Volume XIX, Number 14 Monday, October 8, 2012

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

IOM Endorses Continuous Improvement, Lean

IT IS ONE OF THE IRONIES OF HEALTHCARE that it has taken the prestigious **Institute of Medicine** (IOM) more than three decades to fully recognize the necessary and essential role that continuous improvement and the associated disciplines of Lean, Six Sigma, and process improvement must play if the American healthcare system is to meet the challenges ahead.

On September 6, the IOM issued a report: "Best Care at Lower Cost: The Path to Continuously Learning Health Care in America." In many ways, this report excoriated the entire American healthcare system for taking inordinately long amounts of time to learn about innovations and service enhancements developed by non-healthcare industries and introduce them into healthcare.

Of course, this is not news to you readers. Over the past 17 years, these pages have often highlighted how progressive clinical laboratories and pathology groups have been first to adopt and implement an innovation developed by another industry, with ready acceptance by physicians and patients. And, consistent with the IOM's findings, despite tangible evidence that first-mover labs had raised the service and performance bar, few other labs proved interested in adopting those same innovations.

But now—at the highest levels of healthcare policymaking—the performance improvement worm may be turning. In its description of this report, the IOM writes that: "Achieving higher quality care at lower cost will require *fundamental commitments to the incentives, culture, and leadership that foster continuous 'learning'*... and "The product of the committee's deliberations, 'Best Care at Lower Cost,' ...points out that emerging tools like computing power, connectivity, team-based care, and systems engineering techniques—tools that were previously unavailable—make the envisioned transition possible... Applying these new strategies *can support the transition to a continuously learning health system*, one that aligns science and informatics, patient-clinician partnerships, incentives, and a *culture of continuous improvement* to produce the best care at lower cost." (Italics by THE DARK REPORT.)

To me, this message is unmistakable. American healthcare providers will be encouraged—and given incentives—to establish a culture of continuous improvement. This may be one reason why our upcoming *Lab Quality Confab*, to be held in San Antonio on November 6-7, is growing in size and participation. TDR

Process Improvement Coming to Healthcare

New publication by Institute of Medicine recommends continuous improvement mindset

CEO SUMMARY: One new byword coming to healthcare in the United States is the "continuously-learning healthcare system." At the upcoming* Lab Quality Confab *in San Antonio next month, lab managers and pathologists can learn more about how to achieve and sustain continuous improvement in their laboratory organization. Pathologists and lab managers who have been active practitioners of Lean and process improvement will be interested to learn about this new national call to action by the IOM.

IT APPEARS THAT CONTINUOUS IMPROVEMENT IN HEALTHCARE IS POISED to become the next policy priority of health policymakers. For many Lean and Six Sigma practitioners in the nation's laboratories, this is welcome news.

Powerful evidence of this development is the publication of a study titled "Best Care at Lower Cost: The Path to Continuously Learning Health Care in America" by the **Institute of Medicine** (IOM). The report was issued on September 6, 2012.

If this IOM report gets the same attention as "To Err Is Human" did back in 1999, then major changes lie ahead for all providers, including clinical labs and pathology groups. Among other things, this new IOM report declares that "by one estimate, roughly 75,000 deaths might have been averted in 2005 if every state had delivered care at the quality level of the best performing state."

Similarly, "To Err is Human" estimated that between 44,000 and 98,000 hospital patients died each year due to medical and other errors. Thus, the authors of "Best Care at Lower Cost" are putting down the same marker: patient lives are at stake if the healthcare system fails to drive out the sources of errors and mistakes that directly contribute to unnecessary deaths of patients.

Lab administrators and pathologists should consider publication of this IOM report as the opening round of a national campaign designed to move hospitals, physicians, and all providers to adopt and embrace an organizational culture of continuous improvement.

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

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

SUBSCRIPTION TO THE DARK REPORT INTELLIGENCE SERVICE, which includes THE DARK REPORT plus timely briefings and private teleconferences, is $14.10 per week in the US, $14.90 per week in Canada, $16.05 per week elsewhere (billed semi-annually).

The key term you are going to hear more about is the "continuously-learning healthcare system." This term is salted throughout the IOM report. Clinical laboratory testing may be front and center in the effort, as one example cited by the study's authors focuses on the patient experience with lab test results.

In one of its illustrations, the IOM report notes two facts about patients and lab tests. First, "20% of patients reported that test results or medical records were not transferred from one place to another in time for an appointment." Second, "25% of patients said their healthcare provider has had to re-order tests to have accurate information for diagnosis." (No source study identified).

However, the IOM pointed out that, "in other industries, online banking allows customers to view their entire financial history and conduct transactions in seconds." This contrast in how consumers access banking information versus getting lab test data and other diagnostic results is a direct challenge to healthcare providers.

A New Management Culture

In a concluding statement, authors of the IOM report wrote "The entrenched challenges of the U.S. healthcare system demand a transformational approach." They urge providers to adopt continuous improvement techniques and embed this management approach into the organization's daily culture.

The good news for many clinical laboratory administrators and pathologists is that their respective lab organizations already have established some type of ongoing process improvement or continuous improvement program. Often these programs are anchored in the methods of Lean, Six Sigma, and a quality management system (QMS) like ISO 15189.

Further, there are many examples of hospital or health systems where the clinical laboratory was first to adopt Lean and process improvement methods in its workflow. As the benefits from these improvement projects became known, the lab's process improvement team was often asked to work with other clinical service departments within the hospital.

Learning About Lean

For lab managers and pathologists wanting to learn more about continuous improvement, the upcoming Sixth Annual *Lab Quality Confab* will take place in San Antonio, Texas, on November 6-7. (Visit *www.labqualityconfab.com.*) More than 50 speakers will participate in 40 sessions—all focused on effective use of Lean and process improvement methods.

For example, at **Henry Ford Health**, in Detroit, Michigan, the anatomic pathology department is working to achieve the Lean goal of single piece/small batch workflow in both the histology laboratory and with the surgical pathologists. Richard Zarbo, M.D., Chair of Pathology & Laboratory Medicine, will speak about the remarkable progress his team is making to achieve this goal.

One lab that is a leader in the deployment of QMS is **Laboratory Corporation of America**. LabCorp now has five lab sites accredited to CAP 15189. Kathy McCloy, Quality Assurance Director, will conduct a special session to share how the adoption of the 15189 QMS is helping these five 15189-accredited labs reduce errors, speed lab test turnaround times, and better meet client expectations.

Head Start At Lab Confab

Given publication of this new IOM report, it would be timely for all clinical labs and pathology groups to send their management and staff leaders to *Lab Quality Confab* next month. It is a unique opportunity for them to acquire needed skills while learning from case study presentations and networking with other lab professionals already committed to achieving the continuous learning culture in their labs. TDR

More IVD Consolidation As Danaher Acquires Iris

Danaher to pay $338 million to buy Iris in a transaction expected to close by year's end

CEO SUMMARY: Danaher Corporation continues to fuel growth by continually acquiring* in vitro *diagnostics (IVD) companies. Its latest purchase is Iris International, which manufactures automated urine microscopy systems. Danaher also has $5 billion available that it could spend in the next two years on acquisitions. Because of its acquisitions over the past decade, Danaher now generates a combined $6.4 billion in annual revenue just from its life sciences and diagnostics business units.

IT'S THE LATEST BIG ACQUISITION among major *in vitro* diagnostics (IVD) companies. **Iris International, Inc.**, of Chatsworth, California, has agreed to be acquired by **Danaher Corporation** of Washington, DC.

Announced last month, Danaher will pay a reported $338 million for Iris and the deal is expected to close by year's end. Iris is a major player in automated urine microscopy and chemistry systems. It has placed 3,800 such systems in 50 countries and had revenue of $118.3 million for 2011.

IVD Consolidation Trend

Danaher's purchase of Iris is notable for lab executives for two reasons. First, this deal is the latest example of ongoing consolidation within the IVD industry. Such acquisitions leave fewer companies to compete for the business of clinical labs.

Second, this purchase continues Danaher's own IVD acquisition binge. Its IVD purchases began in 2003, when it paid $730 million to acquire **Radiometer**. In 2005, Danaher did not have a Life Sciences & Diagnostics division. However, since that date, the company has spent almost $9 billion to acquire **Leica Microsystems** (2005), **AB Sciex** (2010), **Molecular Devices Corporation** (2010), **Beckman Coulter Corporation** (2011), and now Iris International.

By following this business strategy, Danaher Corporation has joined the ranks of the largest IVD companies. For 2011, its combined life sciences and diagnostics business generated $6.4 billion in revenue. In fact, Danaher is one of three companies which have become IVD heavyweights in recent years by doing serial acquisitions.

The other two companies with fast-growing IVD businesses are **Alere, Inc.** (formerly **Inverness Medical Systems**), of Waltham, Massachusetts, and **Hologic, Inc.**, of Bedford, Massachusetts. For 2011, revenue from their diagnostic divisions was $1.7 billion and $566 million, respectively. *(See sidebar on page 6.)*

Financial analysts commenting on these IVD acquisitions are generally bullish on the prospects for the IVD industry. They put forth three reasons for this opti-

Inverness Medical Systems Morphs into Alere As It Regularly Snaps Up Various IVD Companies

BY FOLLOWING A STRATEGY of serial acquisitions, Alere, Inc., has built its diagnostics business into a billion-dollar powerhouse. As noted elsewhere on these pages, along with Danaher Corporation and Hologic, regular acquisitions allow these three companies to consistently build market share and revenue for their respective *in vitro* diagnostics (IVD) businesses.

For Alere of Waltham, Massachusetts, (formerly Inverness Medical Systems), 2003 was the seminal year in its IVD acquisition strategy. Alere began a string of purchases that one analyst describes as an "acquisition rampage." Reflecting strong growth through acquisitions, Alere's company-wide net revenue grew by 11% last year from $2.1 billion to $2.4 billion, **Hoover's** reported. About $1.7 billion of this is from its diagnostics businesses.

Alere already had a significant presence in the point-of-care testing business when it spent $375 million last year to acquire **Axis-Shield**. This UK company develops point-of-care diagnostic tests for bacterial and viral infection, cardiovascular disease, and diabetes.

In 2010, it purchased a majority interest in **Standard Diagnostics** of Korea, a company that makes reagents for diagnosing infectious disease. Also in 2010, Alere paid $263 million for **Epocal**, which makes blood analysis systems. Epocal adds to Alere's portfolio of point-of-care diagnostic testing products for use at the bedside, in physicians' offices, and in hospitals.

Also that year, Alere bought **Kroll Laboratory Specialists** for $110 million and renamed it Alere Toxicology Services. Alere added to this division when it spent $270 million for **eScreen**, a company that makes optical scanning systems to analyze urine samples and report results within minutes.

In the previous year (2009), Alere spent $76 million to buy **Concateno**, a company in the UK that makes drugs-of-abuse tests.

The big acquisition was in 2007. That is the year that Alere out bid Beckman Coulter to purchase **Biosite Incorporated** for a purchase price of $1.7 billion. *(See TDR, April 23, 2007.)* Also that same year, Alere bought **Cholestech Corporation** for $326 million.

mism. First, the population of the United States and other large developed countries is aging. This will create an increased demand for clinical laboratory testing.

Second, financial analysts point out that the emphasis on preventive measures in healthcare will be a future driver to the utilization of lab tests. More lab tests will be ordered as physicians strive to detect disease earlier and to monitor patients with chronic diseases.

Third, Congress passed the Affordable Care Act in 2010, and one element of this legislation is to provide health insurance coverage to 30 million Americans who are currently uninsured. Financial analysts expect that the utilization of lab tests will increase as physicians begin to provide care to these newly-insured patients.

It is because of these market trends that IVD companies have the capital they require to fund their acquisition strategies. In turn, the ongoing pace of IVD acquisitions means that clinical laboratories often find fewer sources for the lab instruments, reagents, and consumables they need to purchase.

THE DARK REPORT believes that the pace of acquisitions within the IVD sector will continue. Moreover, the pattern is one of a conveyor belt. Small IVD companies emerge with innovative technology and products. As they grow and add to their market share, they become attractive acquisition candidates for the larger IVD companies. That is another reason why more IVD acquisitions can be expected. **TDR**

—By Joseph Burns

CDC Surveys Docs' Use of Laboratory Test Results

Physicians identify challenges associated with lab test ordering and result interpretation

CEO SUMMARY: There's a treasure trove of information and insights about how physicians use clinical laboratory tests contained in survey data recently collected by a team from the Centers for Disease Control and Prevention. Designed to identify challenges in how physicians utilize laboratory tests, the survey findings offer a road map about how innovative clinical labs could deliver added value to physicians, particularly in providing consultative services and better access to laboratory expertise.

RATHER THAN CONSULT with laboratory professionals, referring physicians almost always seek other sources of information when uncertain about clinical laboratory test results. This is one significant finding of a survey conducted by the **Centers for Disease Control and Prevention** (CDC).

The survey has other useful insights for lab administrators and pathologists interested in learning how to deliver more value to physicians. Among other findings, the survey reveals that physicians have many frustrations when they seek to get certain types of information and support from clinical laboratories.

The survey was conducted by the CDC's Division of Laboratory Science and Standards (DLSS), Clinical Laboratory Integration into Healthcare Collaborative (CLIHC). Data from focus groups of primary care physicians served as the basis for questions in the survey. Responses were gathered from 1,700 primary care and internal medicine physicians. Results are being analyzed and will be published in a peer-reviewed journal.

THE DARK REPORT asked the CDC about the results and received replies by email from Julie Taylor, Ph.D., Project Lead for CLIHC. Her responses are the basis of this article.

One goal of the survey was "to explore the challenges in laboratory test selection and result interpretation [by primary care physicians] with potential strategies to address those challenges," wrote the CDC. Among other notable insights, the survey determined that physicians tend to go to other sources of information before reaching out to their laboratory testing provider.

Docs Consult Other Sources

"When clinicians experience uncertainty about test ordering and result interpretation, they reported that they consult many resources before asking a laboratory professional," noted the CDC in its written answer to THE DARK REPORT. "The results showed they frequently review published references (electronic and/or paper) and guidelines, refer the patient to a specialist, or see how the patient's presentation evolves. Consultation with a laboratory

professional was the least frequent approach."

This finding is certainly a challenge for clinical laboratories. Physicians reported that they consistently went to other sources *before* they would then contact a clinical laboratory professional. However, this situation is also an opportunity, because it shows that once physicians receive a patient's lab test results, they actively look for additional information to develop their diagnosis and come up with an appropriate treatment plan for the patient.

The CDC's survey identified other challenges that physicians have in their relationship with their laboratory test providers. "The most problematic challenges reported with test ordering were related to the cost of laboratory tests (to the patient), lack of comparative information, and insurance limitations," noted the CDC.

Lack Of Uniformity

It will be no surprise to clinical pathologists that the clinical laboratory industry's general lack of uniformity is a problem for physicians. Survey results showed that "other challenges were test panels from different laboratories comprised of different tests, confusion over different test names for the same test, tests that were not available, and conflicting recommendations from different guideline-development organizations.

"Physicians reported they usually review the patient's history and follow-up with the patient when they are uncertain about test result interpretation," continued the CDC. "They expect the laboratory to deliver data. Not receiving results quickly and a lack of previous results were reported as the most problematic issues in result interpretation while difficulty communicating with the laboratory professional was less problematic."

Less complimentary to the laboratory medicine profession are survey responses by physicians that confirm their reluctance to engage clinical pathologists and laboratory scientists for one-on-one consults and conversations about patients and laboratory test results. Survey responses indicate that physicians don't see their lab test provider as an easy source to tap for clinical expertise.

Assistance Not Forthcoming

The CDC wrote that, when referring physicians communicate with laboratory professionals, they do so, "primarily to determine the status of missing results or to obtain preliminary result information. Clinicians infrequently reported communication with laboratory professionals for assistance with follow-up testing or to obtain a medical opinion of test results."

There were some positive aspects about how physicians utilized clinical lab testing resources. "Most survey respondents reported reflex testing, result trending, and interpretive comments were readily available and were useful means for test result interpretation," said the CDC. "Computerized physician order entry (CPOE) with electronic suggestions was least available but moderately useful."

Respondents found these additional lab testing resources to be useful: 1) access to test performance characteristics; 2) a dedicated laboratory phone line for questions; and, 3) clinical testing algorithms. "Lab usage may improve as clinicians have better access to decision support tools," commented the CDC.

Lab Test Interpretation

In the all-important area of interpreting lab test data and developing an action plan, the CDC said that, of referring physicians surveyed, "They primarily utilize electronic/paper references and guidelines, among other methods, when they are uncertain about test ordering. They go back to the basics of care and review information about the patient when they are uncertain about test result interpretation."

Clinical laboratories did not get high marks in how they supported clinicians

with consultative services. "The clinicians responding in our survey did not readily contact the laboratory professional when unsure about test ordering or test result interpretation," wrote the CDC.

Reinforcing this point, it was noted that "one primary care physician in the focus group said, 'You don't talk to a radiologist or pharmacist in a hospital, you talk to a colleague. [But when] you talk to a lab, it's a black box…' When they do communicate with laboratory professionals, the [survey] results show it is primarily to determine the status of missing results or to obtain preliminary result information. Clinicians infrequently reported communication with laboratory professionals for assistance with follow-up testing or to obtain medical opinion of test results."

Daily Clinical Relationship

This early peek at the survey results—prior to the planned publication of a full assessment of the survey and focus groups in a peer-reviewed publication—confirms that there are important gaps in the daily clinical relationship that clinical laboratories have with primary care physicians. Understanding these gaps is a necessary first step before they can be fixed.

This is consistent with the goals of the CDC's survey, which was not designed to ask physicians about how they use laboratory testing in their practices, "but rather to obtain information about what challenges physicians face in test ordering and result interpretation and the resources physicians frequently use to address those challenges."

Innovative clinical pathologists and lab executives who want to position their laboratory organizations at the leading edge of clinical excellence will find much that is useful in the information generated from this CDC survey. Probably the single most useful insight is that—after physicians receive the lab test results for a patient—they spend time accessing other sources, not laboratory professionals, for clinical knowledge. It means that the first call they make with questions is *not* to their clinical pathologist or laboratory scientist. Labs should view this survey finding as an opportunity to change the status quo.

Opportunities For Labs

As healthcare evolves toward new models of integrated clinical care, the insights generated by this CDC survey of the challenges physicians encounter with lab testing can be a useful road map for the lab testing profession. The survey results show opportunities for clinical laboratory professionals to work more closely and productively with referring physicians. More will be reported on this survey when the full presentation is published. TDR

—By Joseph Burns

Contact Linda Carnes at 404-717-6277 or lxc3@cdc.gov.

CDC Survey Sought Insight on PCP Practices

IT WAS LAST YEAR when the Centers for Disease Control and Prevention announced that it wanted to investigate how the rapid evolution of laboratory medicine was affecting primary care physician practices. To do so, it reported in the *Federal Register* the intent to conduct the "Quantitative Survey of Physician Practices in Laboratory Test Ordering and Interpretation."

"This proposed survey follows a series of qualitative focus groups with primary care physicians that identified common concerns and problems with laboratory test ordering and test interpretation," the CDC said in its *Federal Register* announcement. "This survey will quantify the prevalence and impact of the issues identified within the focus groups. Understanding the relative importance of physician issues in the effective and efficient use of laboratory medicine in diagnosis will guide future efforts of the CDC to improve primary care practice and improve health outcomes of the American public."

Labs will handle vast amounts of genetic data

Unprecedented Growth Rates for Molecular Testing

➤➤ *CEO SUMMARY: There will be an expanding role for innovative clinical labs as healthcare moves forward on its path toward personalized medicine. However, to capitalize on this opportunity, pathology groups and clinical labs will need to beef up their information systems. They will also need to recruit lab staff who are skilled in interpreting molecular and genetic test data expressly to advise and consult with referring physicians. One experienced industry consultant predicts that oncology will be the first medical specialty to make extensive use of molecular and genetic testing in this way.*

Genetic testing is poised to transform medicine and foster unprecedented growth in molecular diagnostics. At the same time, most clinical labs and pathology groups are unprepared to deal with the informatics overload that is heading their way.

That is the prediction of Katherine Tynan, Ph.D., President of **Tynan Consulting, LLC**, in San Carlos, California. Her firm provides strategic business planning for diagnostic and pharmaceutical companies that are developing molecular and companion diagnostics, including product development and pricing, reimbursement, and market entry strategies.

"It takes less time now for advances in molecular diagnostics to find acceptance in clinical use," observed Tynan. "This spring the **American College of Medical Genetics** issued a practice guideline suggesting that whole exome sequencing and whole genome sequencing be used for the diagnosis of idiopathic pediatric cases.

"As such testing moves into the clinical front line, labs will see a potential avalanche of data coming at them," she noted. Tynan was speaking at The Dark Report's *Executive War College* in New Orleans in May. "This will require a significant response by clinical laboratories," she added.

"To make clinical use of the vast amounts of data generated by these types of diagnostic tests, labs will need to do two things," she advised. "First, labs must hire specialists in molecular medicine so that they can advise and consult with treating physicians on the results of these tests. Second, labs will need to invest in more robust information systems to store and analyze the data produced by molecular and genetic tests.

"Many pathologists may be aware that a large managed care company recently assessed how much money would be spent on molecular diagnostics in the next five to 10 years," Tynan said. "**UnitedHealthcare's** report, *UnitedHealth Center for Health Reform and Modernization 2012,* noted that spending on molecular diagnostic services is currently in the range of $6 billion to $8 billion per year," she said. "The report predicts such spending will climb to $15 billion to $25 billion by 2021.

"Pathologists and molecular scientists will be at ground zero in this trend," predicted Tynan. "As molecular medicine grows, one major driver in this spending will be the expanded use of tumor genome profiling. This trend is being driven by relatively cheap sequencing and the biological understanding that cancer, for the most part, is an acquired somatic genetic disease. Deriving value from this spending will require clinical labs to re-evaluate workflow and how they interact with referring physicians.

➤Re-Evaluating Workflow

"As they re-evaluate workflow, clinical labs and pathology groups will recognize the need for two significant investments," commented Tynan. "First will be the need to invest in more robust information systems.

"That is because the existing information technology (IT) infrastructure used by many clinical labs and pathology groups today will struggle under the avalanche of data generated by molecular and genetic testing," she added. "Fortunately, information technology is getting faster, better, cheaper—and it will continue to do so.

"Second, and of greater importance, is the need for labs offering molecular diagnostics to invest in more sophisticated clinical expertise," continued Tynan. "Few of the 17,000 pathologists working today have been trained in molecular pathology.

"That is why demand for pathologists who are board-certified in molecular pathology will outstrip the supply for many years to come," she said. "Laboratory medicine must respond with different ways to encourage more lab professionals at all levels of certification to train and work in molecular pathology and genetic testing.

"Another problem exacerbates these two deficiencies," stated Tynan. "The business models are not defined in this space. This is true for clinicians delivering gene-based medical services as well as the pathology laboratories that provide them with molecular and genetic testing.

Financial Incentives

"In addition, financial incentives and reimbursement are not yet in alignment," she declared. "As a member of the Economic Advisory Committee for the **Association of Molecular Pathology**, I can say that workable solutions for each of these significant issues have yet to be developed.

"There are several reasons why the financial incentives are not aligned," said Tynan. "Many types of molecular tests come with a very high cost, as do some targeted therapies. Payers have yet to address this new clinical use of expensive companion diagnostic tests with expensive therapies. And the future will only see an increase in the number of high-priced genetic tests and targeted therapies.

"But if patients can't afford one of these expensive interventions now, how can they possibly afford a cocktail that includes several of these expensive medications?" asked Tynan "This question will be particularly problematic if combinations of targeted treatments are required earlier in the care cycle to minimize resistance or if the treatment of cancer makes it a chronic disease, as many experts believe will be the case.

Opportunities For Labs

"Along with these significant challenges, however, will be opportunities for pathologists and clinical lab professionals," she added. "Within the next three to seven years, labs will need to hire expert intermediaries who can interpret and integrate the data produced by genetic and molecular testing. One positive aspect of this development is that we are approaching an inflection point where pathologists could play a significant role in changing how medicine is practiced."

Tynan was very specific in her recommendations about the skills and capabilities that clinical labs and pathology groups should be developing. "Good decision support tools are years away," she observed. "Thus, in the short term, labs will rely on expert intermediaries who can take that genetic and molecular information and derive the valuable clinical insights that help the referring physicians.

"At the same time, labs also need to give their IT departments the capabilities to handle and combine numerical, morphological, molecular, and image data so this information can be presented in a single report," Tynan explained. "Oncologists cannot do this for us.

Oncologists Are Overloaded

"In fact, it's already incredibly difficult for oncologists to keep up with developments in the literature," she observed. "It will be high value-added for pathologists and molecular geneticists to deliver that information to oncologists in a digestible format so they can make treatment decisions for their patients.

"Having explained the challenges that labs face as genetic medicine and molecular diagnostics become more sophisticated, it will be helpful to remember how laboratory medicine got to this point," noted Tynan. "Current treatment protocols for HIV offer a useful example.

"It is now common that, during the course of treatment for an HIV-positive patient, a sample will be collected and sent to the lab for sequencing," commented Tynan. "Medications will be adjusted based purely on the genotype of the virus. And, as the virus acquires resistance to certain therapeutic drugs, the patient's mix of different medications will be changed appropriately.

"In many ways, the treatment model for patients with cancer will be similar to

Predictions Are That Oncology Will Evolve To Manage Cancer Like a Chronic Disease

CLINICAL LABS AND PATHOLOGY GROUPS are positioned to play ever more important roles as personalized medicine becomes a reality, particularly in oncology. That's the prediction of Katherine Tynan, Ph.D., President of Tynan Consulting.

"Personalized medicine will expand the role of laboratory professionals," she stated. "One role will be the classic opportunity to assist oncologists in diagnosing disease. Another role will be in helping oncologists to manage the long-term care of patients dealing with a chronic disease.

"If we're truly successful with personalized medicine, then cancer will become a manageable chronic disease," explained Tynan. "In this scenario, if pathologists are not engaged in working with oncologists in molecular diagnostics, then those pathologists will not be involved in the lifetime treatment and the lifetime testing of that patient.

"This will occur because it will be necessary for laboratories to identify the individual molecular signatures specific to each patient's disease," she added. "The tip of this iceberg today is circulating tumor cells (CTCs). However, disease markers that are even more specific are on the horizon.

Translational Medicine

"Oncologists will want to run tests to check those signatures every few months to monitor patient response and disease progression. If your lab is not involved in establishing that molecular signature, your lab won't be involved in the ongoing testing required to provide future care to that patient.

"Progress can be seen in published studies," noted Tynan. "One example is an article from the *New England Journal of Medicine* about a group of physicians and other providers at the **Johns Hopkins School of Medicine** (*NEJM 364:4 Jan 27 2011*).

"The authors described how individual molecular signatures were identified at the time of disease diagnosis, then were used to monitor disease over time," she explained. "This approach allowed them to get early insight into disease recurrence. This knowledge was used to change that therapeutic intervention and bring the disease back down to a more manageable state.

Translational Medicine

"Similar progress is being made in other translational medicine programs," continued Tynan. "One study published in *Translational Medicine* (Sequist et al., *Sci Transl Med* 3 75ra26 (2011)) described how a handful of patients carrying specific EGFR mutations acquired resistance via two independent pathways. One pathway was an additional EGFR mutation which interfered with binding of the drug to the receptor. A second pathway were mutations in PIK3CA that resulted in a morphological shift to a mesenchymal cell type that responded well to chemotherapy.

"In each case, by virtue of having the molecular definition of disease, the researchers could alter the treatment and reduce the tumor burden," she explained. "Technically, it wasn't a stasis on the disease but rather resistance or insensitivity developed to a drug. As was reported, the tumor could flip back and forth between being sensitive or insensitive to TKI's.

"These examples show the progress clinicians are making in treating these diseases," noted Tynan. "At the same time, this progress is opening new doors for pathologists and laboratory scientists to provide greater clinical value to physicians."

how we treat patients with HIV," continued Tynan. "Genetic insights now give us deeper knowledge about the taxonomy of different types of cancer. In turn, this allows us to transform treatment based on the taxonomy of disease.

"You will see a shift in the conversation about breast and prostate cancer, for example," she noted. "This will come with better understanding of the specific pathways that are disrupted, along with the specific molecular drivers that drive those particular cancers. After all, cancer is an acquired somatic genetic disease.

Cancer Is Complex Disease

"The problem with cancer is that it is far more complex than many other indications," she said. "Disease heterogeneity is enormous, and this is reflected in complete sequencing data of supposedly discrete cancer states," explained Tynan as she showed data from 25 ovarian cancer patients. "This creates challenges in how to interpret the information produced from genetic and molecular tests.

"That development has a practical consequence," she added. "It means that any pathologist or molecular medicine physician working on a case will need to add a data integration step to the workflow in the lab. The laboratory professional will need to do data integration *before* communicating results to the treating physicians.

> ***"It means that any pathologist or molecular medicine physician working on a case will need to add a data integration step to the workflow in the lab."***

"To illustrate this trend, let me provide you with the hypothetical example of a female patient with non-small cell lung cancer," said Tynan. "This example will give pathologists and clinical lab managers a sense of how cancer treatment is evolving. It will also help me describe how genetic medicine and molecular testing is going to require laboratories to integrate service lines and use information technology in more intense ways.

"Assume the patient relapses 12 months after her initial diagnosis of cancer," noted Tynan. "She was being treated with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs). When the oncologist believes her therapy needs to be changed, he or she will ask, 'what is the best course of action?'

"When treating this patient today, for obvious reasons the oncologist has few options," commented Tynan. "First, many cancers are poorly understood and most treatment guidelines are based on tumor tissue of origin or histopathology.

"Second, lab medicine has a limited number of molecular diagnostic tests directed toward targeted therapies," she said. "Third, the standard of care is population-based medicine—the 'one size fits all' principle that has been the foundation of medicine for decades.

Multiple Limiting Factors

"Despite these limiting factors," continued Tynan, "our female patient actually is fortunate because her non-small cell lung cancer has been identified with an EGFR mutation. That makes her eligible for a TK inhibitor. But now her disease has relapsed and she's entering into a period of uncertainty.

"She likely has a multitude of physicians and connection points to the healthcare system," added Tynan. "This huge care team is deciding which tests to order, how those tests should be interpreted, and how those tests should be integrated into her course of treatment.

"These are complex issues," she stated. "Additional complexity comes from the fact that the patient has multiple physicians and there are arbitrary discipline boundaries between them.

"In this example, when the original biopsy was taken, it was sent to the anatomic pathology laboratory where it was reviewed by the pathologist," she stated. "Then it was sent to the clinical pathology lab where the patient's materials had to be marked, micro-dissected and go through the process of being tested for an EGFR mutation.

Advances in Molecular Testing Give Labs New Ways to Support Physicians, Patients

PATHOLOGISTS SHOULD KEEP IN MIND that the clinical services Katherine Tynan discussed in these pages are already available.

"Currently, targeted oncology gene panels are available at many academic medical centers," she said. "While the cost of this care is high, costs for sequencing and instruments are coming down rapidly. Reagent costs are already relatively low.

"Therefore, we will see more oncologists requesting this type of testing so that they can make ongoing treatment decisions," added Tynan. "One academic medical center has a personalized oncology pilot program that takes about 27 days to complete. They have a sequencing tumor board that discusses and interprets the findings in the context of the patient's clinical presentation.

"Pathologists who believe such work is prohibitive because of high cost will be surprised to learn that this work-up can now be done for $3,600—a dollar amount that is well within the range of many tests in clinical use today," emphasized Tynan.

"The cost of sequencing is no longer a significant barrier when you consider that the typical work-up cost for a leukemia patient is $3,400," she concluded. "The cost of interpretation and data integration in a typical hospital outside of the major academic medical centers is the big unknown. This is one opportunity for local pathologists."

"Questions that arise include: Should we re-test the original biopsy for additional mutations? Can we request a new biopsy? Are there blood-based markers that might inform this next treatment decision analysis?" noted Tynan. "These questions demonstrate how the treatment of cancer will be more complex, along with the need to manage the patient on a longer term basis, like someone with a chronic disease.

Reordering Boundaries

"I would argue that discipline boundaries in medicine today are becoming less relevant because all these steps described above are part of one field—that of molecular medicine," observed Tynan.

"The point is that this current model is unsustainable and that's where the opportunity lies for pathologists," she emphasized. "The iterative testing we do today involves moving samples around and issuing individual reports at various stages.

"Without a sophisticated level of data integration, we pile cost upon cost," continued Tynan. "Current processes and workflows are not particularly helpful for moving the treatment decision forward.

"Consider how different this patient's care will be in three to five years," she said. "Now a rising number of patients—such as this woman—will benefit from more comprehensive molecular diagnostics that repurpose existing and emerging therapies. We'll have a deeper understanding of molecular pathways that drive confidence in those treatment recommendations.

"The combination of mutations and other test findings will be very specific to the individual patient," continued Tynan. "Some of these markers will be actionable and some may not be actionable. The pathologists working with these markers will be aided by very small, clinical studies that will group these patients together.

"This is where information systems become critically important," emphasized Tynan. "It will be incumbent upon us to prospectively track outcomes in these patients because the groups will be narrowly defined based on their molecular profiles. That's the reality of personalized medicine.

"Here is the important change in laboratory medicine," emphasized Tynan. "Going forward, therapy based on tissue of origin will give way to therapy based on a particular pathway or combination of pathways disrupted.

"That is why, in the age of personalized medicine, we need to retain that information for future data mining," she said. "This is the information that helps us understand how the diagnostic testing and the course of treatment benefited individual patients.

Looking Ahead 10 Years

"In seven to 10 years, we will have a deeper understanding of our patient's non-small cell lung cancer and her physician will make more precise decisions about her care," she continued.

"This care will be more precise because we will no longer have a one-size-fits-all approach," she said. "Molecular data from multiple biomarkers will allow pathologists to prepare a list of treatment options.

"Remember that smaller cohorts of patients will generate the rules that physicians will use to prescribe an expanded selection of targeted drugs," observed Tynan. "Clinical labs will need to offer the range of diagnostic tests required to support these therapeutic decisions.

"Expect to see studies produce a growing number of defined molecular signatures that physicians will use to monitor each patient's disease as she/he progresses through treatment," she said. "Testing for molecular signatures expands the lab's role and creates an ongoing clinical relationship with the referring physician.

"Also at this point in the future, I anticipate there will be knowledge databases tracking inputs and outcomes," said Tynan. "There will also be automated interpretation and decision making systems.

"At the 10-year mark, if we don't have systems such as **IBM's** Watson helping us, then we're never going to keep up," she confided. "The rate at which the information is being generated in this field far exceeds our ability to read the literature and stay up to date with it.

"To summarize, laboratories should view these developments in the following time frames," advised Tynan. "During the short-term—meaning three to five years—a deeper understanding of biological pathways will occur that drives new treatment options.

"In turn, this new knowledge will give physicians more confidence in their treatment recommendations," she commented. "Growing numbers of patients will benefit from diagnostics that repurpose existing and emerging therapies. Using these therapies in combinations will become the standard of care. Oncology will be the first medical specialty where these approaches become well-established.

"In the longer term—say seven to 10 years—both labs and clinicians will have access to richer sets of data on patient populations," continued Tynan. "These data will be generated from patients treated by targeted therapeutic interventions.

Two Changes For Labs

"Finally, to serve this evolution in personalized medicine, clinical laboratories and pathology groups will need to make two changes discussed earlier," she stated. "The first is to build a more robust informatics capability to analyze and manage vast quantities of molecular and genetic data and track patient outcomes.

"The second is to hire molecular pathologists and molecular scientists to work with clinicians to interpret the data and help them identify therapeutic options," Tynan concluded. "As this process moves forward, it is likely that one shift in laboratory medicine will be to use individual molecular signatures to track disease and support less-invasive patient monitoring." TDR

—By Joseph Burns

Contact Katherine Tynan, Ph.D., at 650-207-9172 or ktynan@halteresassociates.com.

Lab M&A Update

Ampersand Buys Calloway Labs, Enters Pain Management Market

Acquisition gives Ampersand a stake in lab test niche that has had Medicare/Medicaid compliance issues

URINE DRUG TESTING for pain management may be a challenging business for clinical labs given that compliance officers in the states and in the federal government have successfully pursued lab compliance abuses in this line of business in recent years.

Now comes news that private equity firm **Ampersand Capital Partners** of Wellesley, Massachusetts, is to acquire **Calloway Laboratories Inc.**, a company in Woburn, Massachusetts, that offers pain management and drugs of abuse testing services. The deal was announced last month, but no purchase price was disclosed.

The added twist to this story is that Gail Marcus will be the new President and CEO of Calloway Labs. Marcus was CEO of **Caris Diagnostics** (now **Miraca Life Sciences**) when it was purchased by **Miraca Holdings** for about $725 million. That deal closed in November 2011.

Credibility For Calloway

For Calloway Labs, its prospective new owner and CEO will add credibility to a laboratory company that has run afoul of the Medicaid program. Back in 2010, Massachusetts Attorney General Martha Coakley filed a 42-count indictment involving Calloway Laboratories, Inc., two of its officers, and three individuals. The charges accused the defendants of Medicaid fraud and kickback schemes.

Last spring, Calloway paid $20 million to the Commonwealth of Massachusetts and $7.7 million to the federal government to resolve allegations of kickbacks involving the state Medicaid program and the federal Medicare program. Calloway has operated under a three-year corporate integrity agreement with the Office of Inspector General of the federal Department of Health and Human Services since that time.

Wary Of Pain Management

Many pathologists and lab executives have been wary of pain management testing as it is marketed by a number of lab companies typically started, owned, and managed by individuals who do not have a background in more traditional areas of clinical laboratory testing. There is ample evidence to indicate that these are justified concerns.

Healthcare prosecutors at the federal and state levels have successfully brought enforcement actions against numerous pain management lab companies over the past eight years. A list of some pain management companies named in federal and state enforcement actions is presented in the sidebar on page 18.

Because of this checkered past in Medicare and Medicaid compliance, Wall Street investors have been shy about putting money into this class of lab testing companies. **Ameritox, Inc.,** is a good example.

During the 2000s, Ameritox posted impressive yearly rates of growth in specimen volume, revenue, and operating profit. However, during the past six to

eight years, its investors have engaged investment bankers several times to find buyers for the company—with no takers.

Similarly, the first sales book offering Calloway Laboratories for sale appeared as early as 2008. But despite its record of fast revenue growth, the owners of Calloway Labs were unable to find a buyer until Ampersand showed up last month.

Demand Poised To Increase

Thus, the willingness of Ampersand Capital Partners to acquire Calloway Laboratories at this time—and while Calloway Laboratories is under a corporate integrity agreement with the federal government—may be a sign that Ampersand believes the demand for pain management testing by office-based physicians is poised to take off.

Ampersand does know its way around the clinical lab testing marketplace. In 2007, it invested in **Signature Genomics** of Spokane, Washington. In 2010, **PerkinElmer, Inc.**, paid about $90 million to acquire Signature Genomics.

Similarly, Ampersand had equity interests in two Kansas-based lab companies, which were **ViraCor Laboratories** and **IBT Laboratories**. In 2009, the two firms merged to become **ViraCor-IBT Laboratories**.

Why Physicians Want To Test

Based on its experience with clinical lab testing, Ampersand may see opportunity in pain management testing. After all, physicians have legitimate clinical and medical malpractice liability reasons to use lab tests to monitor their patients' compliance with prescription drugs prescribed to manage pain. Oxycontin is a good example.

Physicians need answers to three primary questions: 1) Is the patient regularly taking a therapeutic dose of oxycontin as prescribed? 2) Is the patient taking too much oxycontin and at risk of becoming addicted? 3) Is the patient not taking the oxycontin because he/she is illegally selling these pills to individuals who are addicted?

Given the rising use of prescription drugs for pain management, accompanied by a recognition among physicians of the need to better manage their patients who are taking these medications, Ampersand may consider that the time is right to serve this market. What will be watched is how Ampersand changes past practices at Calloway Laboratories and what new lines of laboratory testing it may introduce in coming months. TDR

Checkered Compliance Past For Pain Management Testing

AS A NICHE SECTOR, LAB COMPANIES primarily offering urine testing for pain management and drugs of abuse screening have a dismal record of compliance with the Medicare and Medicaid programs.

For example, Amertox, Inc., of Midland, Texas, has been a fast-growing laboratory that provides urine testing for pain management purposes to office-based physicians. In 2010, it agreed to pay $16.3 million to settle a federal *qui tam* lawsuit that had been filed in 2007 by one of its sales representatives. Ameritox denied the claims of the lawsuit.

Starting in 2007, Massachusetts Attorney General Coakley brought enforcement actions against five other laboratories offering pain management testing besides Calloway Laboratories. She won settlements in each of these cases. The labs are:

- **Preventive Medicine Associates, Inc.** (PMA), Brookline
- **Diagnostic Laboratory Medicine, Inc.** (DLM), Bedford
- **Clinical Science Laboratory, Inc.**, Mansfield
- **Life Laboratories**, Springfield
- **Willow Street Medical Laboratory, LLC**, Lynn

INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

Definiens AG, one of the major players in the fast-growing market for digital pathology, raised $12.8 million in additional capital funding. The company, based in Munich, Germany, manufacturers systems for digital image analysis. Definiens stated that the new funds will be used for "commercial expansion of its current business and to develop and commercialize innovative products for clinical digital pathology."

MORE ON: *Definiens*

Definiens has placed its digital pathology systems in most of the major pharmaceutical companies, where a growing application is to support development of tissue-based diagnostic biomarkers. Definiens' systems are also finding acceptance in clinical settings. Pathologists may be interested to learn that one founder of Definiens (back in 1994 when it was called **Delphi2 Creative Technologies**) was Nobel laureate Gerd Binnig. In 1986, he and Heinrich Rohrer shared one-half the Nobel Prize in Physics in 1986 for their design of the scanning tunneling microscope (STM).

TRANSITIONS

• David L. Schultz retired as President and CEO of **Sonic Healthcare USA, Inc.**, at the end of August. In 1989, Schulz was a co-founder of **Clinical Pathology Laboratories, Inc.**, and served as its CEO through its acquisition by **Sonic Healthcare, Ltd.** in 2005.

•**Freedom Imaging Systems** of Ann Arbor, Michigan has named Dennis Hodges as Vice President, Healthcare Sales. Hodges has held executive positions with the **Michigan Co-Tenancy Laboratory**, **Warde Medical Laboratories**, and the **Nichols Institute**.

•Well-known pathologist Jeffery A. Kant, M.D., Ph.D., FCAP, FAAAS, age 65, died September 29, 2012. He was Professor of Pathology and Human Genetics at **UPMC** and the **University of Pittsburgh School of Medicine**. Kant was among the founders of the **Association of Molecular Pathology** and served as its first president. Respected for his expertise in molecular test utilization and coding, he served at the national level in a number of roles for the **College of American Pathologists** and other organizations.

DARK Daily
Clinical Laboratory and Pathology News/Trends

DARK DAILY UPDATE

Have you caught the latest e-briefings from DARK Daily? If so, then you'd know about...

...separate studies by **Fox Chase Cancer Center** and **Aon Hewitt** that found patients were reluctant to pay much money out-of-pocket for expensive genetic tests. This does not bode well for labs when billing these patients.

You can get the free DARK Daily e-briefings by signing up at www.darkdaily.com.

That's all the insider intelligence for this report. Look for the next briefing on Monday, October 29, 2012.

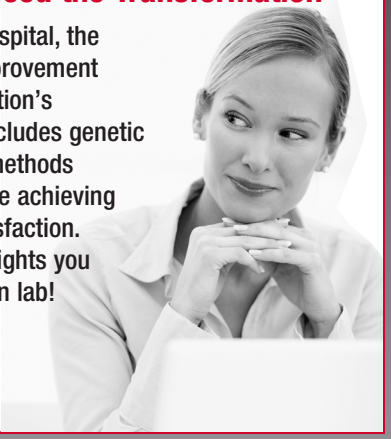
It's New!

Lab Quality Confab

November 6-7, 2012 • Hyatt Regency Hotel• Hyatt Regency Hotel

Anthony Carter, Ph.D. of National Jewish Health on:

Personalized Medicine's Path from Concept to Reality: How Our Lab Uses Lean to Speed the Transformation



At this nationally-respected children's hospital, the laboratory is using Lean and process improvement to rapidly respond to the parent organization's adoption of new clinical services. This includes genetic and molecular testing. Learn how Lean methods give the lab the flexibility to change, while achieving a high level of physician and patient satisfaction. This session is chock-full of practical insights you can take back and implement in your own lab!

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

UPCOMING...

- ***2013's Landscape for Lab Reimbursement: Understanding the Good, the Bad, and the Ugly.***
- ***Outlook for Hospital/Health System Lab Outreach: Why There is Good News for Nimble Labs.***
- ***Unexpected Opportunities in Point-of-Care Testing.***

For more information, visit:

www.darkreport.com

Sign Up for our FREE News Service!

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

Visit www.darkdaily.com

DARK Daily
Clinical Laboratory and Pathology News/Trends