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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

Restricted information, see page 3

COMMENTARY & OPINION by...

R. Lewis Dark

Founder & Publisher

Will Humana's Sale to Aetna Hurt Smaller Labs?

FURTHER CONSOLIDATION AMONG THE NATION'S LARGEST HEALTH INSURANCE COMPANIES is expected following the news on July 3, that **Aetna, Inc.**, and **Humana, Inc.**, had entered a sales agreement calling for Aetna to pay $37 billion to acquire Humana.

Should the proposed sale take place, the consequences are not likely to be favorable to smaller clinical labs and local pathology groups. Post-acquisition, a much larger Aetna would probably continue to narrow its laboratory provider networks while leveraging its larger size to gain further pricing discounts from its exclusive national contract laboratory, **Quest Diagnostics Incorporated**.

Aetna currently has 23.6 million medical members, compared to the 9.7 million medical members at Humana. By contrast, **Anthem** (formerly **WellPoint**) has about 38.5 million medical members and **UnitedHealth** has approximately 36.8 million medical members. Together, following the Aetna/Humana merger, these three insurance companies would be the largest in the United States and would cover 108.3 million, or 74.6% of the 144.7 million people that analyst **Mark Farrah Associates** reported as having medical coverage at the end of 2014.

Financial analysts expect the proposed sale of Humana to Aetna will get intense scrutiny by federal antitrust regulators. As well, a number of state insurance commissioners have voiced concerns about the consequences of this merger. The proposed sale of Humana also now makes **Cigna**, with about 14.7 medical members, an attractive acquisition candidate.

Lab administrators and pathologists should also view these developments among the nation's largest health insurance companies in context with the ongoing enrollment growth in Medicare Advantage plans. CMS data shows that 17.3 million beneficiaries are now in Medicare Advantage. By comparison, as of 2014, there were a total of 45 million seniors enrolled in all forms of Medicare. This means that 38.4% of all Medicare beneficiaries are now covered by Medicare Advantage and predictions are that this percentage will continue to increase.

The rapid enrollment growth in Medicare Advantage plans means proportionately fewer seniors remain in traditional Medicare Part B coverage. Typically, just as the major health insurance companies tend to exclude smaller labs from their provider networks, Medicare Advantage plans do the same by contracting with national labs to access deeply-discounted test prices. TDR

Newer, Smaller Analyzers Will Bring Big Data to Labs

Even smaller labs will handle large quantities of data that contribute to improved patient care

CEO SUMMARY: Clinical laboratories of all sizes are poised to become the source of much of a hospital or health system's "big data." At many academic center labs, greater use of genetic and molecular testing requires that more space and more staff be devoted to data management. At the same time, the latest generation of gene sequencing instruments and molecular analyzers are cheaper, faster, and more automated. These systems make it feasible for even smaller labs to offer sophisticated genetic tests.

DATA IS POISED TO BE A DISRUPTIVE FORCE to the existing model of clinical laboratory testing. That's just one prediction from a lab scientist who has been at the forefront of molecular diagnostics over the past 25 years.

"Not only are clinical laboratories starting to produce much greater volumes of important clinical data than ever before, but the demand from physicians and payers for this data is growing at an equally significant pace," stated Gregory J. Tsongalis, Ph.D., Professor of Pathology and Director of Molecular Pathology at the **Theodor Geisel School of Medicine at Dartmouth College**, in Hanover, New Hampshire.

"Going forward, laboratories of all sizes will be generating essential data in volumes unimagined a decade ago," he noted. "This will be true of both small labs and large labs. It is easy to see the signs of this trend.

"For example, we just opened a new clinical lab facility of 11,000 square feet at the Geisel School," said Tsongalis. "Over 25% of that space will be devoted to data management. The same is true at the **Jackson Laboratory** in Farmington, Connecticut, [where he serves as Director of the Clinical Genomics Laboratory]. Because of the increasing volume of data generated at this site, there are more computational technologists than lab technicians."

According to Tsongalis, laboratories will make significant data contributions in healthcare big data for multiple reasons. "First, larger numbers of clinical labs—both large and small—are using more automated lab testing systems. Lab automation makes it easier and cheaper to

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perform greater lab test volume, thus producing more data," he noted. "Second, new diagnostic technologies are giving labs and physicians additional tools to diagnose disease while providing more precise guidance on therapies, and helping them monitor patients with greater accuracy.

Huge Volumes Of Lab Data

"Third, new diagnostic technologies are producing huge volumes of data in the clinical lab," he continued. "This will not be limited to genetic testing and molecular diagnostics, where analysis of exomes and genomes generates hundreds of millions, even billions of data points. But it appears likely that clinical assays for testing the human metabolome and human microbiome will become common.

"All of these elements are why medical labs will be generating huge quantities of data," stated Tsongalis. "We already have evidence in many academic centers that all of this clinical laboratory test data will be the foundation for the big data efforts of hospitals and health systems."

Tsongalis advised pathologists and lab administrators not to underestimate how the ongoing improvements to automation solutions—including automated lab analyzers with small footprints and lower costs—will benefit even small hospital labs. "Some of this new equipment may even change how reference labs operate," he speculated.

"As laboratory equipment evolves to produce more data on patients' conditions, the role of clinical labs will change," stated Tsongalis. "This will happen concurrent with how labs are paid. Current trends indicate that the role of the clinical lab is poised to change from the entity that keeps specimens to the entity that is the keeper of data. And by that I mean a keeper of big data.

"In many respects our new lab space at Dartmouth—with up to 25% of the space dedicated to data analysis—looks like central command with computer monitors and servers to monitor all of the data being generated," he said. "That data comes from our gene sequencers, from the other molecular analyses we do, and, as we move forward, from the personal health monitoring or wearable devices being developed.

"Another factor that will transform clinical labs is the need for new skills that all the new diagnostic and information technology require," Tsongalis continued. "Labs will need professionals who can do data analysis and who can look at the clinical lab test results from new technologies to flag results of clinical concern or to point out variations and trends.

"At the Jackson Lab, the majority of the staff are computational biologists and curation scientists who process data produced by a small number of laboratory technicians," he said. "Consider this trend as evidence of the game-changing disruptive technology that data represents for all of us working in clinical labs today. It will be essential for every lab to have individuals with the skills to manage and analyze data."

New Uses for EHR, Lab Data

Tsongalis believes that most hospital administrators have yet to recognize that their electronic health records systems will not be able to store the large volumes of data generated by clinical labs. "This is probably one aspect of the big data trend where pathologists and lab scientists are ahead of health system administrators," he observed.

"Should an EHR contain the raw data from a patient's whole genome?" he asked. "Probably not. So where will that data be stored? It will be kept by the clinical lab that performed the gene sequencing. This is just one example of how and why clinical labs will be the repositories for a large proportion of every hospital's 'big data.'

"Take this one step further," added Tsongalis. "The time and expense to sequence a whole human genome is shrinking at a rapid rate. At the same time, the analyzers used in clinical labs are becoming smaller, faster, and more automated. In our lab, we are producing large

Clinical Exome Sequencing Has the Potential To Replace Some Multiple Gene Tests

CLINICAL EXOME SEQUENCING (CES) will be the next game-changing technology in clinical laboratories, stated Gregory J. Tsongalis, Ph.D., Professor of Pathology and Director of Molecular Pathology at the **Theodor Geisel School of Medicine at Dartmouth College**. That's because CES has the potential to replace a long list of tests in every clinical lab.

"Consider that clinical exome sequencing allows us to sequence 4,800 genes, all of which are known to be or have mutations that are causative for some type of human disease," he said. "In other words, it is a rapid way to provide a lot of information quickly.

"This is what distinguishes clinical exome sequencing from whole exome sequencing," noted Tsongalis. "Whole exome sequencing involves sequencing the coding regions of every gene. The clinical exome narrows that down to sequence the coding regions only of those genes identified as being responsible for some type of human disease.

"Here's why CES is important," he emphasized. "Our lab can currently sequence a clinical exome and do the data analysis for less than $1,000. That is much cheaper than what our lab pays when it refers out genetic testing, such as for children with autism, developmental delay, or some type of a syndrome phenotype. When done by an outside lab, those tests cost us between $2,000 to $15,000 each.

"But now we can take this one clinical exome test and run it on every one of those patients," stated Tsongalis. "We don't need to send those tests out. At the same time, our in-house CES test allows us to focus the analysis on the genes of interest, meaning those 4,800 genes. For certain patients there are only 50 or 100 genes of interest and that allows us to narrow the data analysis down specifically to those particular areas.

"We believe that CES testing done in-house will reduce the overall cost of this type of testing tremendously," he continued. "Moreover, the cost savings to the institution will be huge because most payers are reimbursing these genetic and molecular tests at very low rates, if at all. That is why the cost savings and cost avoidance is huge for these cases.

"These are some of the reasons why we are excited about the potential for clinical exome sequencing to allow us to return a faster, more accurate answer that improves patient outcomes while holding down the cost of this testing when compared to using reference labs," concluded Tsongalis. "Our expectation is today's send-out genetic disease panel has the potential to be replaced by one test—the clinical exome sequence—because of still-falling costs, automated systems to produce the sequence, and more robust informatics to store and analyze the data."

amounts of genetic and molecular data in one day or less.

"There is another development that works in favor of smaller clinical labs," he added. "What many lab professionals have yet to realize about molecular diagnostics is that it is a universal technology. That means we don't need one instrument to do genetic testing and another instrument to do infectious disease testing and a third instrument to do cancer testing. The tools—the analyzers—are all the same. The only thing that changes is the chemistry, meaning the primers or the probes used to detect the sequences that are our target, regardless of the actual test.

"This is a significant factor for small hospital labs, for reference labs, and in fact for the entire clinical lab industry," he said. "Look at the test menu when I joined the staff at Dartmouth in 2004. At that time, there were just a handful of molecular tests being done routinely in the clinical lab. There was no automation or high-throughput systems yet because the volume was low and the costs of these tests were high.

"At that time, we had three tests in genetics (FII, FRAX, and FV), three tests

in heme-onc (Bcl-2, IgH, and TCR), and two tests in infectious disease (*B. pertussis* and Parvo B19)," he recalled. "There were no routine molecular tests in oncology or pharmacogenomics.

"Today, of course, the list is much longer," continued Tsongalis. "There are 14 tests in genetics, 10 tests in heme-onc, 13 tests in ID, 22 tests in oncology, and six tests in PGX. In all five categories, the demand for new clinical tests, markers, genes, and mutation profiles went through the roof.

"In response, we automated the testing and developed high complexity testing," he said. "Now our lab has a long list of different tests for genetics, heme-onc, infectious diseases, and oncology. This all happened in the past three to five years because of the explosion of new therapeutics and advances in precision medicine.

➤Multigene Panels Offered

"Notice also that our lab quickly went from single gene and single mutation tests to panels of tests in hematology where we routinely sequence 54 genes for all patients," he explained. "In oncology, it's similar. We offer a 50-gene cancer hot spot panel. One hereditary cancer panel, HCP, is in validation now and has 94 genes in it that we will sequence routinely."

Pathologists and lab administrators working in community hospitals and smaller labs are poised to benefit from the latest generation of sophisticated, automated analyzers now available. "These new analyzers are why we have gone from hands-on, labor-intensive technologies to some automated platforms that can do everything," observed Tsongalis.

"Today, systems exist where the sample is added into a cartridge, and the cartridge extracts the DNA, does the PCR, does the quantification, then generates a result," he continued. "These are game-changing technologies for clinical labs, whether the lab is small, medium, or large. Why? Because these instruments can have a big impact on patient care due to faster turnaround time.

"**Cepheid** has the GeneXpert System, which was one of the first to offer this concept of sample-to-answer with a compartmentalized cartridge," commented Tsongalis. "In each compartment a different step of the assay takes place and a flywheel moves the reagents from one compartment to the next. When it is time for the PCR reaction, the cartridge is then plugged into the instrument and the results of the assay are available within an hour or so.

"Other companies followed with similar technologies because of the huge market represented by smaller hospital labs," he stated. "These labs get great benefit from offering more genetic tests that contribute to improved patient care.

"Another example is the **BD** Mac System, which is all cartridge-based," he added. "Systems like these provide a way to perform fast, real-time PCR assays even though the through-put is low because it's one sample at a time. The latest generation of these instruments is fast and—in the right settings—provide test results that have a major impact on how a patient is diagnosed and treated at specific moments in time. It is why these genetic and molecular technologies are changing how laboratories operate.

"These machines are simple to operate and offer rapid turnaround times," noted Tsongalis. "They use a single-use consumable that's closed, which is important because it eliminates the potential for contamination. Any size lab can use these machines and there is a huge cost-benefit ratio for this equipment.

"In addition, these new cartridge-based analyzers solve a big problem for our clinicians who are unwilling to wait three or four days for results," emphasized Tsongalis. "They want a much more rapid turnaround time. These are all reasons why I believe these technologies will become even quicker and cheaper." **TDR**

—Joseph Burns

Contact Gregory Tsongalis at 603-650-5498 or Gregory.J.Tsongalis@hitchcock.org.

Theranos, Capital Blue Sign Lab Test Agreement

Clinical laboratory company also announces FDA approval of its LDT for herpes simplex 1

CEO SUMMARY: With each passing month, Theranos is looking more like a traditional clinical laboratory company, based on how it is expanding its patient service center network and courier/logistics system into different regions while pursuing managed care contracts with health insurers. Meanwhile, respected laboratory scientists and physicians are using peer-reviewed medical journals to point out that Theranos has yet to publish details about the performance of its diagnostic technology to enable independent validation.

IT'S BEEN A BUSY MONTH for **Theranos, Inc.**, the ambitious clinical lab testing company based in Palo Alto, California. Last week, Theranos and **Capital Blue Cross**, of Harrisburg, Pennsylvania, announced an agreement that would give the clinical lab testing company access to the 725,000 members of Capital Blue Cross in Harrisburg and in Central Pennsylvania.

The week before, on July 2, Theranos issued a press release that it had "received the U.S. Food and Drug Administration's (FDA) clearance of its test system and test for herpes simplex 1 virus IgG. The FDA's decision provides independent validation of Theranos' patented finger stick and venous blood testing technology and the ground breaking Theranos System upon which the HSV-1 IgG test is run, as well as the approach that the company has supported for FDA review of Laboratory Developed Tests (LDTs)."

Also of interest is the announcement Theranos made on June 23 that it had entered into an agreement with the **Carlos Slim Foundation** of Mexico City, Mexico, "to provide Theranos' innovative laboratory testing services in Mexico."

The press release issued by the two organizations further stated that:

> *The Carlos Slim Foundation has developed and implemented a new model for healthcare service centers, CASALUD, which emphasizes prevention of diseases such as obesity, diabetes, and hypertension, and an associated program called MIDO, which evaluates risk factors for those conditions. By incorporating the Theranos system for testing, CASALUD will be able to provide lower cost, more accessible testing than is currently available. The resulting impact in earlier diagnosis for people in Mexico who may unknowingly suffer from diabetes or hypertension will allow these individuals to reduce the risks of these diseases.*

This may represent significant market access in Mexico for Theranos. That's because Carlos Slim is the wealthiest individual in Mexico and, between 2010 to 2013, was ranked as the richest person in

the world. His companies represent 40% of the listings on Mexico's stock exchange.

News that Theranos had a lab testing agreement with Capital Blue Cross in central Pennsylvania caught the attention of many pathologists and lab administrators across the country. It represents the first expansion of the company outside California and Arizona, where it operates Theranos Wellness Centers in certain **Walgreens** pharmacy stores.

Service Centers in PA

According to the press release, Theranos lab testing will be offered in the two Capital Blue Wellness Centers. These are located in retail malls. One is in Enola, a town in the Harrisburg metro. The other is in Center Valley, a community in the Allentown-Bethlehem metropolitan area.

The press release also noted that there would be "a network of Theranos Wellness Centers across the region" to serve the Capital Blue Cross beneficiaries. That may mean that, under its existing national agreement with Walgreens, Theranos would locate its specimen collection centers in Walgreens pharmacies in central Pennsylvania.

The assumption is that Theranos intends to service patients in Pennsylvania from its CLIA laboratory in Newark, California (or eventually from its laboratory in Scottsdale, Arizona, that has applied for CLIA registration). That will add the cost of cross-country transportation to laboratory specimens collected in Pennsylvania, not to mention extend the turnaround time before results can be reported.

Direct-Access Testing Law

Also, with this foothold in Pennsylvania, it can be expected that Theranos will lobby the state legislature to amend existing laws that require lab tests to only be ordered by a "member of the healing arts licensed to practice" in the Commonwealth. If Theranos follows the pattern it used in Arizona, it will send CEO Elizabeth Holmes to Harrisburg to identify a state legislator willing to sponsor a bill to permit consumers to order their own medical laboratory tests without the need for a physician to sign the lab test order. Theranos will then initiate a lobbying and public relations campaign to support passage of this legislation.

In response to the announcement Theranos had obtained FDA clearance of its LDT for herpes simplex 1, press coverage ranged from laudatory to dismissive. On one extreme, *USAToday* reporter Marco della Cava wrote, "In a ringing endorsement of its technology and a counter to its critics, Silicon Valley biotech company Theranos announced Thursday that its proprietary blood-testing system has received clearance." On the other extreme, reporter Jonah Comstock of *Mobihealthnews* titled his story, "Theranos gets unnecessary FDA clearance for its cheap, fingerstick blood tests."

FDA Review Of LDTs

Pathologists and clinical laboratory directors will recognize that Theranos did not need to get FDA clearance for its test. As Lauren Friedman reported for *Business Insider*, "Theranos' technology isn't necessarily such a departure from what's already been proven, though they have likely made significant improvements. In the FDA's letter to Theranos, which was provided to *Business Insider*, the agency noted that "the device is substantially equivalent" to existing technology. "You may, therefore, market the device," it said.

Given that applying for FDA clearance of an LDT is voluntary, that means, "Theranos went above and beyond to validate their tests—or at least one of them—something that might help to beat back the steady stream of critics," Friedman wrote in *Business Insider*. "The technology still has not been subjected to formal peer review, and the details of how it works remain secret. But the FDA approval is an important step toward validating the company's technology." TDR

—Joseph Burns

Respected Pathologists and Experts Ask: Why Don't We Know More About Theranos' Technology?

IN AN ARTICLE ABOUT THERANOS PUBLISHED last month in *Clinical Chemistry and Laboratory Medicine,* Eleftherios P. Diamandis, M.D., Ph.D., wrote an Opinion Paper. He stated "I analyzed the Theranos technology and their promises, and contrast this information with the currently used technologies, to show that most of the company's claims are exaggerated." *(Clin Chem Lab Med 2015; 53(7): 989–993.)*

Diamandis is the Section Head of Clinical Biochemistry in the Department of Pathology and Laboratory Medicine at **Mount Sinai Hospital** in Toronto, Ontario. He is also a Professor and Head, Division of Clinical Biochemistry, Department of Laboratory Medicine and Pathobiology, **University of Toronto** and Biochemist-in-Chief, Laboratory Medicine Program, U**niversity Health Network**, Toronto, Ontario.

After evaluating what is known about Theranos' technology, Diamandis wrote:

> *The following comments apply: The quality of the results are not known since the Theranos system has not been independently evaluated, nor do any published results exist to compare with conventional technologies. New diagnostic tests must be evaluated for their accuracy, precision, specificity and long-term robustness. Trueness and precision (accuracy) need to be maintained over months or years, and monitored by external quality assurance programs, so that patient's data can be directly compared over long periods of time. Without independent validation, Theranos technology's quality and robustness will remain in question.*

In an editorial in the same issue, CCLM Editor-in-Chief Dr. Mario Plebani describes Diamandis' work as the first scientific article to explore the diagnostic technology of Theranos. He wrote:

> *Diamandis raises serious concerns regarding the Theranos technology, maintaining that the system has not been independently evaluated, and as none of its results have appeared in the literature, it cannot be compared with conventional technologies. Nor has it provided evidence on the trueness, reproducibility, specificity, and long-term robustness of the innovative technology used; the finger prick process presents challenges because its commutability and correlation with traditional venipuncture has not been verified.*

Plebani is a full Professor of Clinical Biochemistry and Clinical Molecular Biology at the School of Medicine, **University of Padua**, in Italy. He is also Chief of the Department of Laboratory Medicine at the **University Hospital of Padua** and Chief of the Center of Biomedical Research.

JAMA Story About Theranos

Earlier in the year, John P.A. Ioannidis, M.D., the C.F. Rehnborg Chair in Disease Prevention at **Stanford University**, raised questions about Theranos in an article he wrote for perhaps the most prestigious peer-reviewed journal in the nation, the *Journal of the American Medical Association*. In his article, he explained that, because so little has been written about Theranos in peer-reviewed journals, scientists have not had the opportunity to evaluate its technology.

Ioannidis described the lack of peer-reviewed publications based on Theranos' technology as "stealth research," which "creates total ambiguity about what evidence can be trusted in a mix of possibly brilliant ideas, aggressive corporate announcements, and mass media hype." He also wrote that, "…unless stealth research adopts more scientific transparency, investors, physicians, patients, and healthy people will not be able to judge whether some proposed innovation is worth $9 billion, $900 billion, or just $9, let alone if the innovation will improve the health and well-being of individuals."

Microbiology Lab Handles 900,000 specimens yearly

Combining Lean with Lab Automation to Get Impressive Results

CEO SUMMARY: By combining total lab automation with Lean techniques in a comprehensive makeover of its microbiology lab, one of the largest labs providing hospital acute care and community microbiology services in North America achieved major benefits. Benefits ranged from improvements in lab result turnaround time and reduced errors to significant gains in staff productivity and the quality of lab test results. Productivity improvements allowed the micro lab to absorb a 15% increase in specimen volume while staff levels were reduced by six full-time equivalent MLTs.

Probably no area of clinical laboratory medicine is experiencing the dramatic transformation happening in microbiology. From rapid molecular testing to the full automation of traditional manual processes, significant changes are happening in microbiology labs.

Moreover, the smart use of Lean and quality management techniques magnify the positive effects of these new diagnostic technologies and automation in microbiology.

One early-adopter laboratory leveraging all of these trends to deliver more value with microbiology testing services is **DynaLIFEDx Diagnostic Laboratory Services** in Edmonton, Alberta, Canada. DynaLIFEDx was one of the first two labs in North America to implement total lab automation (TLA) in its microbiology lab and the first to go live in September 2013 with patient specimens being processed on the BD Kiestra TLA system from **Becton Dickinson** (BD). The DynaLIFEDx microbiology team concurrently used Lean to optimize processes in its microbiology department and obtain added productivity from automation.

Another notable aspect about this microbiology lab makeover is that it involves one of the largest microbiology laboratories providing hospital acute care and community patient services in Canada and the United States. DynaLIFEDx processes 900,000 microbiology specimens annually for more than 120 hospitals and health centers across Alberta, Saskatchewan, and the Northwest Territories.

Among the benefits DynaLIFEDx realized were improved turnaround time, reduced errors, standardization of specimen handling and processing, streamlined operating procedures, improved patient and staff safety, and enhanced antibiotic stewardship.

The metrics from the combined use of Lean and total lab automation are impressive. Productivity gains supported a specimen volume increase of 15%, in addition to MLT staffing reductions of six full-time equivalent positions over 18 months. Also, workflow in microbiology has become much more efficient. DynaLIFEDx expects to realize further staff reductions as the lab continues to optimize the TLA system, further improve workflows, and implement new features and components.

"We are a private laboratory within an integrated laboratory service and work closely with **Alberta Health Services,** the public health system," stated Norma Page, the laboratory's Vice President of Clinical Operations. "We provide anatomic pathology, microbiology, and a wide array of other lab testing, including referrals, consultation, and support services.

"From our large referral laboratory in Edmonton, and from labs we operate in regional and rural hospitals within Alberta, we service an area about the size of California," she continued. "We employ 1,200 professional laboratory staff, including 40 pathologists, medical microbiologists, biochemists and other medical laboratory specialists."

➤ Improving Quality and TAT

"We provide microbiology testing for dozens of hospitals including large acute-care facilities, and regional, community, and rural hospitals and health centers," she added. "Those hospitals don't have microbiology departments, but they do have rapid response or stat labs."

"Over the years, DynaLIFEDx has consistently had a forward-looking approach toward innovation," commented Page. "Consequently, we look first for opportunities to use new tools rather than increase the number of hands needed to handle the steady expansion in specimen volume along with increases in our scope of service. Because of our focus on innovation, we often realize big leaps forward when there are new opportunities in technology, automation, systems, or internal innovation.

"These management philosophies supported the major changes implemented in the microbiology lab. Late in 2012 we recognized a need to automate our microbiology department," stated Page. "Over 40% of the 900,000 microbiology specimens we test each year are for acute care patients. We saw the opportunity to combine automation

and new technologies with Lean to improve turnaround time, quality, and productivity.

"Our team started with a thorough analysis of the available automation options," explained Page. "We chose the BD Kiestra system because it had a multi-year track record in various labs in Europe and it offered more flexibility in terms of handling different specimen types. By comparison, other automated systems we considered were early in their development at that time.

"Our business case was approved in early 2013 and by September of that year we installed one of the first two BD Kiestra TLA systems in North America," she recalled. "Two months later, in November 2013, it was fully implemented."

"This microbiology automation system has changed—or facilitated changes—to almost every component of our Microbiology laboratory," said Page. "It does automatic plate barcoding, automated processing of liquid specimens, semi-automated processing of non-liquid specimens, and automated incubation and imaging.

Benefit Of Standardization

"One major benefit that came with this total laboratory automation solution is standardization," added Page. "For us, it allowed us to standardize many aspects of microbiology. This was important to us because our previous traditional microbiology processes were manual with significant differences from person to person and specimen to specimen. We had variations in operating procedures affecting everything from the size of the inoculum to how the plates were streaked and how long culture plates were actually in incubators.

"Perhaps the most interesting technology in the BD Kiestra system is how it uses magnetic beads to streak the plates," she stated. "Underneath where the culture plate sits, there's a magnet that drives the streaking pattern. A magnetic ball rolls across the media in various patterns spreading the specimen on the culture medium. We spent a lot of time determining which pattern was best for each specimen type. This streaking system optimizes colony isolation.

No Need For Subculture

"This is clinically important because when the colonies are isolated, our lab team can go directly to pathogen identification and then to susceptibility testing," continued Page. "Thus, it is not necessary to do a subculture, which reduces turnaround time and supports better patient care.

"That's the first key advantage: standardized culture plates," emphasized Page. "The module that does this process is BD Kiestra's InoqulA automated specimen handling system. It delivers standardized inoculum size, standardized streaking patterns by specimen type, and isolated colonies which support immediate pathogen identification.

"There are two sides to the InoqulA module," she explained. "The automated side takes any liquid specimen, removes the lid, picks up a defined volume of the specimen, inoculates the plates, sends the plates to the streaking system, and then transports them along the track to the incubator.

"The other side is the semi-automated section," stated Page. "We currently do not use this side because in Canada, as in the United States, microbiologists don't manually handle specimens except in a biological safety cabinet.

"We worked with BD to develop a biological safety cabinet (BSC) version, of the InoqulA," she noted. "The first one was installed at the **Royal Jubilee Hospital** in Victoria, British Columbia, and we will install ours in a few months. This customized BSC module gives us the same benefits of the standardized system but it can be used for plating as many as five specimens at one time or doing five plates on the same specimen.

"The second key advantage is improved plate management, and we consider this to

Combining Total Lab Automation with Lean Helps Microbiology Lab Reduce TAT and Errors

Traditional Microbiology	Primary Culture	Sub-Culture	Pathogen Identification	Antibiotic Susceptibility	Total time to Report
	1 – 2 days	1 day	1 day	1 day	4 - 5 days
Microbiology Automation	Primary Culture	Path ID and Susceptibility	Total time to Report		
	18-25 hours	20-24 hours	1.5 to 2 days		

Greater than 50% reduction in TAT

TWO TABLES ARE PRESENTED which show the improvements in turnaround time and error rates at the microbiology laboratory at DynaLIFEDx in Edmonton Alberta, after a new total laboratory automation system was installed and Lean methods were used to improve workflow. The table above shows how, with automation, DynaLIFEDx was able to reduce average microbiology test TAT from four to five days to under two days. The table at right shows the reduction in error rates for different processes due to automation.

Pre- and Post-Lean Error Rates	March 2012	March 2014
Labelling Error	28	0
Media Missed	18	1
Missed Information	16	5
Missed Order	14	0
Specimen Mix	14	4
Wrong Media Labelled	10	3
Plates Not Labelled	6	0
Total # Errors	**106**	**13**
Total # Specimens Processed	70,523	77,951
Total Error Rate	**0.150%**	**0.017%**

Source: DynaLIFEDx Diagnostic Laboratories, Edmonton, Alberta.

be a significant benefit of this automated system," said Page. "Prior to installing this automation, our microbiology lab had an average of 5,000-plus culture plates in motion on any given day. And multiple people handled many of those 5,000 plates. That's a lot of non-value added handling.

"Now our automated system does it all," she explained. "It barcodes the media, matches the specific specimen when it arrives, sends the inoculated media to the correct incubator (CO2 or O2), accurately times the incubation of the culture media, sends the plates for imaging at the ideal time, and pulls the plates out of the incubators when the specimen is completed and ready to be discarded. These processes are fully-automated and specimens are transported via the track system.

"The third key advantage is smart incubators," she said. "For each specimen type, we define standard incubation times to eliminate over-incubation and under-incubation. Both over- and under-incubation can interfere with colony isolation and pathogen ID. Moreover, the system tracks precisely how long every plate was incubated. We now know how old every colony is before we send it for susceptibility testing.

Incubators Get Smart

"Before we made these improvements, we ran a traditional microbiology lab," explained Page. "That meant the staff arrived in the morning and pulled that day's plates out of the incubators onto the bench. A substantial number of the plates were either underdone or overdone. This lack of standardization complicates processing as specimens move through the lab each day.

"In traditional microbiology labs, there are times when a pathogen may not be incubated optimally," noted Page. "Possibly it incubated for 13 or 14 hours when it

should have had 18 or 20 hours. Or maybe susceptibility testing was performed on an isolate without accurately knowing how many hours those colonies had been growing. Our automation and Lean workflow improvements have greatly reduced that source of error.

"Another benefit of our new automated workflow is that we no longer have cultures sitting on the bench instead of being incubated at the right temperature and in the right environment," she added. "With the TLA, plates are kept in the incubators—except for the brief periods when imaging or follow-up work is being performed. This adds a further layer of standardization and quality compared with previous processes.

"The fourth key advantage is digital imaging of the plates," explained Page. "Digital imaging enhances plate reading and provides a detailed audit of follow-up testing.

"We have a reading room where the technologists read the images and interpret the plates," she continued. "When reading these high-resolution images, they can circle a colony to work up and then use a series of codes to indicate what further testing they want and why. On average, it takes 37 seconds to read a plate and put all the indications on it for what needs to be done next—whether further work-up or susceptibility testing.

Seeing Impressive Results

"Our lab is like many microbiology labs today in that we do pathogen ID with mass spectrometry using MALDI-ToF (matrix assisted laser desorption ionization time-of-flight) technology which is capable of accurately identifying more than 2,200 bacterial pathogens," stated Page. "We use the automated Vitek MS from **Biomerieux** to complete the identification of a recognized pathogen in minutes. We have two of these instruments that fit nicely into our microbiology automation system workflow.

"All these improvements in microbiology workflow and standardization have generated another major benefit: improved turnaround time. TAT in microbiology can be improved dramatically compared to the TAT in a traditional microbiology lab," declared Page. *(See sidebar on page 13.)*

Traditional Micro Lab

"In a traditional microbiology lab working from 8 am to 4 pm, it typically takes a day or two to do the primary culture, depending on when the specimen arrived; potentially a day to do the subculture; a day to do the pathogen ID by traditional methods; and then another day for antibiotic susceptibility," she noted. "Thus, the total TAT for a positive specimen in a traditional system could be four to five days. Or, with a complex organism, it could take even longer to produce a final result.

"But now we have automated systems and our lab operates 24/7," observed Page. "Those factors reduce turnaround time and we also save time by having accurate incubation times. Further, we have significantly reduced the need to do a subculture. That means we can go directly to pathogen ID and susceptibility testing from the primary culture plate. That can save up to two or three days, supporting more rapid patient treatment."

Page acknowledged that the microbiology laboratory operates much differently today because of the use of Lean and automation to streamline workflows. "So many of our processes are different from how we handled specimens in early 2013," she said. "At that time, we did batch processing, manual labeling of media, and mostly manual plating.

"Formerly, there were wide swings in workload, and the average elapsed time to process a specimen from the time it was received in the lab was 180 minutes," she recalled. "A significant amount of rework and photocopying took place every day.

"Compare that to how we handle specimens now," continued Page. "We have single-piece flow with automated plate labeling and positive specimen identifica-

tion. Throughout the day, workloads have been leveled and the average elapsed time to process a specimen fell to 56 minutes. There was a huge reduction in duplication and rework. The net result was a 69% reduction in process lead time."

The new workflow and automation has benefited the lab staff as well. "Now we schedule the right number of people for the volume of specimens arriving in the lab," stated Page. "That has made a huge difference because no longer is one person overwhelmed by incoming specimens. Staffing matches demand, which has improved our lead time. For example, from the arrival of an unaccessioned specimen in the microbiology lab to being inoculated used to take about three hours. Now, with automation and the other changes we made, it takes less than one hour, saving two hours of turnaround time.

Dashboard Management

"One more advantage of the BD Kiestra system is the ability to manage many aspects of testing in real time via the dashboards and reports," she observed. "As an example, from these sources, we learned that 30% of our specimens arrive from midnight to 6 am every day.

"Using this information, we staggered our staffing to more precisely match incoming specimen volumes at given times of the day," noted Page. "Steady distribution of work improves TAT. Even with the longer incubation times required for chromogenic agars that we have implemented, we have realized faster TAT. For example, we saw reductions in TAT for MRSA by 7 hours; superficial wounds by 10 hours; urine testing by 5 hours; and VRE by 31 hours compared with a traditional microbiology lab without advanced automation.

"Error reduction has been equally impressive," continued Page, "especially as a result of single-piece flow in specimen processing.

"Another significant result was improved antibiotic stewardship," she stated. "This happened partly because we reduced the turnaround time and partly because the results are more accurate (through use of the MALDI-ToF analyzers)." TDR

—Joseph Burns

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Lean Had Major Role in Planning for Automation

"IT WAS IMPORTANT TO USE LEAN TO STREAMLINE WORKFLOW IN MICROBIOLOGY as we implemented the total lab automation project at DynaLIFEDx," stated Norma Page, the lab's Vice President of Clinical Operations. "To accomplish this, we used Lean approaches and tools to design the layout and the workflow. That required our team to change from the traditional 'batch mentality' to single piece flow in our specimen handling.

"As a first step, we built a mock microbiology lab before we got the new Kiestra automation," noted Page. "We did a cardboard mock-up of where all the equipment would go. We also matched the mock-up to the spaghetti diagrams that came from our value stream maps. We know that technologists hate making mistakes and so we wanted them to be successful. By having them build workspaces out of cardboard, not only was it fun, but it helped our technical staff be more confident about the changes that would be made.

"In the mock lab, we worked through different layouts and designs," she added. "For example, one day the single piece team was working on one option for a layout to see how it would look and function. We discussed an idea about a conveyor system. Several variants to this idea were tried in the mock-up lab and it was determined that they all fell short of required performance. This helped us avoid purchasing and installing equipment that was not going to succeed."

Managed Care Update

Hit by Many New Genetic Tests, Health Insurers Just Say 'No'

OVERWHELMED WITH REQUESTS TO PAY for new genetic tests, health insurers, particularly smaller and regional insurers, find it easier to simply deny payment for such tests.

This is one of the insights shared during a panel discussion involving several managed care executives at the 20th annual *Executive War College* that took place in New Orleans last May.

To this point, panelist Paul von Ebers, formerly CEO of **Noridian Mutual Insurance Company** (which does business as **Blue Cross and Blue Shield of North Dakota**), explained that medical directors for smaller health insurers such as regional Blue Cross plans and regional non-Blue plans, cannot keep up with the scientific developments behind genetic testing.

"One Blue Cross medical director told me that the science is changing so fast and so many new genetic tests are being offered, that he and his colleagues are just overwhelmed," commented von Ebers, who is CEO of **Prospective Health, LLC**, a consulting firm in Fargo, North Dakota. "When an insurer is not sure if it is paying for value, they make their best efforts to understand the science but the science is moving so fast that if they don't have enough evidence they'll deny it," explained von Ebers.

"As health plans manage costs and quality today, they are mostly concerned with improving patient outcomes," he continued. "That is why insurers are much less concerned about such lab metrics as turnaround time. By itself, that's not important to an insurance company. Instead, health plans want to know the scientific value of tests, meaning can a test produce a difference in clinical outcomes?

"Thus, any lab seeking to get health plans to pay for new genetic tests will need to show a relationship to clinical outcomes on a targeted basis," emphasized von Ebers. "This is linked to personalized medicine, which means that health insurers are not going to pay for broad-brush testing approaches. Insurers will only want to pay for targeted testing where clear clinical indications exist that each genetic test is going to help a particular patient and change the treatment pattern.

"When clinical labs seek payment for new genetic tests, insurers want to know whether the scientific literature can be used to support a lab's assertion that targeted testing will improve outcomes," von Ebers explained. "I've talked to health insurance medical directors around the country and find that, yes, clinical literature makes a difference.

Peer Review Required

"And, I would go one step further. If a test for a particular genetic variation has been demonstrated to be related to a patient's ethnic background, for example, then insurers will want to see evidence that the person being tested is from that demographic group," he continued. "In other words, giving a genetic test to all patients would be inappropriate when the test is best for particular patients with a specific ethnic background. So the scientific literature is important but there are usually more specific rules that go beyond the literature."

Affirming the need for medical evidence to guide appropriate use of genetic tests was panelist Richard J. Gentleman, Senior Director for National Contracting for **Aetna Inc.** in Blue Bell, Pennsylvania.

"Any literature used to support a particular test should be of high quality and peer-reviewed, noted Gentleman. "We use evidence-based guidelines, which means there's got to be a credible article published in a peer-reviewed journal.

"The challenge with molecular testing is that not every marker and not every panel is going to give a clinician a clear direction of what he or she needs to do for that patient," he added. "Not every genetic test provides a result that is actionable and where it is known that the action taken results in improved health outcomes for the member. Some tests have the potential to provide this value to patients, but they are too complex for the patient or the physician to know how to use them properly. Therefore, genetic counseling—which is not being used as much as it should be—needs to be a part of all discussions about genetic tests.

Use of Genetic Counselors

"Genetic counselors should be involved on the front end to explain to patients what genetic tests are available and clinically valuable to them and to help those patients understand their options. They also need to explain what the patient's health plan covers so patients can make informed decisions," he noted. "Aetna spends more than $1 billion annually on lab testing, and most of it is done in hospital-based labs. By contrast, very little genetic counseling is used to support testing, despite its availability as a covered benefit."

Panelist Lynne Currie, Senior Director Statewide Networks and North Florida Regional Market, for **Florida Blue** in Jacksonville, also emphasized the role of genetic counselors when genetic tests are involved. "There is not enough expertise within health plans to identify which molecular or genetic test is appropriate in which setting and for which patients, because it seems there is a new test introduced everyday. Further, one of our challenges in making genetic counseling available is that it is most frequently provided via teleconference, which isn't always a covered benefit.

Florida Toxicology Labs Drive Up Testing Costs

IN RECENT YEARS, EXECUTIVES at Florida Blue have seen growth in two worrisome trends, said Lynne Currie, Senior Director Statewide Networks and North Florida Regional Market, for Florida Blue.

"In Florida, toxicology labs seem to be coming out of the woodwork, and the administrators in these labs are finding innovative new ways to attract customers for toxicology testing," she stated. "In recent years, we've seen rapid growth in the number of 'sober houses.' Entrepreneurs in South Florida have converted empty condominium buildings into sober houses that are very closely tied to specific toxicology labs.

"These sober houses advertise in the Northeast, in Michigan, and in Indiana in the winter when it's cold and snowing. 'Wouldn't you rather be here for your drug rehab program in sunny Florida?' they ask. 'We have jet skis, volleyball.' The FBI raided one sober house that had advertised that its residents would use a million-dollar boat as part of their rehab," observed Currie. "These sober houses offer shuttle vans to take residents to local mental health counseling centers for Alcoholics Anonymous meetings.

"In many instances, the toxicology labs are doing full panel screenings every day—including quantitative and qualitative analysis—on the residents of these sober houses," added Currie. "We had one member from another Blues plan come to Florida and his lab spend exceeded the cost of a 30-day stay in the sober house!

"For our own Florida Blue members, we updated our guidance on the appropriate frequency for qualitative and quantitative testing and that helped to control the spending," noted Currie. "But we have many members from other Blues plans that don't have the rules we have. These out-of-network sober houses refer to out-of-network labs, making it difficult for us to control appropriate utilization."

"We need to come up with a solution to the genetic counseling problem, especially for esoteric tests," added Currie. "Health insurers need trained experts who are totally independent of labs but who are expert in gene sequencing to help insurers identify the clinical differences from one patient to the next and which genetic test might be right for one patient but not the other.

Expert Guidance Needed

"Also, health insurers need guidance from experts on when it is appropriate to use these genetic tests," she said. "For a woman diagnosed with breast cancer, when is it appropriate to have the BRCA test?

"Not every woman needs to have the BRCA test, but most women would rather have that test before a lumpectomy rather than afterward and then risk a second surgery," explained Currie. "With so many genetic tests, health insurers do not have the answers to these types of questions.

"How do we, as health plans, especially one as big as Florida Blue is in Florida, determine what is the appropriate test by the appropriate lab and the appropriate continuum of care that will change the clinical outcome for the member for the better?" asked Currie. "This is why health insurers ask for evidence of clinical effectiveness, especially such evidence that is published in peer-reviewed journals.

"With the limited resources we have, how do we balance coverage for genetic testing with the need to design benefit plans that keep costs down?" she continued. "Another issue is that some health insurers still have a few legacy plans that don't cover genetic testing.

"The reason those plans don't cover genetic testing is because, in the past, when there was a broad panel test, we would evaluate the panel and determine that those tests had no effect on a patient's clinical outcome," noted Currie. "But those rules are not relevant for personalized medicine, when a genetic test may have great clinical value for a small number of patients."

Turning to the practical aspects of payer guidelines for genetic testing in today's healthcare system, Gentleman noted that, "Of course, when anyone is denied coverage, that patient can appeal the determination. Each appeal is handled case by case because, at the moment, determining whether to cover genetic tests is very challenging for insurers. In order for Aetna to expand coverage to a new genetic test, it must be demonstrated in the published, peer-reviewed literature to be clinically valid and clinically useful.

"Additionally, Aetna is often asked to look at specific genetic tests that may have some clinical utility but that do not make a difference in how physicians treat patients," stated Gentleman. "For example, **Quest Diagnostics Laboratories** has a great test that can determine some level of risk for whether certain patients will have Alzheimer's disease.

"But what does a physician do with that test result that shows a patient has a marker showing he or she has a 5% chance of having Alzheimer's disease?" he asked. "Maybe for some people, that's a great test. But that information currently has no effect on the patient's treatment protocol."

Pathologists As Consultants

To address these issues, von Ebers suggested that pathologists could provide more consulting services to providers. "Pathologists could consult with health systems on appropriate ordering and appropriate use of tests, particularly in accountable care organizations," he said. "ACOs already need to develop national sources of expertise that they can share, just as Blue Cross plans have created national sources of expertise that they share." TDR

—Joseph Burns

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INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

In a milestone for advocates of digital pathology, an anatomic pathology laboratory in The Netherlands has been identified as the first in the world to "transition completely to digital diagnosis." The laboratory is **Laboratorium Pathologie Oost-Nederland** (LabPON), located in Hengelo. In a press release announcing the accomplishment, **Royal Philips** noted that, as "the largest pathology laboratory in the Netherlands, LabPON is consulted on more than 54,000 histological cases each year, which translates to more than 300,000 slides of human tissue. The 17 pathologists at LabPon have been using the Philips IntelliSite Pathology Solution since 2012 and used a "structured change management approach to full digital adoption"

MORE ON: *Digital Pathology*

In Europe, Philips' digital pathology system is CE-marked for primary diagnostics, as it is with Health Canada. In the United States, this system is cleared by the FDA "for diagnostic use in the evaluation of HER2 expression in breast cancer and is offered for research use (RUO)." The FDA has yet to clear a digital pathology system for clinical diagnostic purposes. That is one factor inhibiting the adoption of digital pathology in this country. The other is the lack of an effective digital pathology workflow solution that can contribute to improved pathologist productivity.

TRANSITIONS

- **Genova Diagnostics** of Ashville, North Carolina, appointed Christopher S. Smith as its new President and CEO. Formerly Genova's Vice President of Sales and Marketing, Smith has held executive positions with **Orchard Cellmark**, **LifeCodes**, and **Pathology Partners**.

- Ted Hull retired as President and CEO of Genova Diagnostics. Previously he held executive positions at **Quest Diagnostics Incorporated**, **Nichols Institute**, and **Deloitte & Touche**.

- On July 8, pathologist Ronald. D. Workman, M.D., died. From 2000 to 2013, Workman served **Sutter Health** in Sacramento, California, as its Vice President of Pathology and Laboratory Medicine. Previously, Workman held leadership positions at **St. Francis Health System** in Pittsburgh, Pennsylvania, and **Community Medical Centers** in Fresno, California, as well as with the **Compass Group**.

That's all the insider intelligence for this report. Look for the next briefing on Monday, August 3, 2015.