Volume XXV, Number 17 Monday, December 3, 2018

From the Desk of R. Lewis Dark...

THE DARK REPORT

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

Restricted information, see page 3

COMMENTARY & OPINION by...

R. Lewis Dark

Founder & Publisher

If 2019 Is a Tough Year, Blame Government, Payers

TRADITIONALLY, THE NEW YEAR IS A TIME OF OPTIMISM. People make resolutions such as exercising more and losing weight. Companies get to start the year with a fresh budget and the new opportunity to achieve their goals.

Unfortunately, events of the last 90 days of this year are not auspicious for clinical laboratories and anatomic pathology groups during 2019. Let me list just four significant events, each with the potential to have major consequences:

- On Sept. 12, in the whistleblower case of the *United States of America ex rel. Chris Riedel vs. Boston Heart Diagnostics Corporation*, the federal judge ruled that the practices of labs waiving patient copays and deductibles and paying referring physicians for packaging and handling of patients' specimens are issues that could go forward in this lawsuit. This ruling thus became something that labs and their legal counsels need to consider when assessing their compliance with the federal Anti-Kickback Statute. *(See TDRs, Oct. 1 and Oct. 22, 2018.)*
- In November, the federal **Centers for Medicare and Medicaid Services** released the 2019 Medicare Part B Clinical Laboratory Fee Schedule with more fee cuts, along with the amended rule requiring hospital labs using the CMS-1450 14x claims form to report their private payer lab test price data in the next reporting cycle. *(See TDR, Nov. 13, 2018.)*
- Following the October 24 enactment of the federal Support for Patients and Communities Act into law, lab industry attorneys have been discovering language in the statute that would make several common lab business practices illegal for both government and private health plans, such as paying commissions to sales reps, putting phlebotomists into physicians' offices, and providing lab supplies to referring physicians. *(See pages 3-9.)*
- Late last week, we learned that **UnitedHealthcare** was terminating an unknown number of labs as providers. Most of these labs had been in-network for a decade or more. This may be the early sign of a new managed contracting trend that does not favor hospital lab outreach programs and regional laboratories. *(See page 16.)*

These examples above are why, if 2019 turns out to be a tough year for the clinical laboratory industry, much of the blame can be placed on the federal government and major health insurers. TDR

New Opioid Law Hits Labs Paying Sales Commissions

ACLA requests HHS to review safe harbors under 'Support for Patients and Communities Act'

CEO SUMMARY: At the last minute, Congress added all clinical laboratories to a far-reaching anti-kickback provision in the newly-enacted Support for Patients and Communities Act. This provision applies to all payers, both government and private. Lab experts say this new law could have a negative effect on patient care because it could make relatively innocuous and heretofore permissible practices into criminal offenses, such as placing phlebotomists in physicians' offices.

THERE'S A NEW FEDERAL LAW applicable to both government and private health plans that could put every clinical laboratory and pathology group with commission-based sales staff at risk of compliance violations.

Within 24 hours of this legislation becoming law, the **American Clinical Laboratory Association** (ACLA) was communicating its concerns to officials at the federal **Department of Health and Human Services** (HHS). That communication came as part of its response to a request for information from the Office of Inspector General of HHS (OIG) on the Anti-Kickback Statute.

On Oct. 25, the day after the Support for Communities and Patients Act was signed into law, Sharon L. West, the ACLA's Vice President, Legal and Regulatory Affairs, asked the Inspector General of HHS to ensure that healthcare providers would be protected under the new law.

OIG should make clear to healthcare providers and law enforcement agencies, "that conduct protected by a safe harbor under the current Anti-Kickback Statute would not be treated as a criminal offense under a different federal law," West wrote. One point of significant confusion is because the Support Act's anti-kickback provisions cover *all* payers, while the federal Anti-Kickback Statute applies just to federal healthcare programs.

Earlier this year, as the Support Act moved through Congress, the ACLA noticed that, late in the process, language was added that put certain practices at risk even though those practices are common

THIS PRIVATE PUBLICATION contains restricted and confidential information subject to the TERMS OF USAGE on envelope seal, breakage of which signifies the reader's acceptance thereof.

THE DARK REPORT Intelligence Briefings for Laboratory CEOs, COOs, CFOs, and Pathologists are sent 17 times per year by The Dark Group, Inc., 21806 Briarcliff Drive, Spicewood, Texas, 78669, Voice 1.800.560.6363, Fax 512.264.0969. (ISSN 1097-2919.)

R. Lewis Dark, Founder & Publisher. Robert L. Michel, Editor.

SUBSCRIPTION TO THE DARK REPORT INTELLIGENCE SERVICE, which includes THE DARK REPORT plus timely briefings and private teleconferences, is $15.27 per week in the US, $15.27 per week in Canada, $16.05 per week elsewhere (billed semi-annually).

among clinical laboratories, West said in an interview with THE DARK REPORT. Coincidentally, the ACLA was preparing to respond to the request for information from the OIG about the federal Anti-Kickback Statute.

Implications for Clinical Labs

In the weeks since the Support Act became law, healthcare attorneys have begun to learn about its potential onerous implications for laboratories that pay commissions to sales staff, whether they are employees or independent contractors.

In a warning note to clients on Nov. 29, Charles C. Dunham IV, a healthcare attorney with **Epstein Becker Green**, explained that all clinical laboratory managers and pathologists need to be aware of provisions in the Support Act that appear to eliminate the ability of laboratories to compensate sales personnel (including W-2 employees and 1099 contractors) on a commission-based formula related to any third-party payer business they generate, whether from a government health program or a private health insurer.

Originally, the provision in question was called the Eliminating Kickbacks in Recovery Act (EKRA) before it became Section 8122 of the Support Act, he wrote.

Added at the 11th Hour

EKRA was added to the Support Act, he wrote, "at the 11th hour, along with the inclusion of laboratories, and there are a number of unclear and questionable provisions that appear to pre-empt the safe harbors under the federal Anti-Kickback Statute and certain state anti-kickback rules." While the laboratory industry is lobbying for amendments to the statutory language, whether and when such amendments will be forthcoming is unknown, he added.

West cautioned that clinical laboratories need to be aware that the law has potentially negative effects on existing specimen collection arrangements and could make labs criminally liable for placing phlebotomists in physicians' offices to draw patients' blood.

Clearly, the new legislation is a significant concern. "In an effort to address the opioid crisis and some of the bad actors in that space, Congress added these far-reaching and significant anti-kickback provisions that now create confusion and potential liability for labs and those providers that refer [lab tests] to them," West commented.

"Primarily, this language was designed to address potential bad actors working in recovery homes and addiction treatment facilities," West added. "But then language was added to the bill extending that far beyond treatment facilities to include clinical labs. Now the new law extends to all payers and all laboratory testing services provided to patients."

Phlebotomists in Offices

One of the ACLA's concerns involves the Support Act's potentially negative effect on patient care. "It's important to note that these provisions could affect arrangements that are truly beneficial to patients and to the community," West said. She was referring to situations in which clinical labs use phlebotomists to collect specimens in physicians' offices—a practice that this law could make illegal.

"It's fairly common to have a lab provide a phlebotomist in a physician's office to draw the blood and send it to the lab," she added. "Under the federal Anti-Kickback Statute, placing a phlebotomist in a physician's office is not an inducement as long as the phlebotomist is not involved in other tasks that would normally be the responsibility of the physician's office staff.

"This kind of arrangement benefits patients because it increases the chance that the patient gets the test. Not having to leave the office to get the blood work done also speeds turnaround time for physicians who need timely lab test results," noted West.

Lawyer: Support Act Has Broad Implications for All Healthcare Providers, Including Labs

ONE LAWYER FAMILIAR WITH THE SUPPORT ACT said the new law has wide implications for all healthcare providers.

Ken Yood, a partner with **Sheppard Mullin**, a law firm in Los Angeles, said the law originally was intended to apply to sober houses and addiction treatment centers. But Congress included all clinical laboratories to the legislation and not just those labs providing toxicology testing, he added.

"A broad swath of healthcare providers and suppliers should be concerned about this new law," he said. "It's not just recovery homes and treatment facilities. It's clinical laboratories and physician office laboratories too. Also, healthcare providers who work with recovery homes, treatment facilities, and laboratories need to know about this law."

The Support Act itself is complex, in part because of the way it overlaps with the federal Anti-Kickback Statute and other federal laws that target healthcare fraud. "Since the new law does not replace or amend the Anti-Kickback Statute, interpretation of the new law in a way that fits with other existing fraud and abuse laws is challenging, to say the least," Yood commented.

"All providers should seek expert healthcare legal advice and counsel to evaluate the law's impact on their operations and relationships," he added. "There will be many regulations under this law, and providers will need to stay abreast as those regulations are written."

One of the most challenging aspects about this law is that it applies to all providers and all payers, not just federal healthcare programs such as Medicare and Medicaid. "As a result, unlike the federal Anti-Kickback Statute that relates only to healthcare services reimbursed under a federal healthcare program, the new law's application to all payers, providers, and healthcare services means that the scope of potential fraud- and abuse-related liability for laboratories has significantly expanded," Yood cautioned.

"As we all know, the federal Anti-Kickback Statute applies to people who are subject to federal and state healthcare payer programs," he commented. "Therefore, healthcare payers and providers already are educated to think about fraud and abuse routinely when dealing with Medicare- and Medicaid-related arrangements.

"Now, however, laboratories and other applicable providers will need to think routinely about the Support Act too," noted Yood. "Although this will be a new hurdle for impacted providers, it won't be entirely new for them because many state laws targeting healthcare fraud apply to all payers."

Given that the Support Act applies to all private and government payers, fraud enforcement activities may increase, along with an increase in the volume of multimillion dollar fraud settlements, Yood warned. "After all, whereas the investigative and enforcement authority of the federal enforcement agencies were generally limited to the world of government payers, the Support Act gives enforcement agencies a whole new world in which to move," observed Yood.

"The OIG has already said this practice of placing phlebotomists in physicians' offices is not an inducement when implemented correctly," she added. "Therefore, it's hard to imagine that these arrangements should go away. But, the breadth of the way the Support Act is written—covering both government and commercial payers—calls into question this practice."

An issue of similar concern involves specimen collection. "Many labs provide specimen collection devices to physicians'

offices, a topic OIG has addressed," West explained. "The OIG has said providing collection devices to physicians' offices for the sole purpose of collecting and transporting specimens is not necessarily an inducement to refer specimens. But even though it's permissible under the current federal Anti-Kickback Statute, there's no language that says this is permissible in the Support Act."

Of greatest concern to clinical labs may be how they pay sales staff. "In the federal Anti-Kickback Statute, there's an employment exception," noted West. "But under the Support Act, the exception applies only if the employee's payment doesn't vary with the number of tests or procedures performed and billed. Yet that's a common practice for how sales personnel are compensated right now.

Lab Reps' Commissions

"So how does a lab manage that?" she asked. "Must it revise all of its employment agreements? Does it have to change the sales reps' incentive structure?

"These questions about the structure of sales compensation are some of the most difficult to answer," continued West. "The language in the Support Act that addresses sales commissions is a perfect illustration in how overly broad the law is.

"In fact, this is one unintended consequence in the Support Act because it extends to all clinical labs, all medical services, and all payers," said West. "Yet the law was originally intended to solve just one issue that has arisen from the opioid crisis."

It is not known whether any federal agency will issue regulations to explain how healthcare providers can follow this new law. To date, ACLA is not aware regulations are being discussed. "Right now, the law is in effect and we don't know whether or not guidance will be promulgated," she said. "Such guidance is not mandatory. Because these provisions are part of the criminal code, the Attorney General can promulgate regulations in consultation with HHS. But whether that will occur we don't know."

For now, many of the questions lawyers are raising about the Support Act cannot be answered without guidance from OIG, some other office of HHS, or the Attorney General. In the meantime, lawyers are raising still more questions.

"What effect does the Support Act have on regulations that have been issued under other laws that might conflict with the new federal law?" asked West. "And what about other guidance that the HHS has issued that could conflict?

"ACLA continues to dig into the implications of this legislation and has identified that it could have an effect on group purchasing organizations (GPOs)," West said. "Under arrangements with GPOs, clinical labs may pay an administrative fee to make the GPO's services available to GPO members. It's unclear that these arrangements would be permissible under the Support Act."

Clinical labs and other healthcare providers often donate their services to federally qualified health centers (FQHCs). "In theory, Congress would want labs to donate testing services and supplies to FQHCs currently under federal protection," she commented. "Those donations help FQHCs to do more to help those in need, but it's unclear whether such practices would be protected under the Support Act."

Pathologists and clinical laboratory directors wanting advice on how to proceed should seek legal counsel. "Since the law came across our desk, we've been doing what we can to educate our members and raise the concerns about these issues," West concluded. "Unfortunately, there just aren't clear answers right now.

"Having said that, we're seeking clarity as best we can from the administration and from Congress," she said. "But it's just not there yet." TDR

—Joseph Burns

Contact Sharon West at info@acla.com or 202-637-9466; Ken Yood at kyood@sheppardmullin.com or 310-228-3708.

Attorney Explains Risks from New 'Support Act'

Under new legislation, paying sales commissions for clinical lab test referrals could be a criminal act

CEO SUMMARY: Legislation signed into law on Oct. 24 was designed to stem the nation's opioid crisis. But in addition to applying to sober homes and addiction treatment centers, the law also applies to clinical laboratories. Called the 'Support for Patients and Communities Act,' the law could authorize criminal penalties for labs that pay sales commissions to employees. Of particular concern, the law applies to labs that serve all payers, not just federal government health programs, such as Medicare.

Tucked deep inside a recently passed federal law intended to stem the nation's opioid crisis are provisions that are not yet widely known and that threaten common practices among clinical laboratories. In addition, the law applies to labs that serve commercial payers, not just federal government agencies, such as Medicare and Medicaid.

This new law has the potential to increase compliance risk for nearly every clinical laboratory. Plus, it establishes a new precedent because it applies to all payers, not just federal government health programs.

In Section 8122 of the Support for Patients and Communities Act, Congress added a new Section 220 to the U.S. Criminal Code that could authorize criminal penalties for one of the most common practices of clinical labs, paying commissions to employees or independent contractors who do sales and marketing, said lawyers familiar with the new law.

Signed into law on Oct. 24, the Support Act lifts restrictions on medications for opioid addiction, allows more types of healthcare providers to prescribe drugs, and seeks to limit overprescribing of opioid painkillers. Originally it was designed to target practices of sober homes and substance abuse treatment centers. Late in the process of drafting the bill in Congress, clinical laboratories were added to the list of providers named in the act, said Jeffrey J. Sherrin, President of the law firm **O'Connell & Aronowitz** in Albany, N.Y., and General Counsel for the **National Independent Laboratory Association**.

Criminal Liability Penalties

In a section titled, "Eliminating Kickbacks in Recovery," the law tracks the federal Anti-Kickback Statute's prohibitions on payments to induce referrals, but imposes criminal liability penalties on recovery homes, clinical treatment facilities, and laboratories. In addition, the law applies to all payers rather than the usual federal practice of having laws apply only to those medical services covered by federal health programs.

The fact that most labs pay sales staff based on commissions raises serious questions that so far are unanswered, Sherrin

said. "That provision alone will have a tremendous impact on labs," he added. "If labs cannot pay their own employees on a commission basis, that provision could have a bigger impact than PAMA. Commissions are the incentives that generate new business for clinical labs."

PAMA is the Protecting Access to Medicare Act, which has resulted in steep annual cuts in payments to labs. The first of those cuts were effective on Jan. 1 of this year.

"Originally, this new law was intended to address referrals to recovery homes and substance abuse treatment facilities," Sherrin explained. "At the last minute, Congress added labs to the law. It did not explicitly limit the application of the statute to labs that do toxicology testing for recovery homes and substance abuse treatment facilities. Instead, Congress used the same definition of labs that is in the CLIA statute.

"This new law raises many serious compliance questions that need to be answered," he continued. "For example, must labs that pay commissions to sales staff immediately change that compensation arrangement or risk prosecution? And does this law apply to all CLIA labs and not just labs that do toxicology testing for recovery homes or clinical treatment facilities?

"Someone in the clinical lab industry may have to get prosecuted before we get some clarity, unless the Secretary of HHS issues clarifying regulations," he predicted.

No Safe Harbor Provision

One confusing aspect of the Support Act is that it does not include a safe harbor against prosecution for a *bona fide* employment relationship that allows for commission payment, as does the federal Anti-Kickback Statute (AKS), Sherrin explained.

"One way this new law seeks to prevent fraud is by making payments for certain referrals illegal," he noted. "But it may be doing far more damage than good in this one instance. In the face of the current opioid crisis, accessible toxicology testing is critical, but this law can put tox labs out of business.

"By comparison, there is a safe harbor in the AKS that covers compensation paid in the context of a *bona fide* employment relationship," he added. "That's the vehicle that labs use to pay sales and marketing personnel on a commission, based in whole or in part on the business they generate.

Sequencing Technologies

"Under the AKS, your lab can satisfy a safe harbor if it has entered into a *bona fide* employment relationship even when compensation is based on commissions," noted Sherrin. "But your lab doesn't fall into this employment safe harbor if it pays sales commissions to independent contractors."

"That's why our law firm always recommends that, if labs pay sales people on commission, then those sales people should be employees and not independent contractors," he said. "Many clinical lab companies don't follow that advice, but at some risk. Neither the AKS nor the Support Act necessarily makes that practice illegal, but doing so comes with real risk.

"We know that the inspector general believes that under the AKS, sales and marketing people generate referrals from providers and, therefore, if your lab pays them a commission based on those referrals, it's arguably a payment for the referrals," Sherrin added. "The Support Act does not have the safe harbor for employees that the AKS does."

By way of explanation, Sherrin quoted from the new law. "The Support Act says, the safe harbor is 'a payment made to an employee or independent contractor (who has a *bona fide* employment agreement or contractual relationship with such employer) for employment, if the payment is not determined by or does not vary by the number of individuals referred ... or the number of tests or procedures

performed or the amount billed to or received.'

"That seems to say that even if your lab pays an employee on a commission basis, that relationship does not fall within the safe harbor," he explained. "Therefore, the same relationship for which there is a safe harbor under the AKS does not enjoy a safe harbor under this new statute.

"The new statute doesn't say this provision is limited at all," emphasized Sherrin. "In fact, it says that it applies to all laboratories. That raises the important question: How do you read this statute? Is it consistent with the AKS?

"If an employee is paid on a commission basis, does that constitute an illegal kickback under this statute even though there might be a safe harbor under the AKS?" he asked. "It appears so if the commission is paid for business generated from sober homes or substance abuse treatment facilities, regardless of payer.

"The question is whether this potential illegality extends also to laboratories that are not engaged in this area of toxicology," he said. "The legislative history would indicate that it does not, but that battle may still have to be fought."

Confusion over Pre-Emption

Another confusing provision in the Support Act involves pre-emption. Some new federal laws pre-empt state laws and other federal laws, but others do not. The Support Act addresses pre-emption, but in a confusing way, Sherrin said.

"There are two pre-emption provisions, one regarding federal law and one for state law," he explained. "The federal pre-emption provision addresses the section on Eliminating Kickbacks in Recovery by saying it, 'shall not apply to conduct that is prohibited under the AKS,'" he said.

"I don't understand that," he commented. "Instead, it should say that 'this provision does not apply to conduct that is legal under the AKS,' meaning that if it fell within a safe harbor under the AKS, then the new law would not criminalize this activity," he explained. "If it's prohibited under the AKS, meaning it's an illegal kickback, then it would be illegal under the Support Act.

"Based on these and other problems in the statute, it seems safe to say that the law will result in litigation," he concluded. "In the meantime, we need to know more about the scope of this law as it relates to the AKS, and does this law apply to all clinical labs or only to those labs that do toxicology testing?" TDR

—Joseph Burns

Contact Jeffrey J. Sherrin at 518-462-5601 or jsherrin@oalaw.com.

In Letter to HHS, ACLA Raises Concerns About Safe Harbors

IN A LETTER TO THE FEDERAL DEPARTMENT OF HEALTH AND HUMAN SERVICES, the American Clinical Laboratory Association (ACLA) said the new Support Act does not address conduct that is protected under existing safe harbor provisions, such as those in the Anti-Kickback Statute (AKS).

"The legislation adds a new section 220 to the U.S. Criminal Code, titled 'Illegal remunerations for referrals to recovery homes, clinical treatment facilities, and laboratories,' that would authorize the imposition of criminal penalties for some conduct that currently is permissible under Anti-Kickback Statute safe harbors," wrote Sharon L. West, ACLA's Vice President, Legal and Regulatory Affairs. The section in question is section 8122 titled, "Eliminating Kickbacks in Recovery" (or EKR).

"As written, section 8122 of the legislation applies to all laboratories, not merely laboratories that perform testing for recovery homes and clinical treatment facilities, and to all services covered by all payers, rather than only items and services covered by the federal healthcare programs."

CEO SUMMARY: Since 2011, the University of Florida Health System has used pharmacogenetic test (PGx) results to guide physicians when they prescribe certain drugs. This initiative has improved patient outcomes, reduced the overall cost per episode of care, and gained partial reimbursement from health insurers for PGx test claims. As this testing becomes more widespread, clinical pathologists and laboratory scientists have an opportunity to add value because primary care physicians often struggle to master this new clinical discipline.

Many physicians still do not understand pharmacogenetics testing

U of Florida Health Improves Patient Care with PGx Testing

Precision medicine is demonstrating how its effective use can improve patient outcomes. That's been the experience at the **University of Florida Health** (UFH), which initiated a precision medicine program in 2011 that uses pharmacogenetic testing (PGx) provided by the health system's laboratory division.

With seven years of experience and data, the pharmacogenetics testing program and precision medicine initiative at UFH can be a useful road map that other pathologists and clinical lab administrators can follow as they develop similar, added-value activities in collaboration with physicians and pharmacists within their own health networks.

The lessons learned and experience at initiating and sustaining this precision medicine program at the University of Florida, was presented by Julie A. Johnson, PharmD, the Dean and Distinguished Professor in the College of Pharmacy, during her presentation at The Dark Report's *Precision Medicine for Health Network CEOs* conference in Nashville, in September.

Johnson showed that at the University of Florida Health, providers use pharmacogenetics testing to identify and use the most effective medications. Doing so can prevent major adverse cardiac events, such as heart attack, stroke, and death, for patients who have a percutaneous coronary intervention (PCI), a non-surgical procedure to address a narrowing of the coronary arteries.

Pharmacogenetics testing is among the most actionable elements of precision medicine today, said Johnson, the founding Director of the UF Health Precision Medicine Program. Started in 2011, this program involves genotyping patients, then having physicians, pharmacists, and clinical pathologists collaborate to use genomic data to improve care.

Multiple Benefits

The results of a multiyear effort to use pharmacogenetic test results to guide physicians when they prescribe drugs has generated multiple benefits:

- improved patient outcomes;
- reductions in the overall cost per episode of care; and,
- at least partial reimbursement from health insurers for test claims for pharmacogenetic testing.

For this article, the word 'pharmacogenetics' is used in relation to genes determining drug metabolism, while 'pharmacogenomics' (or PGx) has a broader definition that encompasses all genes in the genome that may determine drug response.

As pharmacogenetics testing becomes more widespread, clinical pathologists and laboratory scientists have an opportunity to add value because, by definition, an effective clinical program that incorporates such testing requires collaboration involving the patient's care team, the clinical laboratory, and the pharmacy. What's more, the nation's primary care physicians have struggled to master this new clinical discipline, meaning they need extensive training in a field where new knowledge is added almost monthly.

"The problem in many clinical settings is that physicians treating patients often do not understand pharmacogenetics testing and so may not order these tests for their patients," stated Petr Starostik, MD, the Director of Molecular Pathology for the Pathology Laboratories at UF Health.

"The whole field of pharmacogenetics testing is driven by the need for education, meaning we need to make sure that physicians ordering PGx tests are educated properly," Starostik explained.

Need to Educate Doctors

Recognizing this need to educate physicians and encourage more appropriate use of pharmacogenomics testing, the **National Human Genome Research Institute** issued grants under its Implementing Genomics in Practice (IGNITE) program. UF Health was one of the six medical centers to win such grants.

"Under the IGNITE grant at UF Health, pharmacists use pathology testing results to educate physicians at the point of care," noted Starostik. "At the same time, pathol-

Health Insurers Pay Some Amount for Lab

IN 2011, THE UNIVERSITY OF FLORIDA HEALTH SYSTEM started the UF Health Precision Medicine Program to genotype patients and then have physicians, pharmacists, and clinical pathologists collaborate in an effort to use genomic data to improve care.

One of the first initiatives in this program involved using pharmacogenetic testing to identify how well patients needing percutaneous cardiac intervention (PCI) would metabolize the blood thinner clopidogrel. Since then, UF Health has developed tests to assess patients for metabolizing drugs for hepatitis C and opioids, among other tests. "For all of these implementations we have focused on developing the clinical evidence," Johnson explained in her presentation at THE DARK REPORT'S *Precision Medicine for Health Network CEOs* conference in Nashville.

After the first year, UF Health began billing for this pharmacogenetic testing and had a payment rate of about 85%, Johnson explained. Seven different third-party payers, including Medicare, reimbursed for such testing.

"This means that, of the 85% of bills that we submitted to payers, we got paid something," Johnson said. "The range of what we received was a bit wide. Having health insurers reimburse some amount for this testing was significant." Going forward, accountable care organizations may be inclined to pay for such testing too, she added.

ogists have a critical role in developing these programs and producing the test results in support of the pharmacogenetic program."

In 2012, UF Health's Department of Pharmacy started a precision medicine program using pharmacogenetic testing to identify how well individual patients needing percutaneous cardiac intervention (PCI) will metabolize the medications they need. PCI is a non-surgical procedure used to treat a narrowing of the coronary arteries. For these patients, cardiologists prescribe clopidogrel, a blood thinner.

In 2016, the FDA updated the label for clopidogrel to warn that patients who are CYP2C19 poor metabolizers may have diminished effectiveness of the drug as compared to patients with normal CYP2C19 function. The drug label suggests that a different platelet P2Y12 inhibitor be used in patients identified as CYP2C19 poor metabolizers, note guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC).

➤ Poor Metabolizers

The CPIC guidelines require testing for CPY2C19. They recommend an alternative therapy for poor metabolizers, meaning those patients who carry one or two loss-of-function alleles, Johnson said.

At UFH, patients are tested for genotype and phenotype, Starostik said. When the pharmacists developed the PGx program, they asked pathologists to run the tests and incorporate the clinical test results into each patient's electronic medical record.

"It was great that the pharmacists were so active in implementing this program," Starostik said. "If I had to pull this together without the engagement of the pharmacists, then the Pathology Department would have to answer questions from physicians as they look at these results and don't know what they mean."

When UF Health named Starostik the director of molecular pathology in 2014, the program had been in place for two years. "Since then, it has been a great collaboration between the College of Pharmacy and the College of Medicine,"

Researchers and Clinicians Are Developing Clinical Evidence to Support Pharmacogenetic Testing

"AS MOST CLINICIANS AND LABORATORY SCIENTISTS KNOW, much of the pharmacogenetics data being developed focuses on the drug metabolizing enzymes that have very common genetic variations," Julie Johnson, PharmD, said. "By most estimates, these variations are present in more than 95% of the population. This means almost everyone has some genetic variation in one or more genes that lead people to metabolize drugs differently.

"In clinical terms, people are either normal metabolizers or fall into one of three categories," she explained. "One: they may have no functional protein. Two: they may have reduced function or intermediate enhanced function, meaning they have either a duplication of the allele or increased expression of the protein. Or, three: they are rapid or ultra-rapid metabolizers.

"For this discussion, I'll focus on CYP2C19, which has this whole range, meaning patients have genetic variations that cause both increased metabolism and reduced or no metabolism," she added. "Patients were tested for how they would metabolize clopidogrel, an antiplatelet drug used to prevent heart attacks and strokes in persons with heart disease or peripheral vascular disease.

"We know that clopidogrel has to be bioactivated in a two-step process and the most important enzyme in that activation is CYP2C19," she explained. "We also know that CYP2C19 has a common loss-of-function variation and the *2 allele is the most common of these variations. When we say 'common' we mean 30% of people of European ancestry, 30% to 35% of people of African ancestry, and as much as 70% of Asians carry at least one loss-of-function allele.

"As a clinical pharmacologist, this is the type of evidence I need," Johnson said. "Such evidence tells me that if you carry a reduced-function allele, you are less likely to activate to the active metabolite. There's very clear evidence supporting that hypothesis.

"If you have less of the pharmacological activity (meaning less anti-platelet reactivity), then you have an increased risk of death due to a stroke or heart attack," she added.

At UF Health, clinicians follow the guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC), an international consortium of clinicians dedicated to facilitating the use of pharmacogenetic tests for patient care.

"The CPIC guidelines for CPY2C19 and clopidogrel were published in 2011 and updated in 2013 when new drugs became available as alternatives," Johnson said. "The guidelines said that ultra-metabolizers or normal metabolizers using clopidogrel are fine, but for those who carry one or two loss-of-function alleles, CPIC guidelines recommend an alternative therapy."

he said. "For those of us here in molecular pathology, our role was established under the IGNITE grant to collaborate with the College of Pharmacy here in Gainesville."

To enhance its role in the program, the pathology department invested heavily in new technology to be able to run the tests for CYP2C19. "The department purchased the QuantStudio Real-Time PCR systems from **ThermoFisher Scientific** and ran a whole panel of tests of some 200 SNPs (single nucleotide polymorphisms)," added Starostik. "Then we reported those clinical results directly into UF Health's **Epic** electronic medical record system. Using those results, the Pharmacy Department recommends the appropriate medication based on each patient's clinical test result.

"We also collaborated with the College of Pharmacy in putting together the clinical result," he explained. "The clinical result for a patient shows two elements. One is the genotype and the second is the phenotype, which shows what type of metabolizer the patient is. By that, I mean the clinical test results that would show how the patient will react to the drug. Each patient can be either a normal metabolizer, a low metabolizer, or a high metabolizer."

Patients Ask for PGx Tests

UF Health's pharmacogenetics program is important not only for improving patient outcomes but also because many patients today may be more knowledgeable about pharmacogenetic testing than physicians, Starostik added. "Frequently, a patient will ask the physician to run a genetic test before the physician prescribes the medication," he said.

"But if the physician doesn't understand the specific test needed for this patient's prescription drug, then what happens?" Starostik asked. "For these reasons, the whole field of pharmacogenetics testing requires continuous education of the providers.

"Most providers don't know anything about PGx testing, which means they won't order these tests for their patients," he noted. "And, if the providers don't order this testing, then they can cause patient harm. If the patient experiences harm, however, that adverse event will not be obvious right away.

"Should a physician not order the right PGx test, it won't cause problems such as myocardial infarction or strokes or anything acute like that," Starostik explained. "Nothing will happen in the next five or ten minutes because the consequences of not ordering the test are delayed. They are under the surface where we don't see them. But there is an adverse effect to that patient over time."

Pain management is another opportunity. "Especially now with the opioid crisis, PGx testing could help identify people who do not respond well to pain management with opioids," Starostik explained. "If they don't respond well to opioids, they could overdose because they are hyper-metabolizers and cannot get rid of the pain."

To identify patients who may be poor metabolizers for opioids, the pathologists run the cytochrome P450 2D6 test. "Without this testing, these patients could be harmed," he said.

One problem UF Health encountered when it started the program was how to incorporate genomic data into the health system's electronic medical record system, said Johnson. Physicians wanted to be able to store the genetic information from pharmacogenetic testing so that it could be accessed when needed by the clinicians.

"Was there room for it in the electronic health records? Does that data sit behind a wall versus inside the wall?" she asked. "At the same time, we needed to develop clinical evidence for pharmacogenetics. There was lots of data and much of it was retrospective analyses from clinical trials.

Focus on Therapeutic Drugs

"As a clinical pharmacologist, the data made it obvious to me that A plus B equals C," she said. "However, the average physician doesn't have the same focus on therapeutic drugs that I have and so may need to be convinced that A plus B does, in fact, equal C.

"For these reasons, as we proceeded to implement pharmacogenomics into clinical settings, we've tried to marry that implementation with ongoing evidence development," added Johnson. "Early on, we had three big goals: One, to improve treatment outcomes. Two, to improve safety, and, three—potentially—to reduce the cost of medical care," she stated. TDR

—Joseph Burns

Contact Julie A. Johnson, PharmD, at 352-273-6309 or julie.johnson@ufl.edu., Petr Starostik, MD, at 352-265-9900 or starostik@pathology.ufl.edu.

Researchers with IGNITE Consortium Demonstrate How Pharmacogenetics Testing Boosts Outcomes, Reduces Cost

PHARMACOGENETICS TESTING enables clinicians to identify patients who metabolize medications more quickly or more slowly than normal. This knowledge is particularly important for drugs such as clopidogrel, an antiplatelet therapy that cardiologists use to prevent stroke, heart attack, and other heart problems.

Once researchers recognized the clinical differences between normal metabolizers and slow metabolizers, their next step was to incorporate this information into clinical practice. To do so, they needed to answer the question about how PGx testing would affect patient outcomes and costs.

Last year, researchers from nine sites in the Implementing Genomics in Practice (IGNITE) consortium reported that genotype-guided antiplatelet therapy reduced the risk of adverse cardiovascular outcomes.

Poster Presentation

Building on this effort, researchers presented a poster, "Real World Cost-Effectiveness of CYP2C19 Guided Antiplatelet Therapy in Patients with Acute Coronary Syndrome and Percutaneous Coronary Intervention," at the 39th Annual North American Meeting of the Shared Medical Decision Making conference in Pittsburgh.

Josh Peterson, MD, MPH, Associate Professor of Medicine and Biomedical Informatics at **Vanderbilt University**, and Nita A. Limdi, PharmD, PhD, a professor in the Department of Neurology in the **University of Alabama at Birmingham**, are IGNITE researchers who are involved in the study on the effectiveness of using antiplatelet therapy based on CYP2C19 testing.

To evaluate the effectiveness of using PGx testing for 1,815 patients with percutaneous coronary intervention (PCI), the researchers compared patient outcomes and the cost effectiveness of four treatment strategies against a base case.

The four strategies involved using clopidogrel for some patients, using ticagrelor (a second blood thinner) for some patients, and switching medications based on PGx test results.

Four Alternative Approaches

For the base case (or reference strategy), researchers used clopidogrel antiplatelet therapy for all patients and then compared those results with results from the four alternative approaches:

- **In strategy 1,** the researchers used ticagrelor for all patients.
- **In strategy 2,** the researchers treated all patients with ticagrelor therapy for 30 days and then switched those patients to clopidogrel.
- **In strategy 3,** the researchers did genotype testing at the time of the PCI, then treated all patients who did not have a loss-of-function (LOF) allele with clopidogrel and treated all patients who had an LOF allele with ticagrelor.
- **In strategy 4,** the researchers did genotype testing after 30 days of treatment with ticagrelor for all patients and then switched non-LOF patients to clopidogrel and maintained those with an LOF allele on ticagrelor.

For the study, researchers used a measure of clinical outcomes called quality-adjusted life years (QALY).

"In the study, we demonstrate that genotype-guided escalation was cost effective at the widely-referenced willingness-to-pay threshold of $50,000 per quality-adjusted life-year gained," they wrote. The study, with updated results, is currently being considered for publication.

Managed Care Update

UnitedHealth Rumored to Be Excluding Labs from Its Network

Early information indicates the health insurer is terminating contracts of regional, indy labs

In recent days, rumors have surfaced that **UnitedHealthcare** has begun to terminate the contracts it holds with a number of regional and non-national clinical laboratories.

This news surfaced just as The Dark Report went to press. Given its importance to the clinical laboratory industry, we wanted to alert lab executives and pathologists to this development as soon as possible. It may be the earliest sign that major health insurers are in the first stages of changing their long-standing managed care contracting strategies with clinical laboratories and anatomic pathology groups in ways that will deny many local labs and independent lab companies access to the beneficiaries of UnitedHealthcare and other major health insurers.

The next issue of The Dark Report will have a more complete presentation of the known facts and an analysis of why one of the nation's biggest health insurers is taking this step—and why now—before the start of the new year.

Labs In-Network for Decades

Information from late last week included statements that many of these labs have been in-network lab providers for UnitedHealth (UHC) for a decade or longer. One source said that he was told by an executive of an independent clinical laboratory company that UHC had said the reason it was terminating its contract with that lab company was because it needed "to adapt to the ever-changing healthcare environment."

Two reasons may be behind this development. First, UnitedHealth, **Aetna**, and **Horizon Blue Cross Blue Shield of New Jersey** all added both national lab companies to their networks during 2018. This may mean that, by including both national lab companies in their respective networks, those two labs together eliminate the coverage gaps that were formerly filled by regional labs. These regional labs can now be excluded from provider networks.

Second, the ongoing shift away from fee-for-service reimbursement and toward value-based payment arrangements may be a factor. This would be particularly true if health insurers were recognizing that the national labs do a more complete job of reporting utilization data and lab test results on the insurer's beneficiaries. Both are necessary for health insurers in their population health management initiatives.

Any administrator, executive, or pathologist working at a lab that UnitedHealthcare is terminating as an in-network provider—or with knowledge of other labs that are being similarly terminated—are invited to contact our Editor in confidence with this information. Such information will help The Dark Report develop a more detailed and accurate analysis of this developing situation, along with remedies that may be available to labs that have recently received a notice terminating them as a provider for UHC or another health insurer. TDR

Contact Editor-in-Chief Robert Michel at labletter@aol.com or 512-264-7103.

IVD Sector Update

Illumina to Pay $1.2 Billion to Acquire Pacific Biosciences

Deal gives Illumina ownership of two different technologies for sequencing whole human genomes

It's an acquisition that brings together two different gene sequencing technologies into one firm. On Nov. 1, **Illumina, Inc.**, announced an agreement to acquire **Pacific Biosciences** (PacBio) for $1.2 billion.

This deal will bolster Illumina's already-dominant position in the market for DNA-sequencing machines. Wall Street analysts quickly pointed out that this gives Illumina control of two gene sequencing technologies. Illumina will be able to complement its short-read DNA-sequencing technology with PacBio's ability to do long reads of DNA. The timing of the deal also is significant because PacBio's long-read technology is expected to get a boost in the coming months.

Illumina agreed to pay $8 per share for PacBio, a premium of 79% over the closing price of PacBio stock on Oct. 31, according to a report in *Forbes*. The deal is subject to approval from regulators and from both boards. Illumina said it expects to close the transaction in the middle of next year.

Short and Long DNA

By uniting their technologies, the two companies will deliver, "a more perfect view of the genome," said Illumina CEO Francis deSouza. Based in San Diego, Illumina had a profit of $726 million on sales of $2.75 billion last year.

The much smaller PacBio, based in Menlo Park, Calif., had sales of $93.5 million last year, representing an increase of 19% over sales in 2016 of $78.6 million.

In its most recent quarter, PacBio reported on Nov. 1 that it had a net loss of $25 million, up from a net loss of $22 million for Q3 2017 and that it had revenue of $18.2 million, compared with $23.5 million in the same period of 2017. The decrease in revenue resulted from lower sales of instruments and consumables, PacBio said. *Motley Fool* reported that PacBio has never made a profit.

Sequencing Technologies

The key to the transaction will be the ability to unite the two companies' technologies, according to Matthew Herper who interviewed deSouza for *Forbes*.

Illumina has a dominant position with an estimated share of 75% of the market for gene-sequencing instruments and has driven down the cost of sequencing a human genome to less than $1,000 today from $10 million just 10 years ago, according to the *San Diego Union-Tribune*.

Eventually, deSouza expects Illumina will drive the cost of sequencing a genome down to $100 per person, Herper wrote. But its instruments are based on sequencing by synthesis (SBS), which is what's called a "short-read" technology in which machines assemble and analyze many small fragments of DNA.

"For most parts of the human genome this works fine, but it is not as useful in cases where the DNA has been structurally rearranged, or in areas where a pattern in the DNA repeats again and again, making it harder to puzzle

Combining Two Gene Sequencing Technologies Could Deliver Genomes That are More Complete

BY USING THE TWO TECHNOLOGIES TOGETHER, the combined companies of Illumina and Pacific Biosciences are poised to produce more complete genomes of any organism, according to published reports.

While there are other companies that do work similar to that of Pacific Biosciences in the long-read market (such as **Oxford Nanopore**), PacBio has distinguished itself by producing highly accurate results, according to Illumina CEO Francis deSouza. In an interview with Matthew Herper in *Forbes*, deSouza said of PacBio, "It's accuracy profile is really better than anything else in the [long-read] market."

On a conference call with analysts on Nov. 1, to discuss Illumina's pending acquisition of PacBio, deSouza explained that improvements in PacBio's technology were one of the reasons for Illumina's interest in PacBio.

"The accuracy that you can now achieve with long-read technologies essentially is on par with what you can achieve with SBS short-read technology. For us, that was critically important," stated deSouza during the conference call with stock analysts and reporters on Nov. 1, according to a report in *Genetic Engineering and Biotechnology News*.

"For us, that was the threshold," deSouza added. "You had to be able to get to roughly about a Q50 consensus accuracy for the technology to fit within the portfolio of what we were looking to do. From our perspective, Pacific Biosciences was the only long-read technology that met that threshold."

Under the Phred Quality Score, a level of Q50 is said to be 99.9999% accurate, meaning the probability that the base is inaccurate would be 1 in 100,000.

By combining the two companies' instruments, over time Illumina and PacBio will attract more researchers and clinicians as customers, wrote Jim Crumly for the *Motley Fool*, an investor site. In that way, Illumina will continue to dominate the sequencing market, he added.

the code together from tiny pieces," deSouza explained.

Using what's called "long-read" technology, PacBio has pioneered a different approach. To analyze a single molecule of DNA, PacBio's machines decode long stretches with high accuracy, Herper reported, adding that at $12,000 to sequence a single human genome, PacBio's method is costly.

To date, the high cost of long reads has been a barrier to higher sales, according to an article by Jim Crumly writing for investor site *The Motley Fool*. Next year, PacBio expects to use a new core chip in its systems that could cut the per-genome cost to $1,000 per genome, which would open up the market for PacBio's Sequel machines, the site said.

Analysts pointed out that if PacBio can hit that $1,000 price for a whole human genome sequence using a method that produces longer reads of DNA, it would be poised to significantly expand its share of the market.

"PacBio executives believe that the improvements in throughput and cost that the new chip will bring will expand the accessible market for the company's sequencers from $660 million in 2017 to $2.5 billion in 2022, a 30% annualized growth rate," Crumly wrote.

Currently Illumina has an installed base of more than 11,000 instruments, while PacBio has 425 systems in place. PacBio's machines cost about $350,000 each and Illumina's instruments sell for about $1 million each, he added. **TDR**

—Joseph Burns

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

Another long-established regional laboratory company is about to be acquired. On November 27, **Boyce and Bynum Pathology Laboratories** of Columbia, Mo., disclosed that it had entered an agreement to be acquired by **Quest Diagnostics Inc.** Notably, the press release about the agreement states that the anatomic pathology division, **Boyce and Bynum Professional Services, Inc.**, and the long-term care business of the clinical lab company, are not included in this purchase. The two companies said the transaction is expected to close in the first quarter of 2019.

MORE ON: *Boyce and Bynum*

This is the first significant lab acquisition disclosed by either of the two blood brothers since several lab purchases were announced in the early months of this year. With only four weeks left before Dec. 31, there may be additional deals announced because lab sellers want to finalize the sale by year-end for tax purposes, and the public lab companies want to acquire the assets early enough in 2019 to contribute to their revenue and earnings.

DOCUMENTARY FILM ABOUT THERANOS WILL SCREEN IN JAN.

Medical laboratory professionals continue to be fascinated by **Theranos** and how its former CEO, Elizabeth Holmes, managed to hoodwink savvy investors, the national media, and others for several years. Now comes news that a documentary film, titled, "The Inventor: Out for Blood in Silicon Valley," was accepted and will be screened at the Sundance Film Festival in Park City, Utah. The festival starts on Jan. 24. The film was directed by Alex Gibney and produced by Gibney, Jessie Deeter, and Erin Edeiken. **HBO** participated in the production of this film.

TRANSITIONS

•**ACM Global Laboratories**, a division of **Rochester Regional Health** in Rochester, N.Y., appointed Brian Wright to be its new President. Wright previously held executive positions at **SP Industries**, **Remedi SeniorCare Pharmacy**, **TE Connectivity Medical Products**, **Stryker**, and was a captain in the U.S. Army.

•Glenn Miles is the new Chief Financial Officer at **Cancer Genetics, Inc.**, of Rutherford, N.J. He formerly held positions at **Catalytic Consulting LLC**, **Pfizer**, **Lehman Brothers**, **AT&T Mobility**, and **Grant Thornton**.

That's all the insider intelligence for this report. Look for the next briefing on Monday, December 24, 2018.

24 YEARS

REGISTRATION Now Open!

EXECUTIVE WAR COLLEGE

April 30-May 1, 2019 • Sheraton Hotel • New Orleans

CMS includes hospital labs in 2019 price data reporting..

What Your Hospital Lab Needs to Know to Report PAMA Price Data, Avoid Fines

In 2019, nearly all hospital labs will be required by CMS to report lab test prices paid by private payers to meet the PAMA law. Failure to report, or to provide inaccurate data, or to provide incomplete data can trigger federal fines of up to $10,000 per day!

To help your hospital lab get it right, we're scheduling sessions by experts in lab billing/collections, LIS and informatics, compliance, and legal. Included will be a full-day workshop on Thursday, May 2, to prepare your lab team to successfully report your lab data to CMS. **Register today to guarantee your place at this valuable session!**

For updates and program details, visit www.executivewarcollege.com

UPCOMING...

- ***'Support for Patients and Communities Act' makes paying commissions to lab sales reps illegal.***
- ***Quest Diagnostics to Buy Boyce & Bynum Labs: Are More Lab Acquisitions Happening by Year-end?***
- ***Newest Lab Automation Solutions: Picking Winners in Chemistry, Microbiology, and Histology.***

For more information, visit:

www.darkreport.com

Sign Up for our FREE News Service!

Delivered directly to your desktop, *DARK Daily* is news, analysis, and more.

Visit www.darkdaily.com

DARK Daily

Clinical Laboratory and Pathology News/Trends