon's global metabolomics expertise and integration of multiomics data within MJFF's research environment, researchers will have access to unprecedented analytical depth across plasma, urine, and cerebrospinal fluid samples, the company said.

Together, MJFF and Metabolon will study proteomic, lipidomic, and metabolomic data from PPMI participants. Researchers will look for patterns, including those that may reflect *LRRK2* activity. Such insights could help identify biomarkers that support patient stratification and target engagement in future clinical studies, Metabolon said.

ILLUMINA AND LABCORP PRECISION ONCOLOGY EXPAND TESTING COLLABORATION

Illumina and Labcorp recently announced an expanded collaboration to advance precision oncology through innovative application of next-generation sequencing solutions across the healthcare ecosystem.

The expanded collaboration's projects are expected to promote equitable access to cancer biomarker testing by bringing it closer to patients through new distributed test offerings, evidence to facilitate payer coverage, and tests to address areas of unmet need.

The collaboration will involve the companies commercializing Labcorp's Food and Drug Administration (FDA)-authorized liquid biopsy assay, PGDx elio plasma focus Dx, alongside Illumina's FDA-approved TruSight Oncology Comprehensive for solid tumor profiling.

Together, these distributed test kits are intended to expand access to tissue and liquid biopsy testing for hospitals and community health systems, bring advanced biomarker testing closer to patients, help provide more specific diagnoses, and identify eligibility for targeted treatments and clinical trials, the companies said.

This distributed offering also aims to provide pharmaceutical companies with differentiated opportunities for companion diagnostic development and to support tissue and liquid biopsy needs for targeted therapy approvals.

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Product Spotlight

Advancing cardiovascular risk evaluation with Diazyme Lp(a) Assay

Reliable lipoprotein(a) testing is designed to support accurate cardiovascular risk assessment in clinical laboratories.

The Diazyme Lipoprotein(a) Assay enables quantitative measurement of lipoprotein(a) [Lp(a)] in human serum or plasma using routine clinical chemistry analyzers. The assay utilizes a latex-enhanced immunoturbidimetric method, in which Lp(a) particles in the sample bind to antibodies coated on latex particles, forming agglutination that is measured photometrically. The resulting signal is directly proportional to the concentration of Lp(a), which allows laboratories to incorporate Lp(a) testing into cardiovascular risk evaluation workflows.

Why choose the Diazyme Lp(a) Assay?

- Rapid turnaround time: Delivers results in less than 10 minutes, supporting efficient laboratory workflows.
- Low sample volume: Requires only 6 µL of serum or plasma, allowing testing even when sample availability is limited.
- Liquid-stable reagent format: A dual-vial liquid reagent system simplifies handling and preparation in the laboratory.
- Designed for routine chemistry analyzers: Enables laboratories to perform Lp(a) testing without requiring specialized instrumentation.
- Automated immunoturbidimetric method: Provides quantitative measurement of Lp(a) concentrations with reliable analytical performance.

Measurement of Lp(a) can provide important insight when evaluating lipid metabolism disorders and assessing risk associated with atherosclerotic cardiovascular disease. With rapid assay time and compatibility with routine clinical chemistry analyzers, the Diazyme Lp(a) Assay offers laboratories a practical solution for expanding cardiovascular biomarker testing while maintaining operational efficiency.

Every year, laboratorians produce billions of test results—valuable data that can unlock smarter workflows, more efficient lab operations, and better patient outcomes.

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COLLABORATION AIMS TO IDENTIFY NOVEL BIOMARKERS FOR CANCER IMMUNOTHERAPY

Pixelgen Technologies recently announced a research collaboration with a group at the department of oncology-pathology at Karolinska Instituet in Sweden to discover novel biomarkers for cancer immunotherapy response.

The collaboration will focus on the spatial distribution and abundance of more than 150 cell surface proteins in patients with nonsmall cell lung cancer who undergo immunotherapy with immune checkpoint inhibitors.

The project will use Pixelgen's Proximity Network Assay. The assay may give new insights into the organization and interactions of cell surface proteins, project leaders said. That knowledge could aid in the discovery of new biomarkers for immune checkpoint inhibition response and consequently inform treatment regimens for patients.

STUDY EXPLORES CARDIOVASCULAR RISK PREVENTION IN VETERANS

The United States Department of Veterans Affairs (VA) has partnered with the precision medicine company Allelica on a clinical genomics study aimed at reducing cardiovascular risk in veterans, Allelica recently announced.

The trial aims to improve therapeutic interventions for heart disease prevention using clinical genomic testing provided by Allelica. The trial will enroll veterans at risk for cardiovascular events who do not currently take cholesterol-lowering medications. Participants will receive either standard care or a genomic risk assessment. Researchers will use polygenic risk scores (PRS) for coronary artery disease and *SLCO1B1* pharmacogenetics testing to assess statin tolerance.

Allelica will provide eligible veterans with clinical, multiancestry PRS and *SLCO1B1* pharmacogenetic testing, as well as genomic risk assessment. Using the test results, investigators will determine whether personalized lipid-lowering therapy can improve adherence and statin effectiveness and reduce adverse effects.

The study's results have the potential to inform how healthcare professionals prescribe lipid-lowering drugs, reduce unnecessary side effects, and improve long-term health outcomes. This approach could be scaled across the VA healthcare system and beyond, benefiting millions of individuals at risk for cardiovascular disease, Allelica said.

PARTNERSHIP TO DEVELOP HLA-BASED COMPANION DIAGNOSTIC FOR CANCER IMMUNOTHERAPY

A recently announced collaboration between GenDx, based in the Netherlands, and Treos Bio, based in the United Kingdom, aims to develop the next generation of effective off-the-shelf peptide cancer immunotherapies.

The collaboration's goal is to accelerate the clinical development of Treos Bio's active immunotherapies while enabling precise patient selection through an integrated companion diagnostic approach, the companies said. The collaboration involves the development and validation of an integrated companion diagnostic (CDx) human leukocyte antigen (HLA) typing test for Treos Bio's off-the-shelf peptide cancer immunotherapy candidate, PolyPEPI1018, for the treatment of microsatellite stable colorectal cancer.

The CDx will combine GenDx's NGSgo HLA-A, HLA-B, HLA-C typing kits and NGSengine analysis software with Treos Bio's proprietary PEPI Test predictive software platform in compliance with ISO13485, European Union In Vitro Diagnostic Regulation, and relevant Food and Drug Administration requirements. The companies plan to integrate HLA typing workflow and PEPI Test predictive software and clinically validate them during Treos Bio's anticipated phase 3 clinical trial of PolyPEPI1018.

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Ask The Expert

The inside scoop on inhalants of abuse

By Laura M. Labay, PhD, F-ABFT, DABCC(TC), FADLM

What is an inhalant of abuse?

a: An inhalant of abuse is any volatile substance that produces psychoactive effects when intentionally inhaled to achieve intoxication or euphoria. These substances typically are not intended for human consumption and can be found in household, industrial, or medical products. Inhalants act rapidly on the central nervous system (CNS) due to pulmonary absorption and produce effects within seconds to minutes, generally lasting only a short duration. This rapid onset and brief effect contribute to their misuse potential, as repeated inhalation may be required to maintain the desired effect.

Experts broadly classify inhalants into four major categories. Volatile solvents are liquids that vaporize easily, such as toluene, acetone, and hexane, commonly found in paint thinners, glues, and cleaning agents. Aerosols include propellant- and solvent-containing sprays, often hydrocarbons such as butane and propane, found in spray paints and air fresheners. Gases include anesthetic agents and industrial or household gases, such as nitrous oxide and butane, obtained from whipped cream chargers, lighters, or medical sources. Lastly, nitrites, such as amyl nitrite and isobutyl nitrite, act as vasodilators and smooth muscle relaxants rather than acting as classic CNS depressants.

What makes inhalants particularly difficult to detect?

Laboratorians find inhalants challenging to detect because many are highly volatile, rapidly absorbed, and quickly eliminated from the body. Routine toxicology screens often do not include these substances, and confirmatory testing typically requires techniques such as headspace gas chromatography. Sample type and handling are critical, because volatile compounds can be lost during collection, storage, or transport, leading to negative results.

Interpretation is further complicated by the lack of standardized reference concentrations and the difficulty in distinguishing intentional abuse from incidental environmental or occupational exposure. Both clinical and forensic assessment relies heavily on contextual information, including patient history, scene investigation, and observed signs of intoxication, rather than laboratory results alone. Awareness of pharmacokinetics, analytical limitations, and proper specimen handling plays an essential role in detection and accurate interpretation.

What emerging inhalants of abuse are labs encountering?

Emerging inhalants of abuse are largely influenced by changes in product formulation, accessibility, and user behavior rather than entirely new chemical classes. Laboratories continue to see intentional inhalation of propellant gases from compressed air dusters containing 1,1-difluoroethane. These substances produce rapid euphoria but carry significant health risks, including fatal cardiac arrhythmias, multiorgan injury, and sudden death.

How are nitrous oxide and alkyl nitrites currently used?

Nitrous oxide continues to be misused recreationally. Its rapid onset and short duration of psychoactive effects make it appealing for recreational use but also complicate detection. Alkyl nitrites, commonly known as "poppers," are frequently used in the context of chemsex — the intentional use of drugs to enhance or prolong sexual activity — often in group or party settings. In this context, nitrites act as vasodilators and smooth muscle relaxants, demonstrating that inhalant misuse may occur not only for recreational intoxication, but also in specific social contexts. These emerging trends also reflect shifting patterns among adolescents and young adults because of easy access, low cost, and perceived safety, as well as new aerosol formulations, online product purchases, and social media-influenced use.

Interested in learning more? Attend the ADLM 2026 roundtable, "Inhalants of abuse: Analytical, clinical, and forensic perspectives," on Monday, July 27 in Anaheim, California. Find out more at meeting.myadlm.org.

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