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From the Desk of R. Lewis Dark...

THE DARK REPORT

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

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COMMENTARY & OPINION by...

R. Lewis Dark
Founder & Publisher

Lab Profession's 'Haves,' 'Have Nots,' and Thieves

ONCE AGAIN, THE LATEST NEWS OF IMPORTANCE in the clinical laboratory industry includes disparate topics that include legal/regulatory, new technology in anatomic pathology, fraud involving lab testing, and more consolidation in the *in vitro* diagnostics (IVD) industry.

You will find coverage on all of these topics and more in this issue of THE DARK REPORT. Each intelligence briefing presented here contains actionable insights you can use to position your laboratory for success. However, one thing in particular stands out. The developments in recent weeks perfectly illustrate how the market is stratifying the winners and losers in diagnostics and lab testing.

For example, the "haves" are strengthening their financial position and market share. This is affirmed by the fourth quarter and full year 2020 earnings reports of the major IVD manufacturers that are covered on pages 6-9. In specific ways, these clinical lab suppliers have prospered during the COVID-19 pandemic, as demand for analyzers, automation, and collection kits for molecular SARS-CoV-2 testing soared. Added to this is the substantial funding directed to these companies by the federal government and many states.

The "have nots" are clinical labs throughout the country that were at the end of the supply chain when the pandemic arrived last March. They continually struggle to acquire the instruments, kits, and collection supplies they need to provide COVID-19 testing to their communities. Consequently, they also lost the cash flow and revenue that would come from performing these vital tests.

Next are the bad actors in the clinical lab industry. You'll read on pages 16-18 about the resolution of two separate federal fraud cases involving lab testing. In one case, the defendants will pay restitution totaling millions of dollars. In the other case, four owners and managers from one lab pled guilty to criminal charges and the medical director of the lab will soon go to trial in his case. Unfortunately, these fraud and abuse cases taint all labs in the eyes of the **Department of Justice**, **Centers for Medicare and Medicaid Services**, and Congress.

Collectively, the news and analysis presented in this issue remind lab leaders that the clinical laboratory marketplace continues to change in a dynamic way. It is a reminder that all labs should be nimble and innovative to sustain clinical excellence and financial stability. TDR

Federal Judge Rules Against ACLA in Its PAMA Lawsuit

Dismissal of PAMA lawsuit raises questions about next steps for clinical laboratory industry

CEO SUMMARY: Now that a federal judge has ruled that the American Clinical Laboratory Association's lawsuit is moot and dismissed the case, it is unclear what next steps are open to ACLA and the clinical laboratory industry in their challenge to how the federal Centers for Medicare and Medicaid Services is implementing the Protecting Access to Medicare (PAMA) statute. Two experienced lab industry attorneys provide insights into what the lawsuit did accomplish and some possible next steps.

DISMISSAL ON MARCH 30 of the **American Clinical Laboratory Association's** (ACLA) lawsuit against the federal **Department of Health and Human Services** (HHS) over the 2016 PAMA Medicare reimbursement rate regulation raises the question about what other avenues the clinical laboratory industry might pursue in seeking to remedy concerns with PAMA Medicare payment rates.

"ACLA could appeal this decision by Judge Berman, as it did her previous decision in 2018," says David Gee, a partner with **Davis Wright Tremaine LLP**. "The industry could also continue to advocate for Congress to recognize the great value of state-of-the-art laboratory innovation, based upon the industry's front-line role throughout the COVID-19 public health emergency."

Jeffrey Sherrin, Esq., an attorney with **O'Connell Aronowitz**, says one can never know what Congress or the Department of Health and Human Services has in store for statutory or regulatory changes. "With COVID-19 opening up so many challenges and opportunities for labs, the discussions right now are not as much about PAMA as they are adapting to the new COVID-19 era."

ACLA filed the lawsuit in 2017 against HHS Secretary Alex Azar (who has since been replaced by Xavier Becerra). The lawsuit challenged a 2016 rule promulgated by HHS that defined "applicable laboratory" as one that "bills Medicare Part B under its own NPI." ACLA contended that the rule's definition of applicable labs was "arbitrary and capricious" because it "excluded significant numbers of hospital laboratories that provide outreach services

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from the Secretary's data collection … because most hospital laboratories bill under their hospitals' NPIs rather than their own," the court said in its ruling.

Judge Amy Berman Jackson of the **District of Columbia District Court** initially dismissed the case for lack of subject matter jurisdiction, but ACLA appealed. On Nov. 23, 2018, HHS issued another rule that revised the "applicable laboratory" definition to include "hospital outreach laboratories" that use a billing method used by hospitals for non-patients. On July 30, 2019, the D.C. Circuit Court overturned the dismissal of the case, remanding the matter to the lower court "to address in the first instance the merits of petitioner's arbitrary-and-capricious challenge."

In her March 30 ruling, Judge Berman said that the challenge is now moot since HHS modified its definition of "applicable laboratory" in its 2018 rule. The only other available remedy would be back pay for any past reimbursements that were calculated using the 2016 rule's definition, which would have changed the pay rate, the court noted.

"But PAMA provides that 'payment amounts under this section shall not be subject to any adjustment (including any geographic adjustment, budget neutrality adjustment, annual update, or other adjustment)," Judge Berman wrote. "So, even if the Court were to rule in plaintiff's favor on the merits, it could not order the agency to revise any payment amounts."

Problematic Decision

Sherrin says the decision is problematic. "The Court could have gone either way on the mootness question. Other courts have held that a change in regulation—since it is an administrative and not a legislative act—does not moot the controversy. ACLA can appeal this decision, but whether it decides to do so, or perhaps feels that the chances of winning are not good enough, remains to be seen."

Julie Khani, ACLA President, said the ruling is a disappointing outcome for ACLA member laboratories and the millions of patients they serve. "We are currently reviewing our legal options and we will continue to work with policy makers to establish a [Medicare] Clinical Laboratory Fee Schedule that is truly representative of the full market and supports continued innovation and access to vital laboratory services, as Congress originally intended. Now is the time to strengthen our laboratory infrastructure and support continued access to the high-quality lab services that our nation depends on."

Could Ruling Be Favorable?

Gee says this ruling could actually be seen as a win for ACLA and the clinical laboratory industry as the original lawsuit ultimately led to CMS revising the definition of "applicable laboratory."

"Generally speaking, the decision confirms that the ACLA lawsuit succeeded in achieving one of the lab industry's primary objectives, albeit by prompting the 2018 regulatory changes broadening the regulatory definition of 'applicable laboratory' to ensure that the PAMA data reporting requirement includes pricing data from hospital labs, which comprise a very significant sector of the marketplace," Gee said.

"For this reason, the post-2018 PAMA rate-setting process must factor in higher reimbursement levels paid to hospital labs. The good news is that the rule change took effect well before it would have if compelled by judicial ruling," said Gee. "The bad news is that Judge Berman did not agree with ACLA that the United States District Court for the District of Columbia has the authority to rule on the adequacy of the pre-2018 definition of 'applicable laboratory' or to compel the **Centers for Medicare and Medicaid Services** to undertake a corrected data gathering and reporting process." TDR

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Lab Market Update

Amazon Sells COVID-19 Test Kit for At-Home Use by Consumers

Experience at selling a COVID-19 saliva test could encourage the compay to offer other lab tests

QUIETLY AND WITHOUT MUCH ATTENTION, online retailing giant **Amazon** began to sell a COVID-19 molecular test to consumers for at-home testing. This is consistent with other actions Amazon has taken to generate revenue during the SARS-CoV-2 pandemic.

The test Amazon sells is the DxTerity COVID-19 Saliva at-Home Collection Kit. The test was developed by **DxTerity**, a company based in Rancho Dominguez, Calif. DxTerity has an Emergency Use Authorization (EUA) from the **Food and Drug Administration** (FDA) for this test. It performs the tests in a CLIA-certified lab facility.

$110 for COVID-19 Test

Amazon charges $110 for a single COVID-19 test kit. It also will sell a 10-pack bundle for $1,000. On its website, Amazon says, "Prepaid express return shipping is included with the test. Results are available within 24 to 72 hours of sample receipt at the laboratory. Refund policy: the kit is not returnable once purchased and must be used within 60 days of purchase."

Currently, the DxTerity COVID-19 test kit is the only COVID-19 test offered by Amazon on its website. However, Amazon has a full section devoted to selling businesses a range of products they can use during the pandemic. These products range from protecting patients and staff to maintaining clean facilities and implementing social distancing.

Another national retailer selling at-home COVID-19 saliva test kits is **Costco**. **Walmart** and **Sam's Club** also are selling at-home COVID-19 test kits, however, at time of purchase the customer must complete a survey. If appropriate, a physician's order is generated to allow the purchase to proceed. The test collection kit is mailed to the customer who then self-collects the sample and mails it to the lab for results.

To provide SARS-CoV-2 tests for its own employees, as early as last May, Amazon began building and operating multiple clinical laboratory facilities located near its distribution centers across the United States. Amazon employs almost one million people, so this COVID-19 testing program is of significant size and scale. *(See TDR, Aug. 3, 2020.)*

THE DARK REPORT predicts that Amazon is unlikely to close down its clinical laboratory facilities once the pandemic has subsided. With one million employees, plus their family members, the company would have substantial economies of scale to perform routine lab tests for its employees and beneficiaries.

It would be consistent with Amazon's business strategy to enter the clinical laboratory market and attempt to disrupt it. Further, with the experience it gains from selling at-home COVID-19 test kits to consumers during the pandemic, it may believe it can also develop a lucrative consumer direct access testing (DAC) business in coming years. TDR

IVD Update

IVD Firms Report Strong Growth Because of COVID-19 Testing

For most of the world's in vitro diagnostics (IVD) companies, 2020 shaped up to be a stellar year.

To no one's surprise, those *in vitro* diagnostics (IVD) manufacturers that produce molecular tests, instruments, and automation used for COVID-19 testing reported strong growth in revenue and profits during 2020.

In recent weeks, these companies issued their earnings reports for the fourth quarter 2020 and full year 2020. As expected, most companies announced substantial increases in revenue and financial performance.

However, probably of greater interest to clinical lab managers and pathologists are the statements and predictions IVD executives made to financial analysts and investors during these earnings calls about the ongoing COVID-19 pandemic. Some IVD leaders called COVID-19 an endemic disease similar to influenza. They see continuing demand for COVID-19 diagnostic testing through 2023 and perhaps beyond. Antigen rapid testing is key, they said.

IVD company executives are watching the pace and effectiveness of vaccines and their roll out. They are concerned, too, about SARS-CoV-2 variants and how that may create the need to develop related assays and clinical lab tests to help manage new COVID-19 variants.

Here is a recap of recent data reported by top IVD companies *(See also "The Dark Report's Ranking of 2019's Top 10 IVD Companies," December 28, 2020).*

These summaries include select comments made to IVD company investors, which are likely to be helpful to clinical laboratory leaders developing strategies.

Roche

ROCHE: Diagnostics Division Sales Grow 28% in Q4, 14% in 2020

Continued demand for COVID-19 testing in Q4 drove impressive growth in **Roche Holding's** diagnostic division. The Basel, Switzerland, IVD leader reported diagnostic division sales growth of $14.6 billion, an increase of 14% for the year and 28% in Q4. Molecular diagnostics drove the growth, swelling 90% during the full year 2020. Roche acknowledged that the growth offset a decline in routine testing during the pandemic.

During 2020, Roche introduced 15 molecular and immunodiagnostic tests for clinical laboratories and point of care.

Thomas Schinecker, PhD, CEO, of Roche Diagnostics, told investors during an earnings call Q&A session that the company's repeat of positive financial indicators in 2021 may depend on COVID-19 vaccines and SARS-CoV-2 variants. "How quickly is the roll out of vaccines? Is this going to take longer? Then, the question is really on the different variants and what kind of level of vaccine rate do you need to get to herd immunity?

"So, we will definitely see very strong [COVID-19] testing, particularly in the first half year [of 2021]; likely some testing also in the second half of the year and for the years to come, simply because this virus is endemic," continued Shinecker.

"It mutates frequently. So we will have to monitor this."

Severin Schwan, Roche CEO, added, "COVID-19 will continue to stay with mankind like the flu virus."

ABBOTT LABORATORIES: Diagnostic Sales Grow 110% in Q4-2020 with $2.4B in COVID-19 Test Sales

Abbott Laboratories, announced company sales in Q4 grew about 28.7% to $10.7 billion including $2.4 billion of COVID-19 testing. For the full year 2020, revenue was $34.6 billion, compared to $31.9 billion for full year 2019, an increase of 8.5%.

"In total, we delivered more than 400 million COVID tests since the start of the pandemic, including more than 300 million tests in the fourth quarter alone," said Robert Ford, President and CEO during an earnings call. "We exited 2020 with tremendous momentum, including total sales growth of more than 28%. Our diagnostic business grew nearly 110% in the quarter, driven by $2.4 billion of COVID testing-related sales."

During a Q&A session, Ford said he anticipates continued COVID-19 testing demand as vaccines become available. "I expect testing demand is still going to remain high even as the vaccines roll out. I don't think we've even seen testing demand peak yet," Ford said.

"Even if COVID-19 testing starts to mature a little bit in 2022, we believe there's a significant portion that's still very sustainable. Can we predict it perfectly today? No, I can't—not to the level that you're accustomed to getting from us."

Commenting on the future demand for COVID-19 tests, Ford observed that one trend that the pandemic has accelerated is the shift away from the dominance of core lab testing. "I also think that the ability to do testing in a decentralized manner ... people talk about how the pandemic has accelerated digital transformation and businesses, and accelerated transformation in the business models."

On that point, Ford mentioned that Abbott received in 2020 a $760 million federal contract for 150 million rapid antigen tests called BinaxNOW. And the company also launched Panbio COVID-19, a CE-marked rapid antigen test.

DANAHER–BECKMAN COULTER, CEPHEID: Cepheid Increases Installs 35% in 2020

At **Danaher Corporation**, full year 2020 revenues increased 24.5% to $22.3 billion. For Q4-2020, revenue for the diagnostics division was $586 million, an increase of 66% over Q4-2019's $352 million.

For the full year 2020, diagnostics division revenue was $1.5 billion, compared to $1.1 billion for full year 2019, a growth rate of 36%. Danaher's diagnostic division includes **Beckman Coulter**, **Cepheid**, **Leica Biosystems**, and **Radiometer.**

During the earnings call with investors, Rainer Blair, President and CEO, described Q4 highlights in the diagnostics division and called attention to the performance of Cepheid. During 2020, "Cepheid's installed base [increased] by more than 35% year-over-year to over 30,000 instruments globally. Cepheid achieved a significant milestone in December for passing $2 billion in annual revenue, just one year after hitting the $1 billion mark."

One analyst asked Blair. "...not only has Cepheid replaced a ton of instruments, but a lot of your competitors—all the other companies selling molecular diagnostic tools—have placed enormous numbers of instruments. Are you worried that there is going to be a glut of [molecular testing] machines out there that don't get used ... once we're past [the demand] for COVID-19 testing?"

Blair answered that question as follows. "... we've been very thoughtful about the placement of those [molecular] instruments. First, to help during the pandemic ... At the same time, we've been thinking about those placements for the long-term ... We placed those instruments primarily where we see that, even in a post-COVID world, they would find great utilization based on [Cepheid's] full testing menu."

SIEMENS Healthineers

SIEMENS HEALTHINEERS: Diagnostics Revenue Grows 23% to $1.4B in Q1-2021

Siemens Healthineers' most recent report reflected performance during Q1 ending Dec. 31 for FY 2021. The diagnostics division's revenue of $1.4 billion was up 23% year-over-year.

"Q1 revenue increased by 13% on a comparable basis, with outstanding 23% growth in diagnostics, but also very good growth in our imaging and advanced therapies businesses with 9% and 6%, respectively," Bernd Montag, CEO, said in an earnings call.

"Diagnostics has seen nice margin improvement thanks to a strong uptake of profitable rapid antigen tests, but also improving margins in our routine care business where procedure volumes returned to growth again," he added.

Siemens boosted assumptions for fiscal 2021, stating it now expects antigen test revenue to be about $350 million instead of $117 million.

During a Q/A session with investors, Montag addressed whether testing capacity is sufficient going forward. "When it comes to the antigen tests, capacity is not the limiting factor. Capacity is where it needs to be. It is now really about how does the need for the tests develop? What are programs in society, in programs by government? And also how fast is the progress on the vaccination front?" he said.

ThermoFisher SCIENTIFIC

THERMO FISHER: 200% Growth in Diagnostics/Healthcare in Q4, 100% Growth in Full Year 2020

Thermo Fisher Scientific reported Q4-2020 revenue grew 54% to $10.5 billion. The company's revenue for the full year 2020 was up 26% to $32.2 billion.

"In diagnostics and healthcare, we had another incredible quarter, delivering more than 200% growth. Our COVID-19 testing revenue continued to accelerate in the quarter as customer demand for our sample preparation, PCR solutions, and viral transport media remained very robust," Marc Casper, CEO, said during an earnings call. "For the full-year, diagnostics and healthcare grew by more than 100%, driven by our leading role in supporting COVID-19 testing," he continued.

Looking to 2021, Stephen Williamson, Senior Vice President and CFO, said, "We're assuming vaccine and therapy revenue is fairly linear in 2021. The testing-related revenue is assumed to be very front-end loaded with Q1 levels similar to Q4 2020. Our guidance assumes [COVID-19] testing demands may begin to moderate in Q2 and potentially moderate further as the year progresses."

Casper shared projections for COVID-19 testing in 2022 and 2023. "Based on what we see with the pandemic and what our customers are telling us, we would expect demand for COVID-19 therapies and vaccines to be very substantial in 2022, and likely to have some level of revenue going into 2023, maybe even longer."

BIOMÉRIEUX

BIOMÉRIEUX: Sales Increased 20.5% in Q4-2020

bioMérieux said sales were $3.6 billion in 2020, which was up 19.7% over 2019. Sales in Q4 increased 20.5%, led by molecular biology reagents.

During the call, executives singled out the company's BIOFIRE molecular product, noting that sales increased 76% in Q4 due to demand for the respiratory 2.1 panel.

The company says this panel tests for "19 viruses including SARS-CoV-2, and four bacteria that cause respiratory tract infections in 45 minutes."

"...our BIOFIRE has proven to be a key diagnostic solution in the fight against COVID-19 with an impressive growth of around 80%. It's worth noticing that the installed base in terms of units will increase from around 10,000 to 17,300 units worldwide. It's a major achievement," declared Alexandre Mérieux, Chairman and CEO.

BECTON, DICKINSON AND COMPANY: Integrated Diagnostics Solution Revenue Grows 106% for Q1-2021

Becton, Dickinson and Company (BD) had revenue of $4.7 billion in the fiscal Q4 ending Sept. 30, 2020, a growth of 4.4% over Q4 2019. COVID-19 testing was associated with more than $440 million in Q4-2020 sales.

BD's noted life sciences segment revenue was $1.4 billion during Q4-2020, an increase of 31% over Q4-2019. The company associated the sales bump with COVID-19 diagnostic testing on the BD Veritor and BD Max platforms.

Earlier this month, BD reported its first quarter 2021 earnings. For its Integrated Diagnostics Solutions (IDS) business unit, revenue was $1.7 billion, up 106% over Q1-2020, which was the start of the SARS-CoV-2 pandemic.

In looking to 2021, BD said it sees "no significant change in utilization or procedure volumes associated with COVID-19 resurgences."

Tom Polen, Chief Executive Officer and President, said, "I think there remains uncertainty around the effectiveness and timing of the [COVID-19] vaccines, especially with additional variants that are out there, et cetera. But we can't predict what is going to happen there on the second half of the year. And so we continue to project that there will be very strong demand for antigen testing in the first half of the year and that the second half of the year is less certain."

HOLOGIC: 89.3% Growth in Q1-2021 Compared to Q1-2020

Hologic issued its earnings report for Q1-2021, which ended on Dec. 31, 2020. The company said revenue increased 89.3% for the quarter to $1.6 billion, compared to $850 million in Q1-2020.

Hologic has a substantial presence in women's health and related diagnostics. But it also has a flourishing business in molecular diagnostics.

In its earnings report, Hologic said, "Worldwide molecular diagnostics revenue of $995.3 million increased 457.6%—or 448.7% in constant currency—exceeding expectations based on increased production of, and strong global demand for, the company's two SARS-CoV-2 assays that run on the fully-automated Panther and Panther Fusion systems."

Hologic believes there will be an ongoing demand for COVID-19 testing. "... we've been in close contact with most of the major governments around the world, [as well as] all of the key labs and health experts," stated Stephen P. MacMillan, Chairman, President, and CEO. "We believe [there will be] ongoing COVID-19 screening programs ... that use the most sensitive [diagnositic] tools out there ... hospitals are going to want to continue to test patients coming in ... everybody who is going to go in for a hip and knee cardiac, any other procedure, we think will probably to be tested [for COVID-19]." TDR

➤➤ ***CEO SUMMARY: Use of artifical intelligence (AI) to analyze digital pathology images and aid in diagnosis—or even in making the primary diagnosis—is much discussed. Experts in pathology regularly predict that use of AI in image analysis will transform the pathology profession. But that leaves one important question unanswered: When will AI be ready for prime time in the diagnosis of digital pathology images? In this exclusive interview, one expert explains how AI developers are tapping decades of lab test results to develop AI solutions for two common types of cancer.***

Expert in digital imaging anticipates wider use of AI in image analysis

Artificial Intelligence Ready for First Use in Anatomic Path

By Robert L. Michel

FOR ALMOST TWO YEARS, anatomic pathologists have been bombarded by a seemingly-endless stream of press releases trumpeting some company's new algorithm or image analysis solution that uses artificial intelligence (AI) to diagnose a whole-slide image (WSI).

However, these press releases leave two essential questions unanswered for pathologists interested in digital pathology. One: Is the AI in any vendor's product robust and consistently accurate in the answer it produces? Two: Is the product truly ready for daily use in diagnosing cancers and other diseases?

Artificial intelligence is regularly touted as the most important technology poised to revolutionize anatomic pathology since pathologist Rudolf Virchow's work with light microscopes in Germany 130 years ago. But surgical pathologists still wait for the first AI-based pathology product that, when used, transforms the basic diagnostic processes that pathologists use every day.

That day may not be far off, given the ongoing improvements to products that incorporate artificial intelligence, particularly in image analysis and diagnostics. For this reason, it is important for pathologists to understand the development curve for artificial intelligence.

One individual who is uniquely qualified to explain the technology development curve of artificial intelligence and its capabilities for use in anatomic pathology is Ajit Singh, PhD, a partner at **Artiman Ventures** in Palo Alto, Calif. He has a unique career trajectory involving imaging and informatics. In the 2000s, he was the CEO of **Siemens Medical Solutions Image and Knowledge Management Group**.

In 2008, Singh became CEO of **BioImagene**, one of the early entrants in the digital pathology marketplace. BioImagene was sold to **Ventana Medical Systems**, a division of **Roche Diagnostics** in 2010. Early in 2011, Singh joined Artiman Ventures. Over the past decade, he has been involved in diagnostic startups, several of which incorporate image analysis and artificial intelligence in their systems intended for use by pathologists.

Artificial Intelligence in 2018

In 2018, Singh was the closing speaker at the *Executive War College* and gave attendees a comprehensive presentation on artificial intelligence and its then-current state of development.

During his session, Singh pointed out that the capabilities of AI at that time made it effective for use in situations where there were not more than 15 to 20 variables in the problem to be solved. He gave the example of a patient who presents at the physician's office. Singh observed that the AI technology of 2018 was effective at managing the variables of:

- Who is the patient?
- Does identification presented to the physician match a real person?
- As of that date, does the patient have active health insurance?
- What is patient's co-pay/deductibles with his/her coverage?
- How much of the yearly deductible/out-of-pocket has the patient met and how much of the patient-pay requirement does the physician need to collect?

To illustrate why the 2018 technology version of AI was not ready for use in anatomic pathology, Singh used the example of breast cancer. Because of the complexity of breast cancers, Singh observed that an AI solution would need a data base of five billion breast cancer cases before the current technology of AI could reliably diagnose a breast cancer case with comparable accuracy to a trained pathologist.

Fast forward three years to today. What is different about artificial intelligence in 2021, compared to 2018? How has AI gained capabilities that make it ready to be a prime-time tool for pathologists in their daily work?

Singh has answers to these questions. In this recent interview with THE DARK REPORT, Singh explained that multiple

companies are bringing digital pathology analytical systems to market that utilize AI and demonstrate the ability to diagnose whole-slide images for at least two of the less complex types of cancer.

True of Prostate Cancer

"This is particularly true of prostate cancer, which has far fewer variables compared to breast cancer," he said. "It is now possible to do a secondary read, and even a first read, in prostate cancer with an AI system alone.

"In cases where there may be uncertainty, a pathologist can review the images," he continued. "Now, this is specifically for prostate cancer and I think this is a tremendous positive development for diagnostic pathways.

"Why and how did AI find its first success with prostate cancer?" asked Singh. "There are two reasons and they are familiar to all surgical pathologists. One, as noted earlier, the number of variables is less.

Ajit Singh, PhD

➤"Why and how did AI find its first success with prostate cancer?" asked Singh. "There are two reasons and they are familiar to all surgical pathologists."

"Second is the pool of data about prostate cancer testing and outcomes that spans at least 35 years," he noted. "Let me explain. The first FDA clearance for the PSA test was in 1986, and since then men have had PSA exams, even though this test is highly inaccurate for diagnosis. The inaccuracy of these PSA tests are recorded in medical records, along with the results of prostate needle biopsies and prostatectomies.

"Today, there are some 35 years of data that include PSA test results, prostate biopsies, prostatectomies, and diagnosis codes sitting in various electronic patient records and non-electronic patient records," stated Singh. "In recent years, it became possible to digitize and assemble this data. From all that data comes an unexpected and exciting development for the use of artificial intelligence in prostate cancer diagnosis.

"Researchers and AI developers went back and looked at the prostate cases and began to identify the variables common to the cases that could be associated with the PSA scores," he explained. "There were instances where the PSA test would say positive, but the patient's biopsy showed no cancer. There were also cases where the PSA test showed negative, but the doctor observed hematuria or other symptoms and decided to do a prostate biopsy and discovered that the patient actually had a partial carcinoma.

"This was a gold mine of useful diagnostic data for the AI developers," Singh said. "For large numbers of patients, they could look at the PSA scores, see the diagnoses, then look at the slides made from the biopsies to see what features and characteristics of the tissue could be associated with the PSA test variables.

"Working retrospectively with this data, the AI developers were able to identify the tissue structures consistent with the different variables," added Singh. "Was it a positive PSA test and a negative biopsy? Was it a negative PSA and a positive biopsy? Researchers could now identify the tissue characteristics consistent with each type of diagnostic outcome and program the AI to accurately recognize and classify these different elements in a prostate cancer."

State of Development

According to Singh, AI algorithms have reached the state of development where they also can be used in the diagnosis of skin cancers.

"AI is happening quickly in dermatopathology because melanomas have been tested and diagnosed in similar ways to prostate cancer," noted Singh. "There are decades of patient cases where an ini-

How an Early Image Analysis Solution Created the TC-PC Model That Changed Anatomic Pathology

ONE CHALLENGE FOR ALL CLINICAL LABORATORY ADMINISTRATORS and pathologists is to know the definition of artificial intelligence (AI) and use that definition to correctly assess if any lab test system, product, software, or image analysis algorithm truly uses AI.

Pathologists with long memories recall **ChromaVision Medical Systems**, Inc., founded in 1993. At the time, Chromavisions' flagship product—the ACIS System—was an image analysis tool that allowed pathologists to "detect, count, and classify cells of clinical interest based on recognition of cellular objects of particular color, size, and shape." Its FDA clearance was as a staining device for cytokeratin 18.

Era of TC-PC Arrangements

Although this was not true artificial intelligence used to diagnose a digital pathology image, the ChromaVision system did transform anatomic pathology in a fundamental way. The ACIS was quickly adapted for use in measuring estrogen receptors in breast cancer. When used in this manner, the ACIS system became an essential tool in the earliest versions of the TC-PC (technical component-professional component) business model.

The TC-PC model was simple in concept and execution. Pathologists at community hospitals sent their breast cancer biopsies to a centralized laboratory. The referral lab processed the tissue to produce the glass slides and the images used by the ChromaVision system and billed for the TC. The lab then transmitted the digital images back to the referring pathologists, who then used the ChromaVision system to diagnose the case, thus allowing them to bill for the PC.

US Labs, a pathology company company based in Irvine, Calif., was fastest to jump on this TC-PC model in the early 2000s. It became the biggest buyer and user of ChromaVision ACIS systems.

Meanwhile, executives at nearby Chromavision Medical Systems watched the growth and profits at US Labs. They decided to restructure their company. They renamed it as **Clarient, Inc.**, and converted their instrument manufacturing company into a pathology laboratory organized around the TC-PC model. *(See TDRs, January 3, 2005, and August 30, 2004.)*

The TC-PC model was so attractive that **LabCorp** acquired US Labs in 2005. **GE Healthcare** described Clarient as a "molecular diagnostics and imaging firm" when it purchased the company for $580 million in 2010. GE divested Clarient to **Neogenomics** for $275 million in 2015. *(See TDR, Oct. 26, 2015.)*

The saga of ChromaVision and its pioneering system, which could do basic analyses from a digital image of a pathology slide, might be considered one of the earliest applications of a computer algorithm being used with a digital image of a pathology slide in support of clinical care.

Early Image Analysis

Of course, this happened with technology that dates back to 1993. Because the current generation of image analysis algorithms and artificial intelligence systems are much more robust and capable, the pathology profession may be poised for widespread adoption of AI for use in digital image analysis.

There is another lesson that pathologists and pathology practice administrators should take from ChromaVision's role in expanding use of the TC-PC business model. That lesson is that there is fast adoption anytime pathologists recognize something new can increase the revenue they generate from the cases they read.

tial indication caused the dermatologist to take multiple skin biopsies from the patient," noted Singh. "However, when these biopsies were read by dermatopathologists, many of them were negative for cancer.

"Consequently, there are huge numbers of cases where researchers can see the initial symptoms that caused the physician to do skin biopsies, along with the final diagnoses. They then compare the slides made from the biopsies to see characteristics of the tissue associated with the negative diagnoses and positive diagnoses.

"Melanoma is a much less complex type of cancer than, say, breast cancer, so the decades of diagnoses and slides provided an immense amount of relevant data that AI developers could use to build their image analysis algorithms. Like with prostate cancer, this is an exciting development," he emphasized.

➤Coming Next in Diagnostics?

What may come next with AI and cancer diagnostics? "Pathologists might want to watch the development of AI for use in diagnosing the types of cancers where diagnostic tools often trigger unnecessary biopsies," predicted Singh. "The frequency of lung cancer and colon cancer would make each a good candidate for an accurate AI-powered diagnostic tool.

"Awareness of smoking as a cause of lung cancer gives that disease high visibility," he continued. "Colon cancer is an interesting opportunity for AI because there is very low compliance on colonoscopy and there are frequent overcalls on colon cancer. For example, if polyps are found, it creates a concern for the physician and the patient. That concern leads to unnecessary biopsies."

Singh also noted that cervical cancer—especially the type caused by the human papillomavirus (HPV)—is another type of cancer ripe for development of an AI diagnostic tool. "Like with prostate cancer and melanomas, there exists decades of HPV test data, Pap smear results, biopsy results, and patient outcomes," observed Singh. "This huge volume of data is what allows researchers to develop and tune AI to acceptable performance for use diagnosing digital pathology images in support of clinical care."

Ajit Singh, PhD

➤"Pathologists might want to watch the development of AI for use in diagnosing the types of cancers where diagnostic tools often trigger unnecessary biopsies."

Because of the growing numbers of companies entering the anatomic pathology space with image analysis algorithms, machine learning products, and artificial intelligence tools, The Dark Report was interested to learn which companies or academic centers Singh would single out as worth watching.

"There many companies coming into the pathology AI market," noted Singh. "Of these, I think three are farthest along with their AI offerings for analysis of pathology images. They are **Ibex Medical Analytics** (Tel Aviv, Israel), **Paige.AI** (New York, N.Y.), and **PathAI** (Boston)."

➤Ongoing Development of AI

Pathologists and clinical lab administrators following the development of artificial intelligence capabilities and how they are used in different aspects of healthcare—including surgical pathology—need to remember that the AI's enabling technologies are being improved at a steady pace. We may still not have the self-driving car that was promised just a few years ago, but, as Singh points out, where there are fewer variables, artificial intelligence can already be used to great success and that is happening already in certain sectors of healthcare. TDR

Contact Ajit Singh, PhD, at ajit@artiman.com.

Lab Briefs

Roche to Acquire GenMark Diagnostics

LAST MONTH, **Roche** and **GenMark Diagnostics** announced a definitive merger agreement for Roche to acquire GenMark in a transaction valued at $1.8 billion.

Roche called attention to GenMark's syndromic panel testing portfolio and said this line of molecular tests would strengthen its products for infectious disease testing in hospitals, particularly for identifying antibiotic resistance.

GenMark's proprietary eSensor detection technology is used in its molecular diagnostic tests to detect multiple pathogens from a single patient sample. Roche wants to use GenMark's ePlex system to increase lab efficiency through streamlined order-to-reporting workflow, while also contributing to better patient outcomes because of a faster time-to-answer, particularly for infectious diseases.

Pathology Group Hacked, Protected Health Information Was Accessed

ONCE AGAIN, HACKERS HAVE TARGETED the protected health information (PHI) of a medical laboratory. This time, the target was **ProPath**, the large regional pathology group in Dallas.

As required by federal law, once ProPath discovered the breach of its data systems, it reported the event to the federal government. It then reported the event to news outlets and began notifying patients whose confidential data was exposed during the breach. ProPath said it alerted 39,213 patients that an unauthorized party had accessed email accounts within the ProPath system.

ProPath disclosed that it discovered the breach on Jan. 28 and determined that the unauthorized access of either or both email accounts occurred between May 4 and Sept. 14, 2020. In its press release, the company said:

- accessed emails contained patients' social security numbers, birthdate, financial account information, and more.
- patients affected by the breach were offered free access to a credit monitoring system.

This latest hack involving a medical laboratory and the breach of protected health information is a reminder that all clinical laboratories and pathology groups are vulnerable to this type of cybercrime.

Thus, regular reviews of security of practice computers and digital systems is recommended.

Thermo Fisher Buys Mesa Biotech

AT THE END OF FEBRUARY, **Thermo Fisher Scientific** of Waltham, Mass., announced that it finalized its purchase of **Mesa Biotech** of San Diego. Thermo Fisher paid $550 million for the healthcare test and data company. Mesa has about 500 employees and in 2020 reported revenue of about $45 million.

Mesa's diagnostic products include nucleic acid PCR amplification assays designed for use in non-core medical lab settings, such as ERs, rural hospitals, urgent care clinics, and pharmacies.

Last March, Mesa obtained an emergency use authorization (EUA) from the federal **Food and Drug Administration** (FDA) for its Accula molecular COVID-19 test system. The desktop PCR instrument works with a single-use cartridge to produce a SARS-CoV-2 result in 30 minutes. **TDR**

Restitution and Guilty Plea in Two Lab Fraud Cases

Outcomes in separate cases alleging fraud involving lab tests were announced last month

CEO SUMMARY: In one case, owners and a sales rep agreed to pay restitution totaling almost $10 million. In the second case, three defendants pled guilty to federal charges involving payment or receipt of kickbacks and illegal inducements. A fourth defendent in this second case, a physician, awaits trial. These smaller cases come just months after the announcement last fall of two huge fraud investigations that involved labs and genetic testing and represented about $6 billion in fraudulent Medicare claims.

THE **US Department of Justice** (DOJ) recently announced decisions in two separate fraud cases involving clinical laboratories. In one case, the defendants agreed to pay restitution for their roles in the fraud and in the other case, several co-defendants pled guilty and are scheduled for sentencing this summer.

Neither of the two cases filed by federal prosecutors involved fraud on the scale of, say, the **Health Diagnostics Laboratory** (HDL) case of 2015, when the Department of Justice claimed that fraudulent actions by operators of that lab company had defrauded federal health programs of as much as $500 million in just 48 months. *(See TDRs, Apr. 20 and Jun. 22, 2015.)*

Feds Prevail in Both Cases

What is significant about those two cases is that they show that DOJ prosecutors are willing to file charges in federal court against the operators of even smaller clinical laboratory companies that violate federal laws, particularly the Anti-Kickback Statute. The outcomes of both cases show that these federal court actions can have teeth and result in criminal convictions and even jail time for lab owners, managers, and sales representatives who are alledged to have violated federal laws by illegally inducing test referrals from physicians and other providers.

The DOJ announced in late March that two former owners of a now-defunct North Carolina laboratory known as **Physicians Choice Laboratory Services** (PCLS), agreed to pay more than $7 million in reparations for allegations that they violated the federal Anti-Kickback Statute (AKS) and swindled taxpayers with fraudulent medical claims involving urine tests.

The Anti-Kickback Statute makes it illegal for any person to knowingly and willfully solicit or receive, or offer or pay, any remuneration in exchange for the referral of items or services that are paid for by a federal healthcare program. In this situation, the federal **Centers for Medicare and Medicaid Services** (CMS) were fraudulently billed for unnecessary medical tests.

One of the former owners of PCLS, **Douglas Smith**, agreed in federal court to settle claims against him for $4.5 mil-

lion. Prosecutors alleged that Smith violated the AKS by paying kickbacks to a Knoxville medical practice in exchange for drug-testing referrals.

Smith's Business Partner

His former business partner, Philip McHugh, agreed to pay $2,021,795.57 in restitution for his part in the AKS fraud scheme. Federal prosecutors alleged that McHugh participated in several AKS violations including:

- Providing free urine drug testing equipment to two physicians,
- Paying volume-based commissions and a salary to an individual in exchange for that person's influence over medical practices, and
- Providing loans to two doctors to convince them to refer drug-testing business to PCLS.

"This laboratory used prohibited financial instruments and giveaways to physicians for patient referrals," said Derrick Jackson, CFE, Special Agent in charge at the **US Department of Health and Human Services** (HHS), Office of Inspector General (OIG) in Atlanta, in a statement. "Such *quid pro quo* arrangements are kickbacks that stifle competition and steer business to the company offering the inducements."

'Illegal enticements'

Court filings indicate that McHugh's use of these illegal enticements resulted in numerous fraudulent claims, totaling millions of dollars, to Medicare between 2013 and 2015.

Acting US Attorney Bill Stetzer added that the actions of the defendants damaged the credibility of labs and an important diagnostic procedure, particularly with regards to urine testing and drug abuse.

"Offering financial incentives to medical providers in exchange for performing these tests not only violates the law, it undercuts the significant efforts that the medical and law enforcement communities have made to combat the opioid crisis in America," Stetzer said in a statement following the announcement of McHugh's settlement, *The Charlotte Observer* reported.

The DOJ did note that the aforementioned resolved claims are allegations only and that there has been no determination of liability.

"The Anti-Kickback Statute is meant to protect patients and federal health programs from medical decision-making corrupted by financial motive," said Andrew Murray, JD, former United States Attorney for the **Department of Justice (DOJ) Western District of North Carolina**, in a statement. "My office will aggressively pursue such claims."

Lab Sales Rep

Previously, **Manoj Kumar**, a former sales representative and manager at Physicians Choice Laboratory Services (PCLS), consented to pay $649,407 in restitution for claims that he also participated in ploys to encourage physicians to send medically unnecessary urine drug tests to PCLS.

"Tests and other services should be ordered by physicians based on sound medical judgment, not on financial benefit," said Murray in the DOJ Western District of North Carolina statement. "Paying inducements to obtain orders for tests and other services corrupts medical decision-making and causes unnecessary costs to federal healthcare programs."

Federal prosecutors filed the complaint against PCLS after the company had been named in two separate whistleblower lawsuits in Tennessee and Florida. The two cases were later consolidated and transferred to the Western District of North Carolina in 2017.

In a separate case, a Pennsylvania man, Jeremy Richey, admitted guilt for his involvement in a conspiracy to receive kickbacks and bribes from several laboratories in exchange for patient referrals

of DNA samples and genetic testing in violation of the AKS.

According to documents in this case, Richey and his co-conspirators operated **Ark Laboratory Network LLC** (Ark), a company that claimed to operate a network of labs that performed genetic testing. The suit alleged that Richey and others entered into kickback agreements with certain clinical laboratories where bribes were paid to Ark in exchange for delivering DNA samples and orders for genetic tests.

Counterfeit Invoices

Ark concealed these kickbacks through the issuance of counterfeit invoices to other labs that reflected fictitious services being provided at an hourly rate, even though the involved parties had already agreed upon the amount of the bribes. The total sum of each bribe was based on the revenue the labs received from Medicare or a predetermined amount paid for each DNA sample.

Between January 2018 and January 2019, Medicare paid these laboratories approximately $4.6 million for genetic tests that were the result of these bribes. Ark received at least $1.8 million in kickbacks for these inducements.

Richey's sentencing is scheduled for August 9 and he faces up to five years in prison and a fine of $250,000.

Three Other Guilty Pleas

Three of Richey's co-conspirators, Kacey Plaisance, Kyle McLean, and Edward Kostishion, previously pled guilty to the charges. Plaisance is scheduled for sentencing on June 21 and McLean and Kostishion are scheduled to be sentenced on July 26.

Matthew Ellis, MD, who served as the Chief Medical Officer for Ark, also has been charged for his role in the conspiracy. Ellis allegedly served as the ordering physician for genetic tests and certified that those tests were reasonable and necessary. However, the test requests contained fraudulent information regarding patient medical histories and conditions and patients were provided with misinformation about the genetic testing. Ellis' case is pending.

Although the magnitude of the fraud in both of these cases is not as large as many of the headline-grabbing laboratory fraud cases, the details of cases like these can deliver information to clinical laboratory managers regarding fraudulent practices and how they are used.

This type of information also can help lab professionals understand how federal fraud investigations occur and how DOJ prosecutors build such cases. TDR

$6 Billion Fed Fraud Case Involved Lab Drug Tests

LAST SEPTEMBER, the Department of Justice announced what it described in a press release as a "National Health Care Fraud and Opioid Takedown." It charged 345 defendants and, in court documents, reported that the alleged fraud losses totaled $6 billion.

One interesting aspect of this case is that the DOJ said schemes using telemedicine were responsible for "$4.5 billion in allegedly false and fraudulent claims submitted by more than 86 criminal defendants in 19 judicial districts" that included medically-unnecessary "genetic and other diagnostic testing [and that] durable medical equipment companies, genetic testing laboratories, and pharmacies then purchased those orders in exchange for illegal kickbacks and bribes and submitted false and fraudulent claims to government insurers."

Also, last September, the DOJ announced Operation Double Helix. These cases involved 35 individuals accused of submitting $2.1 billion in fraudulent genetic test claims. The DOJ press release said that nine physicians were charged in these cases.

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

One clinical laboratory company now says it provides COVID-19 testing services to all five of the major men's professional sports leagues in the United States. On April 1, **BioReference Laboratories, Inc.** (BRLI), a division of **Opko Health**, announced a new agreement with **Major League Baseball**. In its press release, BRLI said it will provide COVID-19 testing for "players and staff, stadium employees and league staff for the 2021 Major League Baseball (MLB) season." BRLI will use **Mesa Biotech's** Accula System to provide on-site rapid PCR point-of-care COVID-19 testing to all 30 MLB teams.

MORE ON: *BioReference and Pro Sports Teams*

Every clinical lab company would like to find a unique, profitable market niche. BioReference Laboratories seems to have found that niche in providing molecular COVID-19 testing services to athletic events. In the past year, BioReference provided COVID-19 testing services to the **National Football League**, the **Winter X Games** in Aspen, Colo., **U.S. Soccer's Women's and Men's National Teams**, and the **NBA G League** in Orlando.

FAKE COVID-19 TEST RESULTS IN MEXICO

Fake COVID-19 test results are being sold in hotels and airports in Mexico. The **Mexican Council of Medical Diagnostic Companies** (COMED) publicy called on health regulator **Cofepris** (Federal Commission for Protection against Sanitary Risk) to investigate and levy sanctions on companies and people selling fake COVID-19 test results to international travelers.

TRANSITIONS

• Pathologist Emily Volk, MD, was selected as the new Chief Medical Officer at **Baptist Health Floyd Hospital** in New Albany, Ind. Previous positions were with **University Health San Antonio**, **Baptist Health System San Antonio**, and **William Beaumont Hospital**.

• **Paige** of New York, N.Y., appointed Andy Moye, PhD, as Chief Commercial Officer. Moye previously held positions with **Ontada**, **Caris Life Sciences**, **Philips**, and **CombiMatrix**.

• **EllKay** of Elmwood Park, N.J., announced the appointment of Gretchen Tegethoff as Regional VP of Strategic Relationships. Past positions have been with **CHIME**, **Athens Regional Health**, **George Washington University Hospital**, and **IntelliData**.

• Patrick Turner is the new VP of Sales, USA and Canada, at the **College of American Pathologists** in Northfield, Ill. Prior positions were with **OPKO Health**, **GenPath Diagnostics**, **LabCorp**, **SmithKline Beecham Clinical Laboratories**, and **Quest Diagnostics**.

That's all the insider intelligence for this report. Look for the next briefing on Monday, May 3, 2021.

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