G2 INTELLIGENCE
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DIAGNOSTIC TESTING & Emerging Technologies

New Trends, Applications, and IVD Industry Analysis

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May 11, 2017 – 8 a.m.-5 p.m.
Holiday Inn Airport, Atlanta, GA
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Initiatives Seek to Demonstrate Clinical Utility of Premptive PGx Testing

The application of pharmacogenomics (PGx) into routine, clinical care remains very limited, despite its potential to improve drug and dose selection based upon one's genes. Two new reviews, one published online Dec. 27, 2016 in *Clinical Pharmacology & Therapeutics* (*CP&T*) and one published in the December issue of the *European Journal of Human Genetics*, highlight both the challenges impeding translation of PGx into the clinic, as well as the surging number of implementation initiatives ongoing in the United States and Europe. Experts are optimistic that the evidence generated from these implementation initiatives will not only drive clinical adoption of PGx, but will shift momentum towards implementation of preemptive PGx testing strategies.

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FDA and Health Orgs Renew Focus on LDT Oversight

Late last year, the U.S. Food and Drug Administration (FDA) announced that it would not finalize the guidance on agency oversight of laboratory developed tests (LDTs) that it proposed back in 2014—at least not yet. Instead, the FDA said it would work with the new administration and Congress "to get our approach right." See "FDA Oversight of LDTs Delayed for Consultation with New Administration, Stakeholders," *DTET*, Nov. 2016, p. 1.

With that in mind, on Jan. 13, 2017, the FDA issued a discussion paper summarizing the public feedback it has received on the 2014 draft guidance and outlining the key features of a possible alternative approach to FDA regulation of LDTs. Later that same month, health care organizations emphasized the urgency of addressing LDT safety with a letter urging Congress to act sooner rather than later in addressing oversight.

Here is an overview of these latest developments concerning LDTs.

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Initiatives Seek to Demonstrate Clinical Utility of Premptive PGx Testing, *from page 1*

"Since actionable PGx variants are ubiquitous and the results of PGx testing are life-long, we foresee a future where everyone undergoes PGx testing," writes lead author Cathelijne H. van der Wouden, from Leiden University Medical Centre (the Netherlands), in *CP&T*. "We consider that quantifying the collective clinical utility of a panel of PGx markers to be more relevant than providing evidence for individual drug-gene pairs. This will, however, still require the systematic implementation of a pre-emptive PGx."

Evidence shows the majority of people have at least one actionable PGx variant. PGx testing holds the promise to make prescribing safer, more effective, and, in theory, more cost-effective by eliminating trial and error prescribing patterns. Yet, barriers exist to implementing widespread PGx testing because of inadequate understanding about testing selection, limited guidelines directing clinical use, and inadequate integration of information technology with clinical workflow.

Commercial genotyping microarrays can inform PGx-related treatment decisions at a cost of less than $50. This price point, experts believe, is low enough to encourage wide-scale augmentation of electronic health records with PGx information, even before the need for medication arises. However, the authors caution that the evidence base remains limited for demonstrating the clinical utility and the cost-effectiveness of pre-emptive testing.

Filling the Evidence Gaps

To date, PGx investigations have disproportionately focused on clinical discovery and validation instead of clinical translation, which must address barriers both at the clinic level (workflow and IT implementation challenges) and at the national level (reimbursement policies and development of guidelines). Now, though, there are an increasing number of large-scale initiatives implementing PGx in clinical settings, including how to integrate PGx test results into electronic health records and clinical decision support systems.

The newest initiative, the Ubiquitous Pharmacogenomics Consortium, which has been funded (€ 15 million) by the European Commission's Horizon-2020 program, aims to fill in evidence gaps related to patient outcomes and cost effectiveness of pre-emptive PGx in real-world settings. The consortium is conducting a prospective, block-randomized, controlled clinical study called PREPARE (PREemptive Pharmacogenomic testing for prevention of Adverse drug REactions), in which 8,000 patients throughout Europe (United Kingdom, the Netherlands, Austria, Greece, Slovenia, Italy and Spain) will undergo pre-emptive genotyping using a polymerase chain reaction-based panel of 50 variants in 13 pharmacogenes to guide drug and dose selection for 43 drugs. Prior to the launch of the trial, organizers developed clinical decision support systems, clinical guidelines, and provider training and education regarding PGx. The consortium believes that implementing PGx-guided drug and dose selection will decrease clinically relevant adverse drug reactions by 30 percent.

In the United States, there are more than eight ongoing implementation efforts. Some, including Right Drug, Right Dose, Right Time (RIGHT) at the

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As of Dec. 8, 2016 there are 233 drugs labels on the FDA's Table of Pharmacogenomic Biomarkers in Drug Labels.

	Genetic Testing Required	Genetic Testing Recommended	Actionable PGx*
FDA	46	5	143
EMA	31	-	14

* Drug label does not mention gene, protein, or chromosomal testing, but it contains information about changes in efficacy, dosage or toxicity due to such variants

Source: *Adapted from "Drug Labels" by PharmGKB.*

Mayo Clinic, the 1,200 Patients Project at University of Chicago, PG4KDS at St. Jude Children's Research Hospital, INdiana GENomics Implementation: an Opportunity for the Under Served (INGENIOUS) at Indiana University, and the multi-center Pharmacogenomics Research Network (PGRN) Translational Pharmacogenetics Program are all putting pre-emptive PGx testing into clinical practice.

Takeaway: While PGx has seen slow uptake in routine, clinical practice, experts believe evidence emerging from new large-scale implementation initiatives will demonstrate the clinical utility and cost-effectiveness of pre-emptive PGx testing strategies.

Industry Leaders Form Coalition to Further cfDNA-Based Noninvasive Prenatal Testing

Five major players in genetic testing have joined forces to promote cell-free DNA (cfDNA)-based noninvasive prenatal testing (NIPT). A newly formed organization, Coalition for Access to Prenatal Screening (CAPS) will promote prenatal screening using cfDNA-based NIPT. The five founding companies are: Illumina, Inc.; Counsyl, Inc.; Progenity, Inc.; Natera, Inc.; and Integrated Genetics, a specialty laboratory of Laboratory Corporation of America Holdings.

"NIPT represents a major advance in the screening for fetal chromosomal aneuploidies through the analysis of millions of cfDNA fragments in the blood of a pregnant woman," according to a statement announcing the coalition's formation. CAPS' website indicates the coalition "seeks to improve access to state-of-the-art prenatal screening using cell-free DNA (cfDNA)-based noninvasive prenatal testing (NIPT) that is easily accessible to all pregnant women who choose to pursue aneuploidy screening, regardless of their risk factors, income, age or geographic location."

cfDNA-based NIPT provides a less invasive method for screening pregnant women for Trisomy 21/Down syndrome and other chromosomal aneuploidies. Diagnostic testing such as chorionic villus sampling or amniocentesis must still be used to confirm positive screening tests but cfDNA-based NIPT identifies "a higher proportion of pregnancies affected by chromosomal aneuploidies" than serum-based screening, according to CAPS. A 2011 recommendation of the American College of Obstetricians and Gynecologists (ACOG) stated that cfDNA testing should be offered to high-risk women. A more recent committee opinion from ACOG and the Society for Maternal-Fetal Medicine, however, suggested NIPT using cfDNA offered "tremendous potential" to screen for fetal aneuploidy and any patient regardless of risk should be able to choose the screening—but it still did not recommend universal use of the NIPT with cfDNA as first line screening for pregnant women. See "Obstetric Groups Still

Don't Endorse Universal Use of NIPT, But Expand Access," *Diagnostic Testing & Emerging Technologies*, Feb. 2, 2016).

The coalition's announcement explains that cfDNA-based NIPT has high sensitivity and specificity with low failure rate, and leads to fewer invasive testing procedures for women. The testing can also be performed as early as nine to 10 weeks into a pregnancy.

The coalition will:

- "promote public awareness about the value of cfDNA-based NIPT";
- "advocate for the highest standards of quality, service and education";
- support relevant legislative action; and
- seek reimbursement policies supportive of such testing.

A clinical advisory board—to be named in the first half of 2017—will provide the coalition with "an independent medical perspective."

"As leading providers of cfDNA-based NIPT, CAPS members are working together towards the common goal of ensuring that this innovative and highly accurate screening method is easily accessible to all pregnant women who choose to pursue aneuploidy screening, regardless of their risk factors, income, age or geographic location," said Arnold W. Cohen, M.D., Chairman of the CAPS Clinical Advisory Board, in a statement. Cohen is also Chairman Emeritus of the Department of Obstetrics and Gynecology at the Einstein Healthcare Network. "We recognize the importance of providing reliable and useful information about cfDNA-based NIPT to patients, healthcare providers, and public and private insurers."

Takeaway: Industry leaders collaborate to increase recognition for cfDNA-based non-invasive prenatal testing.

4Q Earnings Show Mostly Gains for Diagnostics

Fourth quarter earnings reports are starting to trickle in. Here is a big picture roundup of some of the key results so far.

Gainers

Companies with strong 4Q diagnostics revenues include:

Abbott Laboratories: Year-over-year (YOY) growth of 3% driven by 4% increase in infectious disease testing and core laboratory sales (from $969 million to $1 billion)—offsetting 1% foreign exchange loss and 8% decline in molecular diagnostics due to wind-down of genetics business;

Quest Diagnostics: Quarterly revenues of $1.86 billion on 0.7% growth (on a reported basis) and full year revenues of $7.52 billion on 0.3% growth;

Luminex: Expected YOY growth of 20% for 4Q and 14% for year with revenues of, respectively, $72 million and $271 million, easily beating Wall Street estimates of $70.3 million and $268.9 million; and

Invitae Corporation: Among best performing of genetic information companies with expected 33% revenue growth (as compared to Q3) driven by

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Christopher Ianelli, M.D., Ph.D.
Founder & CEO, iSpecimen

iSpecimen Creates Marketplace for Clinical Discards

iSpecimen (Lexington, Mass.) can be thought of as a cross between a dating site and an online marketplace for human biospecimens. The company has built a turnkey solution that connects providers, such as hospital systems, commercial labs, and biobanks, to researchers looking to gain access to these specimens and associated data from electronic medical records and other sources. It's a win-win situation, with providers having a new market for both soon-to-be discarded and banked specimens, researchers more efficiently accessing needed specimens and rich clinical data, and patients getting a chance to make a contribution to research.

DTET recently spoke to Christopher Ianelli, M.D., Ph.D., iSpecimen's founder and CEO, to learn about the company's business model, patient preferences for sample donations, and how biobanking is anticipated to evolve in the coming years.

iSpecimen's goal is to reduce research costs and procurement time, while ultimately hastening clinically relevant discoveries. What is the business case for iSpecimen? How do you deliver value to your partners and investors?

> *"Instead of throwing it away, allow iSpecimen to identify researchers across the world who are asking for access to that material because it is perfectly useful for research endeavors."*
>
> — Christopher Ianelli, M.D., Ph.D.
> Founder & CEO, iSpecimen

What I tell investors is that there is real value to the bookends on our business model—the bookends being the health care provider system and the life science research community. We create value on both sides. On the health care provider side we focus on hospitals as the prototypical partner we work with. If you walk into the laboratories of those hospitals, they have very well organized workflows that take in samples and conduct clinical testing to deliver results to the clinicians and patients. Then, those samples are almost always thrown away. In the clinical laboratory it is a matter of days before they throw away a sample that was tested. In pathology labs it is anywhere from days to a decade later that tissue that doesn't get used is thrown away. You can walk into 99.9 percent of hospitals across the country and you can point to the garbage cans and say that there is tremendous value in that garbage can, especially if you can link the material in that garbage can to data.

We give them an opportunity to work with us, before they throw anything away, to help us identify what in their workflow can be utilized beyond the clinical lifespan. Instead of throwing it away, allow iSpecimen to identify researchers across the world who are asking for access to that material because it is perfectly useful for research endeavors. This gives hospitals the choice. Instead of discarding the material, they can take it, pack it, and ship it off to the researcher.

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That sample can yield research results that will ultimately come back and help their patients or patients like them. We will provide all of the tools in the form of technology and processes to make it a very efficient process so that the laboratory does not need to worry about distractions to their core workflow.

> *"Overwhelmingly, more than 80 percent of patients, for no compensation, say 'channel my sample into research.' "*
>
> — Christopher Ianelli, M.D., Ph.D.
> Founder & CEO, iSpecimen

If you go out and talk to life science researchers, in industry or academia, they have long complained about the bottleneck in going from discovery through validation, which can slow getting their product— a diagnostic test or therapeutic—to market. The bottleneck is they can't proceed because they do not have the number of samples they need, or adequate quality of samples. We solve that for them. Instead of calling the 5,000 hospitals across the country to cobble together samples, they can work with just us and we will deploy their request across our partner network to make it more efficient. For researchers, it is a huge defragmentation exercise that helps them get material.

We are compensated by the research community for the matching service when we are successful in identifying samples for them. We share that revenue back with provider partners that sourced the material, and they put this back into their day-to-day operations, including patient care. Our investors like it because from the money we take in from researchers and the money we share with our partners, there is something left over as profit. We are not yet profitable, but we are on our way.

When researchers can't use remnants we have a whole other track where they can make requests of us that they need collection under certain conditions or a specific volume or collected in a certain tube you would not ordinarily use clinically. This track is 'research use only,' where we collect non-remnant samples. These are obtained under patient consent to send directly to the researcher.

iSpecimen By the Numbers

iSpecimen's partner network includes:

- 250+ hospitals and labs
- 10+ biorepositories
- 6 clinical research organizations
- 1 large blood center

With annual access to

- 25 million remnant specimens
- 5 million patient encounters
- Hundreds of thousands of banked samples

How do patients feel about their specimens being used for research?

We explored this question with patients directly. It turns out most patients don't understand what happens to that tube of blood after they give it. They know it goes to a laboratory and test results will be generated, but they don't realize that several days after the results are generated, the sample will be thrown away. More often than not, there is an adequate volume left that is perfectly useful and sought for research. We educat-

ed patients about the process and then asked them, assuming that your privacy and confidentiality are protected, would you rather we throw away the sample or channel it into a research effort. Overwhelmingly, more than 80 percent of patients, for no compensation, say "channel my sample into research."

What legal mandates govern the re-use of clinical samples for research?

In mid-January a ruling was made on proposed changes to the law that governs the use of clinical discards. Under the Common Rule, patient specimens may be used for research without consent as long as they are left over from a clinical process and are de-identified. In September 2015, a Notice of Proposed Rule Making was issued that would have changed this process and mandate consent for de-identified discards. But, President Obama's administration decided to keep the process as is and consent will not be required for these samples.

> *"The first barrier is getting them comfortable that as a company we are compliant with all of the regulations that exist."*
>
> — Christopher Ianelli, M.D., Ph.D.
> Founder & CEO, iSpecimen

Having said that, iSpecimen has always offered consent support for partners who want to implement consent. So, whether or not the law changed we were ready for what ensued. We will continue to operationalize consent for our partners who opt to implement it for discards, as many of our partners feel good about informing and asking their patients.

While the proposed changes did not go into effect, the rationale behind the proposal was that with progress in genetic technology came a little less confidence that de-identification of samples and datasets was really enough to protect each patient's identity because gene sequences and mutations may someday be able to re-identify the patient. Because of that, some believed that we needed to revisit the issue and respect patient autonomy a little bit more than in the original version of the Common Rule. The general sentiment of industry has been that requiring consent for de-identified discards would slow things down and stifle research. Now we know that, at least for now, nothing will change.

2016 appeared to be a year of tremendous growth for the company. What challenges does iSpecimen face as it continues to expand its partner network?

When we go into meetings, the providers bring in their chief of compliance or privacy officer. There are lots of questions around privacy and security, but is not a strict barrier. It is more of a picket fence. They want to understand to what extent we are taking measures to adequately protect patient privacy. They want to understand what we are doing to de-identify patients and what we are doing to protect against re-identification. The first barrier is getting them comfortable that as a company we are compliant with all of the regulations that exist.

We also let them know about the rules and regulations around the use of remnant specimens and that they can, but do not need to, obtain patient consent.

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"Biobanks have collected so much material with the promise of directing it into research, but they don't have the tools and systems in place to share."

— Christopher Ianelli, M.D., Ph.D.
Founder & CEO, iSpecimen

We are set up to give hospitals support for operationalizing consent, so they can decide how they want to handle it.

The next obstacle we face in growing our provider network is information technology (IT). Electronic medical records are being aggressively adopted and implemented across the health care workflow. IT departments are so busy, and since we need to have data transmitted, we need the time and attention from the IT group of the hospital, laboratory, or practice group to implement our solution. We have to wait in line for that to happen. Understandably, they are focused on the systems that are in place for patient care, and then they can get to us.

How will biobanking and specimen sharing evolve in the next few years?

You hear a lot about the challenge of interoperability in the health care system with electronic medical records. Biobanks are even further behind. In the short-term I see standards being applied for what information is collected and how it is collected. It has to change and as biobanks move towards interoperability for sharing, we can play a central role in impacting interoperability discussions.

Biobanks have collected so much material with the promise of directing it into research, but they don't have the tools and systems in place to share. We refer to them as biomuseums because most of the material never finds its way out to researchers. Biobanks are filling up. I think in the coming years, biobanks will be forced to specialize in a way that will align with their center's clinical expertise. General inventory will transition to specialized neuroscience or hematology collections and sharing across systems will be needed to get material into these specialized banks. I see iSpecimen playing a dominant role as a channel partner in helping get samples quickly and efficiently to researchers, which will help biobanks with their long-term sustainability.

Updated Guidelines Emphasize Newer Tests for TB Diagnosis

Patients at risk for tuberculosis (TB) infection should be assessed with newer tests, including interferon-gamma release assays (IGRAs) and molecular diagnostics, according to new guidelines developed by the American Thoracic Society, Infectious Diseases Society of America, and the U.S. Centers for Disease Control and Prevention (CDC). The guidelines, published in the December issue of *Clinical Infectious Diseases*, are the first updates in 17 years and were prompted by advances in testing.

"These guidelines develop a structured approach to testing, recommending that doctors test for latent TB in patients who are at risk for infection and who

"These guidelines develop a structured approach to testing, recommending that doctors test for latent TB in patients who are at risk for infection and who would benefit from treatment, and for TB disease in patients who have signs and symptoms of the disease"

— David Lewinsohn, M.D., Ph.D.

would benefit from treatment, and for TB disease in patients who have signs and symptoms of the disease," said David Lewinsohn, M.D., Ph.D., lead author of the guidelines in a statement. "Even though TB disease is not common in this country, it's important that doctors remember it's still around, and that they should test patients when appropriate."

In 2015 there were just over 9,500 cases of TB reported in the United States, a 1.6 percent increase over the previous year, according to the CDC. Additionally, the CDC says that up to 13 million Americans have latent TB, meaning they are infected with Mycobacterium tuberculosis (Mtb), but are asymptomatic. Eradication of TB in the United States, experts say will require expanding testing and treatment of latent TB.

The new guidelines recommend health care providers consider testing for latent TB in patients who live with a person who has TB disease, immigrated to the United States from a country where TB disease is common, or who are in high-risk settings, such as prison. The guidelines, though, now recommend IGRAs, instead of tuberculin skin tests, for testing for latent TB.

Data shows IGRAs blood tests are more effective at detecting TB disease than a TST, although neither can distinguish active TB from latent infection. IGRAs have the added benefit that they can be performed in one patient visit. Currently, there are two approved and commercially available IGRA platforms. They measure interferon-γ released by sensitized T cells in response to Mtb-specific antigens.

If a patient has active signs of TB disease, the guidelines recommend doctors should order smear (acid-fast bacilli smear microscopy on three samples), cultures (both liquid and solid), and molecular diagnostic testing (diagnostic nucleic acid amplification test on the initial respiratory specimen, as well as rapid molecular drug susceptibility testing), particularly in patients at higher risk, such as those who have HIV or live with a patient with TB disease.

"The ability to rapidly and accurately identify Mtb as well as drug resistance (e.g., through NAAT, line probe, molecular beacon, and Xpert MTB/RIF assays) reflects substantial advances," the authors write. "While rapid tests for TB diagnosis still have a sensitivity of 70 percent to 90 percent, they … also remain relatively expensive, making them difficult to implement in high-burden, low-resource settings. Ideally, what is needed is a simple, inexpensive, rapid (i.e., hours) test that is highly accurate (>95 percent sensitivity and specificity)."

The authors also note that future diagnostic development should focus around accurately identifying those with latent TB at risk for disease progression.

Takeaway: Substantial advances have been made in testing for TB prompting revised guidelines favoring newer tests, including IGRAs and molecular testing.

FDA and Health Orgs Renew Focus on LDT Oversight , *from page 1*

FDA Discussion Paper Analyzes Stakeholder Feedback

As part of the feedback process, the FDA asked stakeholders to suggest how they think the agency should regulate LDTs. The agency summarized the feedback it received in its January discussion paper, noting that the various proposals shared some similar features, including:

- Risk-based approach;
- Premarket review for some tests, with exemptions for certain categories;
- Test approval based on analytical and clinical validity;
- Adverse event reporting;
- Quality systems;
- "Grandfathering" for certain existing tests; and
- Transparency regarding test performance information.

"Based on the feedback received, a *prospective* oversight framework that focuses on new and significantly modified high and moderate risk LDTs would best serve the public health and advance laboratory medicine," the new discussion paper concludes.

FDA Describes Alternative Oversight Model

The FDA discussion paper also sets out the agency's own thinking on LDT regulation and how it has changed since 2014. Over the two years of "engagement," "positions of many groups, including the FDA, have evolved," the FDA acknowledged. The paper then sets out key features that may be incorporated in an alternative to the framework it proposed back in 2014, including:

- Phased-in oversight program over four years rather than the originally proposed nine years;
- Grandfathering for many LDTs already on the market;
- Broader definition of LDTS for unmet needs;
- Collaboration between FDA and third parties to use existing review standards and certification programs—such as the National Glycohemoglobin Standardization Program or the Cholesterol Reference Method Laboratory Network—for evidence standards;
- Potential use of existing review programs for third-party review, such as New York State's Clinical Laboratory Evaluation Program and independent CLIA accreditation programs;
- Clinical collaboration with stakeholders and health care professional organizations on standards for analytical and clinical validity;
- Public availability of evidence regarding analytical and clinical validity;
- Reliance on CLIA certification requirements plus three FDA quality systems requirements regarding test development processes—design controls, acceptance activities, and procedures for corrective and preventive action (CAPA); and

- Postmarket surveillance requiring labs report serious adverse events for tests except for traditional LDTs, LDTs for public health surveillance, specific transplantation related LDTs, and forensic-use LDTs.

"There is no systemic way to be sure of the accuracy and reliability of these tests. The current oversight framework creates inconsistencies in oversight and can leave FDA with limited options to catch and address problematic LDTs."

— American Cancer Society Cancer Action Network

The FDA expressly states that its discussion paper and the proposal it outlines is not a final version of the 2014 guidance and "does not represent the formal position of the FDA, nor is it enforceable. We hope to simply advance the public discussion by providing a possible approach to spur further dialogue."

Health Care Orgs Ask Senate to Address LDTs

Meanwhile, shortly after the FDA released its discussion paper, some health care organizations sought to make sure the FDA's deference to working with the new administration did not mean significant delays in addressing oversight issues. Calling the current regulatory system for LDTs "inadequate and in urgent need of updating," the American Cancer Society Cancer Action Network and 32 other organizations sent a letter to U.S. Senate leaders urging them to update the oversight framework for all molecular diagnostic tests, with an emphasis on LDTs.

"It is imperative that patients and physicians are assured of the accuracy and reliability of these test results when making vital health decisions," write the letter's signees. "Currently, diagnostic tests undergo widely different levels of oversight depending on whether they are submitted to the U.S. Food and Drug Administration for review or are offered as LDTs."

Citing the increased complexity of current LDTs and the fact these tests are increasingly performed in reference laboratories with national reach, the organizations, representing patients, scientists, advocates, caregivers, and health care professionals, say that CLIA regulation does not adequately address the "safety and effectiveness" of LDTs.

Under CLIA, laboratories are required to demonstrate the analytical validity of the tests they offer (the test's reproducibility), but CLIA does not ensure consistent performance for measuring the same analyte across laboratories, the Cancer Action Network says. Additionally, the organizations stress that CLIA does not evaluate the clinical validity of a test—the test's ability to accurately diagnose a condition.

"There is no systemic way to be sure of the accuracy and reliability of these tests," say the signees. "The current oversight framework creates inconsistencies in oversight and can leave FDA with limited options to catch and address problematic LDTs."

As further evidence of the need for updates to the oversight framework, the organizations cite a Dec. 15, 2016 study in *JAMA Oncology* that reported "markedly" different test results from two different commercially available, next-generation sequencing-based tumor profiling tests (See the March issue of *DTET* for more details).

Takeaway: LDTs remain very much a work in progress, one that has evolved since 2014, and you need to stay tuned for further developments.

4Q Earnings Show Mostly Gains for Diagnostics, *from page 4*

200% YOY increase in billable test volume with approximately 59,000 tests for the year. The genomic testing sector was strong with robust quarterly YOY growth reported by:

- T2 Biosystems (+50%) (preliminary);
- NanoString Technologies (+15%) (preliminary); and
- GenMark Diagnostics (+13%).

Decliners

Although gainers generally outnumbered decliners, companies with weaker than expected diagnostics revenues included:

Meridian Bioscience: Decline of 1% for 3 months ended Dec. 31, 2016 (which is actually the company's first quarter) to $46.8 million, well below Wall Street estimate of $51.2 million, due to 4% decline in core diagnostics business which more than offset 3% growth in molecular diagnostics;

Quidel: Expected 4Q revenue of $52 to $53 million, as opposed to Wall Street estimate of $63.1 million, which company attributes to weak sales of influenza kits caused by late start to flu season; and

Fluidigm: YOY decline of 19% (roughly $25 million v. $30.7 million in 4Q 2015) and expected 9% decline in full year revenues.