

From the Desk of R. Lewis Dark...

THE DARK REPORT

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

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R. Lewis Dark
Founder & Publisher



Genome Sequencing Promises to be Disruptive

EVERYONE SHOULD CAREFULLY READ OUR LEAD STORY ON THE FACING PAGE. Titled “Rapid Gene Sequencing Predicted by Mid-2009,” it is a revealing look at the declaration of California-based **Complete Genetics** that, in less than eight months, it will begin delivering full human genome sequences priced at \$5,000 each to interested customers at a cost of only \$1,000 to itself!

Complete Genomics’ announcement represents the same paradigm-shifting earthquake in genetic medicine that occurred back on May 11, 1998. That’s the day when J. Craig Venter, Ph.D., and his partner, **Perkin-Elmer**, announced their plans to map the entire human genome for a cost under \$300 million and do it in within three to four years. At the time, the Human Genome Project was about halfway through a 15-year, \$3 billion project to complete the first full sequence of the human genome.

THE DARK REPORT predicted that Venter’s effort would succeed and, as it did, it would accelerate both the accumulation of genetic knowledge and the speed with which it was converted into clinically useful molecular diagnostic tests. We wrote: “Those laboratories and pathology practices which flourish in the year 2005 will be the ones which were early implementers of emerging genetics-based diagnostics.” (*See TDR, June 15, 1998.*)

Venter achieved his bold goal in just 25 months. It was June 25, 2000, when President Bill Clinton publicly announced the successful sequencing of the human genome and recognized the roles of both Venter and Frances S. Collins, M.D., Ph.D., who had led the Human Genome Consortium, in this accomplishment. For the lab industry, by 2005, a host of new lab companies had emerged to offer a growing menu of molecular tests. Molecular assays for infectious diseases and certain cancers were transforming clinical practices, giving truth to THE DARK REPORT’s 1998 prophesy.

Now THE DARK REPORT sees a parallel moment of disruption in genetic medicine. Complete Genomics and a host of competitors are about to transform human genome sequencing, dropping price and speed while opening the doors to vast amounts of new knowledge about DNA, RNA, and the human proteome. Pathologists and lab directors should prepare for an accelerating flood of new insights about genes and proteins. Many of these discoveries will rapidly lead to new laboratory tests that offer physicians and patients more precise tools for diagnosis, therapeutic decisions, and patient monitoring. **TDR**

Rapid Genome Sequencing Predicted by Mid-2009

➤ **Surprise announcement that California firm is about to achieve a \$1,000 human genome sequence**

➤➤ **CEO SUMMARY:** *In the same way that the Human Genome Project was disrupted by the entry of C. Craig Venter and Perkin-Elmer in what was then a 15-year, \$3 billion project, now Complete Genetics of Mountain View, California, is disrupting the race to the \$1,000 human genome sequence. Developments in this field are moving at rocket speed and the resulting new technologies and instrument systems may give laboratory medicine new clinical assays that are disruptive in their own right.*

TALK ABOUT DISRUPTIVE TECHNOLOGY! The race to achieve the \$1,000 genome was transformed earlier this month when **Complete Genomics, Inc.**, of Mountain View, California, publicly predicted that it would achieve this goal, possibly as early as the spring of next year.

In accomplishing the feat of sequencing the entire human genome for a cost of \$1,000, Complete Genomics will instantly transform the field of genetic medicine. Not only is its gene sequencing technology disruptive, but its business plan appears equally disruptive.

That's because Complete Genomics does not plan to sell gene sequencing instrument systems. Rather, it will create a global network of gene sequencing centers and will sell gene sequencing services to pharmaceutical firms and researchers. Its

first gene sequencing center will cost \$75 million and will be located in Mountain View, California. The company predicts this 32,000 square foot center will produce 1,000 human genomes during 2009 and as many as 20,000 human genomes in 2010.

"We are setting out to completely change the economics of human gene sequencing so that we can do diagnostic quality human genome sequencing at a medically affordable price," stated Clifford Reid, Complete Genomics' President and CEO, during an interview with *Bio-IT World*. "Essentially, [we'll] transform this genome sequencing world from a scientific and research endeavor into a pharmaceutical and medical endeavor."

This statement of intent is clear and unambiguous. Complete Genetics believes its technology and its business plan will

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immediately propel genetic medicine to a higher level of knowledge. It expects the availability of high numbers of human genomes, produced at reasonable cost, will unlock a host of medical breakthroughs that can quickly be adapted into clinical practice.

► Implications For Lab Testing

For pathology and laboratory medicine, the implications of Complete Genomics' technology and business plan are many and profound. Experts observe that, having complete genomes for a large number of humans sharing the same disease will make it possible to identify all the genetic variations that contribute to individual diseases.

Once that knowledge becomes available, new diagnostic assays will be developed that look at thousands—and possibly tens of thousands—of biomarkers that must be present in certain combinations to confirm specific diseases.

THE DARK REPORT observes that an explosion of knowledge is expected to result from the study of thousands of complete genomes of people afflicted with the same disease. This is likely to trigger a flood of new lab tests. The majority of these will involve analysis of DNA, RNA, and proteomics. For that reason, the role of the molecular laboratory will steadily expand as clinicians apply the diagnostic knowledge generated by these laboratory tests to patient care.

► Global Genome Sequencing

After construction of its first gene sequencing center in California, Complete Genomics intends to build 10 similar centers in the United States and abroad during the next five years. These will be developed in partnerships with selected organizations and foreign governments.

Complete Genomics' strategy is to offer its technology via a service model—not by selling instrument systems. It considers itself to be a “wholesaler of human genomes.” It will price a genome sequence at \$5,000 when it opens its sequencing center.

Reid believes the service model has a ready market, particularly among pharmaceutical companies. Not only do they already spend billions on research and clinical trials, but they recognize how outsourcing to the right supplier can both accelerate results and save money.

“The pharmaceutical market has declared very clearly they don't want to buy instruments,” continued Reid in his *Bio-IT World* interview. “They want to buy services, so that they get the data that enables them to do the discovery and development work, without having to own and operate a large-scale genome sequencing center.”

Another factor in selecting the service model is the sheer volume of data generated by genome sequencing. This issue is already well-known to pathologists and scientists operating molecular laboratories and offering molecular testing to clinicians. Reid observed that new sequencing technologies “generate a breathtaking amount of data. Simply selling 10 or 20 instruments to a company doesn't solve the problem. You then have to be able to manage huge volumes of data. We are putting in a Google-style data center to manage the data.”

► Outsourcing By Pharma

According to Reid, in its service model, Complete Genomics will “offload [users] from the operational burden of running all those sequencers; the computational burden of running all those assemblies; and from the capital purchase burden, having to build up these huge genome centers they haven't started building to generate the volumes of data we're talking about. By providing this outsource service, they get access to the data so they can do the science.”

Reid indicates that first customers for this service will probably be pharmaceutical companies wanting to study cancer and mental illness. There is a strong genetic component in both categories of diseases. Further, because of the prohibi-

Who's in the Race to the \$1,000 Genome? Several Companies Have Promising Approaches

SEVERAL COMPANIES ARE RACING TO BE FIRST to sequence the human genome for \$1,000. It is widely acknowledged that, until the cost falls to \$1,000 or less, progress in genetic medicine will be slow.

Some of the main contestants are Applied Biosciences, Inc. (ABI); Illumina, Inc.; 454 Life Sciences (a division of Roche), and Pacific Biosciences. Now Complete Genomics must be added to this list. Helicos BioSciences Corporation and Intelligent Bio-Systems, Inc. are two other companies which have thrown their hats in the ring and declared that their respective technologies will produce the \$1,000 genome sequence. Additional companies working in this field are NABsys, Inc. and VisiGen Biotechnologies, Inc.

One stimulus to this race is the "Archon X Prize for Genomics." (www.xprize.org) Anyone who can sequence 100 genomes in ten days will win \$10 million plus bragging rights. The X Prize for Genomics believes that the ability to sequence 100 genomes in 10 days represents the technology threshold that will enable an explosion of research and new knowledge about the human genome.

Another stimulus is a program offered by the National Human Genome Research

Institute (NHGRI), part of the National Institutes of Health (NIH). In recent years, it has awarded millions of dollars of grants under its "Revolutionary Genome Sequencing Technologies" program. Also called "\$1,000 genome grants," the NHGRI's grants are intended to speed development of sequencing technologies that will accelerate the use of genomics in medical research and health care.

Claims made by the different companies demonstrate the potential of various technologies to reduce both the time and the cost required to sequence the human genome. Intelligent BioSystems, for instance, has stated its plans to have, by year-end, a system that requires only 24 hours and \$5,000 to sequence a full human genome.

However, that impressive prediction is about to be surpassed. At its press conference on October 6, Complete Genomics stated it had sequenced a genome in July that required four days and was completed at a cost of \$10,000. Complete Genomics has also made the public prediction that its technology can eventually drop the cost of sequencing the human genome down to just \$100.

tive cost of using today's generation of sequencers to generate the full genome of the hundreds of people participating in research studies and clinical trials, Reid is confident that he has ready-made customers for his genome-sequence service. "The pharma guys are pretty much sitting on the sidelines, waiting for guys like us to come along," he noted.

With the public announcement of its accomplishment in sequencing a human genome for just \$4,000 this summer,

Complete Genomics intends to leapfrog the competition in the race to achieve the \$1,000 genome sequence. However, the speed of technology and the numerous competitors in this race make it unwise to make Complete Genomics the odds-on favorite to finish first.

Moreover, this unfolding story has immense consequences for pathologists and the entire laboratory medicine profession, for at least four reasons. First, DNA sequencing technologies and instrument

systems to perform this function are improving at what seems to be an exponential rate. Consider, for a moment, what this means.

► Uses In Clinical Testing

The multiple technologies under development by a variety of companies to perform human genome sequencing are likely to find useful applications in clinical diagnostics, particularly where smaller sequences of DNA need to be sequenced and studied. Thus, one likely outcome from the collective efforts to achieve a \$1,000 human genome is for these technologies to find uses for smaller scale DNA sequencing that supports molecular testing for clinical purposes.

Second, the speed with which the cost to sequence the human genome has fallen reinforces an expectation that this technology will be both robust enough for clinical lab tests and cheap enough to be affordable for health plans and labs that perform such tests.

Third, as researchers during the next 36 to 48 months gain access to the complete genomes of hundreds of people with the same diseases, pathologists and lab directors should expect a myriad of new biomarkers to result from this research. That could trigger disruptive forces within laboratory medicine in as few as five years.

► Tidal Wave Of Data To Come

Fourth, genome sequencing generates huge amounts of data. That means lab directors and pathologists will need more robust software and hardware to accommodate what is likely to be an exponential growth in the number of molecular assays offered by hospitals and independent laboratories.

That creates an opportunity for information technology vendors. Clinical laboratories are likely to be voracious buyers of software and systems that do a good job of collecting, storing, and manipulating the data generated by genome sequencing and related molecular assays.

TDR

First Genome Sequence Was Achieved for \$4,000

WHEN THE FIRST COMPLETE HUMAN GENOME WAS sequenced this July using Complete Genomic's disruptive technology, it only cost \$4,000. That cost will fall to \$1,000 and includes instruments, material, labor, and overhead.

"This [genome] ran four instruments for one week," explained Clifford Reid, President and CEO of Complete Genomics in an interview with *Bio-IT World*. "This is a 28 instrument-day experiment. By the launch of our product in Q2 [of 2009], it will be a four instrument-day experiment."

Bio-IT World described the experiment as "the genome coverage was 22-fold from 67 gigabases (Gb) of mapped reads." Concordance with the HapMap was slightly more than 98%. Reid boasted that the speed of his company's instrument "is about 10 times as fast as ABI [Applied Bioscience, Inc.] and Illumina."

The technology used in the Complete Genomics' system was developed using work done by Rade Drmanac, Ph.D., who has been involved in DNA sequencing from its earliest days. He was sequencing-by-hybridization using a ligation strategy and gridded arrays of up to one billion "nanoballs." Drmanac is now Chief Science Officer at Complete Genomics.

Drmanac's work in biochemistry was married to Clifford Reid's experience in computing to develop the sequencing system at Complete Sciences. Reid, a Ph.D., was using MIT's OpenCourseWare (OCW) in 2004 to do self-study on biology, genetics, and molecular biology. Reid became intrigued by the confluence of biology and computation in systems biology. It caused Reid to seek out Drmanac to discuss his ideas on how to blend the two fields of science. As a result of these discussions, Reid and Drmanac launched Complete Genomics in 2006.

ICD-10 Conversion Costs Underestimated by HHS

➤ **Laboratories and physician groups to incur significant expenses when implementing ICD-10**

➤➤ ***CEO SUMMARY: Criticism of the October 1, 2011 implementation date for ICD-10 is building. Last week, a new study was released that highlights how federal officials underestimated the costs and time required to implement the complex new codes for ICD-10. One large national laboratory company estimates it will spend at least \$40 million to prepare for ICD-10 implementation. Officials from groups such as AMA and ACLA are voicing strong concerns on this matter.***

IT WAS IN AUGUST WHEN THE FEDERAL Department of Health and Human Services (HHS) declared October 1, 2011, as the date when use of the International Classification of Diseases, Tenth Revision (ICD-10), code sets will begin. Since that announcement, evidence is accumulating that federal health officials have significantly underestimated the costs that providers will incur to meet this mandate. (See *TDR, October 6, 2008*.)

For example, converting to ICD-10 will cost one large national lab about \$40 million. That includes costs for information technology and staff education. This lab company estimated that implementing the new ICD-10 code sets will be twice as expensive as what it spent to prepare for conversion to the new processes for the National Provider Identification (NPI) system. That changeover caused severe cash-flow problems for labs earlier this year. (See *TDR, June 16, 2008*.)

These costs were disclosed in a new report issued by **Nachimson Advisors, LLC**. This report was commissioned by a group of organizations that represent physicians and laboratories, including the

American Medical Association (AMA) and the American Clinical Laboratory Association (ACLA).

“This study illuminates the fact that adopting ICD-10 will be far more costly for physician practices and clinical labs as well as much more complicated than HHS acknowledges in the proposed rule,” said ACLA President Alan Mertz. “We are hopeful that HHS will review this study closely and revise their compliance strategy to correspond with a more appropriate timeline.”

➤ **Huge Costs For Providers**

In the report, Nachimson estimated that a typical small physician group (three providers) would incur \$83,290 in costs to comply with ICD-10. Those costs climbed to \$285,195 for the typical medium physician group (10 providers), and \$2,728,780 for a typical large physician practice (100 providers).

The transition date for ICD-10 has caught the attention of the **American Medical Association (AMA)**. Joseph M. Heyman, M.D., Board Chair at the AMA stated, “The AMA is deeply concerned that

Nachimson's Report Looks at Financial Costs For Physician Groups to Comply with ICD-10

TO COMPLY WITH ICD-10 CODE SETS, physician groups will need to devote money and resources in six different areas of their business. In the report prepared by Nachimson Advisors, LLC, these expense estimates were summarized in the table reproduced below.

Total Summary of Estimated Compliance Costs

	Typical Small Practice	Typical Medium Practice	Typical Large Practice
Education	\$2,405	\$4,745	\$46,280
Process Analysis	\$6,900	\$12,000	\$48,000
Changes to Superbills	\$2,985	\$9,950	\$99,500
IT Costs	\$7,500	\$15,000	\$100,00
Increased Documentation Costs	\$44,000	\$178,500	\$1,785,000
Cash Flow Disruption	\$19,500	\$65,000	\$650,000
Total	\$83,290	\$285,195	\$2,728,780

Small practice: assumes three physicians and two administrative staff

Medium practice: assumes 10 providers, 1 full time coder, and 6 administrative staff

Large practice: assumes 100 providers, with 64 coding staff, 10 full time coders, 54 medical records staff

Source: "The Impact of Implementing ICD-10 on Physician Practices and Clinical Laboratories," Nachimson Advisors, LLC

HHS is rushing head-first into the transition to a complex coding system without fully recognizing the impact on the healthcare system. Physicians, insurers, medical labs and others are raising the alarm that the costs, documentation, and training required by ICD-10 will be significantly greater than HHS now recognizes.

"We are committed to improving the healthcare system," continued Heyman, "but we cannot let history repeat itself as CMS attempts to quickly implement yet another major HIPAA change without allowing time for physician education, software vendor updates, coder training, and testing with payers—steps that are needed for a smooth transition and cannot be rushed."

"We have known this transition was going to be a big problem for a few years," noted Mertz of the American Clinical Laboratory Association. "The Nachimson study confirms that belief. As well, ACLA

has consulted with our members and some of the larger labs tell us the costs for transitioning to the new codes and then the ongoing costs to use the new codes will be quite high. It will be costly for lab billing personnel to have to go back to the referring physicians to get the right diagnosis codes."

Complicating the transition is another coding deadline: the implementation on April 1, 2010, of the 5010 transaction standards under the Health Insurance Portability and Accountability Act (HIPAA). The 5010 standard must be in place before physicians can use ICD-10. Yet HHS' advisory group, the National Committee for Vital and Health Statistics, has recommended a minimum of two years is required to test and verify the 5010 standards before work can begin to implement ICD-10.

TDR

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Hospital Labs Have New Options for Molecular Dx

➤ **Combination of growing physician demand and new molecular technologies open door for labs**

➤➤ **CEO SUMMARY:** *Laboratories that offer molecular assays continue to see strong growth in four areas: oncology, hematopathology, infectious diseases, and personalized medicine. Further, a new generation of molecular testing systems and analyzers is coming to market which will make it easier for even smaller community hospital laboratories to establish and perform molecular tests that are both clinically useful and financially sustainable.*

“Strong physician demand for molecular tests makes this a hot growth area for hospitals and independent laboratories,” stated Gregory J. Tsongalis, Ph.D., Director, Molecular Pathology, at the **Dartmouth-Hitchcock Medical Center**, in Lebanon, New Hampshire.

“Pathologists are wise to add molecular components to their lab’s menus because these tests are changing the way medicine is practiced,” explained Tsongalis during a conference call sponsored by THE DARK REPORT on September 23, “How Hospital And Health System Labs Can Profit From New Must-Have Molecular Tests.”

However, along with his enthusiasm for the opportunities in molecular testing, Tsongalis provided a caveat. “Molecular testing is a new and developing area of clinical testing—but it offers more pitfalls than other types of testing in the clinical lab because many things can go wrong!”

“One simple example illustrates this point,” added Tsongalis. “In a chemistry lab, I could take a pipette of 10 milliliters of plasma and spin it in the air across the lab and it is improbable that any patient’s results would be affected. This is not the

case in the molecular lab! A worker could contaminate the entire lab with as little as 50 microliters of specimen depending on the instrument systems being used. That is why, when adding new molecular tests in your lab, you must proceed with care and precision.”

➤ **Smart Business Decision**

Notwithstanding this complexity, Tsongalis believes that adding molecular tests represents a smart business decision for labs because of the sustained growth in physician demand for these tests. “Labs that do molecular testing see strong growth in four particular areas: oncology, hematopathology, infectious diseases, and personalized medicine,” he explained.

“Of these, oncology is the single biggest growth area in molecular diagnostics, with assays emerging for diagnostic, prognostic, and predictive applications,” Tsongalis continued. “We used to say that, using traditional methods and depending on experience, a pathologist could diagnose correctly about 96% to 98% of the specific tumor types. But new knowledge of the underlying mechanisms of these

tumors and the new classification of tumors will make it difficult for pathologists to do testing with traditional tools only. Therefore, forward-looking labs should be supporting these new molecular applications for diagnostics.

► Rising Therapeutic Demand

“Further, therapeutic applications are stimulating the demand for molecular testing,” he added. “Look at how molecular testing is involved in decisions to treat a patient with Gleevac or Herceptin. We are now at the point where we can identify patients who need specific therapies. That is a new capability linked to genetic knowledge.

“Steady advances in these technologies are allowing researchers and labs to revisit old questions about genes and the way we have classified different types of cancers,” he said. “This research helps us better understand how certain genetic abnormalities, oncogenes, and tumor suppressor genes affect the diagnosis and prognosis of individual patients. This information is having an effect on therapy and is driving this field forward in a big way.

“For example, in colon cancer, physicians are now looking at the K-ras oncogene as they make therapeutic decisions and evaluate how patients respond to treatment,” Tsongalis explained. “New molecular tests like these give the laboratory a role in changing the way patients are diagnosed and managed. This is a big growth area for our laboratory here.”

► Hematopathology And WHO

Similar advances are under way in the field of hematopathology. “We also have an active service in hematopathology at Dartmouth Hitchcock,” he continued. “This area is important because later this year, the **World Health Organization** (WHO) will publish new classifications regarding leukemia and lymphoma testing.

“These new classifications will be based on very specific molecular targets for these diseases,” he noted, “and they will

affect diagnostic and therapeutic decision making. I expect that testing for these diseases will follow the path that we have seen for Gleevac and Herceptin.

“But even without the forthcoming new classifications, there are ongoing discoveries of new gene mutations involved in different types of cancers,” Tsongalis said. “In turn, this creates a clinical need for molecular tests that support diagnosis—and fast turnaround times for these tests because physicians want to treat these patients in a timely fashion. Pathologists will need to be prepared to identify the targets and to do these tests quantitatively so that physicians can monitor therapies.”

► Infectious Disease Testing

Infectious disease testing was the first fast-growth area in molecular diagnostics. It continues to be a dynamic and changing field. “In the area of infectious diseases, we already have assays for different pathogens that run the gamut of qualitative, quantitative, and genotyping,” he noted. “Just as in oncology and hematopathology, there is a strong clinical demand for these tests, and, again, one important clinical need is for speedy turnaround times.

“For instance, labs batching clinical tests for infectious disease testing two days a week may not be providing the best service,” Tsongalis cautioned. “Labs should expect to see physicians want faster and faster access to test results for infectious diseases. New automated solutions in molecular testing will help the lab meet this demand.”

When discussing the last of the four areas—molecular testing in personalized medicine—Tsongalis described progress in this field as somewhat disappointing. “Personalized medicine is a growth area. But labs should be deliberate in their approach to adopting personalized medicine,” he explained. “For example, last year, targeted therapy programs for patients taking warfarin were instituted. These projects were called the first broad use of personalized medicine, in which a person’s genetic

Consider Overall Cost of Healthcare Encounter When Evaluating Possible New Molecular Tests

MOLECULAR TESTS GENERALLY COST MORE than most traditional laboratory tests. “But that’s not the whole story,” observed Gregory J. Tsongalis, Ph.D., Director, Molecular Pathology, at the Dartmouth-Hitchcock Medical Center. “Pathologists concerned about the cost of these new tests should consider how the results from molecular testing can help control other health system costs and save a lot of money!”

“In a recent review of our contracts with reference labs, we noted that the cost of the molecular tests ranged from \$2,500 to \$10,000,” Tsongalis said. “That’s a lot of money and shows why many clinicians believe molecular testing is expensive. But often an expensive lab test brings about the least-cost outcome.

“Let me explain. At a recent tumor board meeting, the discussion was about a transplant patient who had a particular virus. One oncologist asked about the cost of a PCR assay for a virus. I hesitated, but as an educational opportunity I reported that it would cost the hospital about \$7,500 to run this test. The consensus was, despite this high cost, that’s what should be done for the best management of

the patient. Actually, the test under discussion only cost \$150, illustrating the perception physicians have that new molecular tests are expensive.

“Additionally, despite the increased cost of some of the more elaborate and complex molecular assays, they can have a beneficial effect for the overall finances of our institution. That is something that lab directors and pathologists must consider,” he added. “For example, if the lab performs a particular molecular test, what does that mean for patient management? Will that test result help identify a targeted therapy that allows the patient to go home sooner? If so, then the institution will save the cost of several days in-hospital care for that patient, generating savings that may far exceed the initial cost of the molecular test.

“For too long, the laboratory has failed to consider its total role in the continuum of clinical care,” observed Tsongalis. “As laboratory professionals, we have been isolated for too long. In today’s medicine, we should recognize that what we do has an effect on overall costs and on patient management. In other words, we need to get out of our labs and be contributing at every appropriate step in patient care.”

makeup was used to identify the best medicine or dose for each patient. But the programs did not produce the results expected by researchers. With hindsight, warfarin was not the best choice of a therapeutic to serve as a model for these programs.

“It is in the field of oncology where there is an active demand for targeted therapeutics,” added Tsongalis. “Our molecular laboratory at Dartmouth Hitchcock is focusing on therapeutics in personalized medicine, particularly in oncology. Knowing in advance whether an individual patient will or will not respond in a positive fashion makes a difference in their management.

“Keep in mind that, at the moment, development of these tests is challenging, since there are not many FDA-approved assays for the different conditions,” he said. “The other challenge is for a laboratory to determine the cost-benefit ratio of any new test for personalized medicine.”

Not only is Tsongalis bullish on the future of molecular testing in labs, but he believes new molecular tests coming to market will make it easier for even smaller community hospitals to establish a clinically useful and financially viable molecular testing menu.

TDR

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Molecular Dx Update

LabCorp's Ovarian Cancer Test Generates FDA Warning Letter

WHEN THE FOOD AND DRUG ADMINISTRATION (FDA) sent **Laboratory Corporation of America** a letter in September declaring its marketing of the Ovasure test for ovarian cancer was a violation of the law, the news was widely reported.

Because Ovasure is a test that is being marketed as a home brew test, the fact that the FDA was taking some form of action caught the attention of the biotech industry and the genetic testing community. But with all the news reporting has come relatively little understanding of how LabCorp found itself in this position.

There are several elements to this story which are of interest to any laboratory offering a "home brew" lab test to clinicians. First, the FDA asserts that LabCorp is using materials not manufactured by LabCorp to perform the test. (The test was developed at **Yale University** and LabCorp has an agreement with Yale to market and perform the OvaSure test.) If that is the case, the FDA advises that LabCorp "must have an approved application for premarket approval (PMA)."

► Oncologists Have Concerns

Second, there are a number of vocal critics that are unhappy at LabCorp's decision to market this particular test. Within the ovarian cancer and women's health communities, there are concerns that the patient population used to study the sensitivity and specificity of the OvaSure test had certain biases. These biases mean the test may not be accurate when used in the clinical settings targeted by LabCorp.

In particular, members of the **Society of Gynecologic Oncologists** have questioned the accuracy of the test. Some cancer specialists point out that the test could produce too many false positives, which would encourage women to unnecessarily have either their ovaries removed or exploratory surgery. If the test generates too many false positives, that would give woman a false sense of security.

► Test Launched In June

LabCorp introduced the Ovasure test last June and it is priced at \$220. The test measures six proteins in the blood and uses an algorithm to determine the probability that the woman has cervical cancer.

The FDA letter was sent on September 29, 2008, and was posted on the FDA Web site in October. It was signed by Steven I. Guman, M.D., Office Director of the FDA's Office of In Vitro Diagnostic Device Evaluation and Safety.

Lots of new legal and regulatory ground is likely to be broken as the matter proceeds to resolution. In recent years, the FDA has taken its first steps to place molecular diagnostics under some form of regulatory review and oversight. What may prove a vexing complication for LabCorp as it works to resolve this situation is the fact that elements of the women's health community have lined up to oppose OvaSure as it is currently marketed by LabCorp.

As indicated in this intelligence briefing, there are many other elements to this LabCorp/FDA dispute that go unreported by the major news outlets. For that reason, stay tuned for the next installment in this unfolding story.



Lab Briefs

►► SIEMENS INVESTS IN DIGITAL PATHOLOGY, BUYS STAKE IN BIOIMAGENE

IMAGING AND RADIOLOGY GIANT **SIEMENS** just made an interesting investment in digital pathology systems. On October 16, **Siemens Venture Capital** (SVC) revealed that it had purchased a stake in **BioImagene Inc.** (www.bioimagene.com) of Cupertino, California. The amount of the investment was not disclosed.

The timing of this investment is a point of interest. Just four weeks earlier, BioImagene had recruited its new CEO from Siemens. Anjit Singh, Ph.D., a senior executive and 20-year veteran at Siemens, assumed his CEO duties at BioImagene on September 17. Previously, Singh was the CEO of the Siemens' Image and Knowledge Management business in Erlangen, Germany. (See *TDR*, September 29, 2008.) Thus, just weeks after Singh's arrival at BioImagene, Siemens became an investor.

Another noteworthy fact about Siemens' decision to invest in BioImagene is that it marks the second major imaging corporation in 16 weeks to enter the market for digital pathology imaging systems. Back on June 5, **General Electric** announced a joint venture with the **University of Pittsburgh Medical Center** (UPMC), called **Omnyx, Inc.** GE and UPMC are each investing \$20 million to develop and market digital pathology imaging systems for primary diagnosis. (See *TDR*, June 16, 2008.)

It is not a coincidence that the world's two largest radiology and imaging equipment manufacturers have both bought into a company developing digital pathology imaging systems within weeks of each other. Based on their study of market demand and emerging technologies, each company believes that: 1) digital pathology imaging systems can soon gain regulatory approval and be ready for use in primary

diagnosis; and, 2) that first mover and early adopter pathologists will readily acquire and use these new digital pathology systems.

Taken together, the investments by Siemens and GE in emerging digital pathology companies should catch the attention of pathologists and pathology practice administrators. It is timely for pathology groups to revisit their informatics strategy and look for ways to use digital pathology to gain competitive advantage.

Further, the fact that the world's two largest imaging companies are positioning themselves in the digital pathology marketplace is likely to encourage other investors to invest in these types of products. Should that happen, pathologists may see multiple competitors and, in coming years, enjoy falling prices for digital pathology systems because of this competition.

►► NYC POLICE CHARGE PATHOLOGIST FOR THEFT OF INSURANCE PAYMENTS

BAD APPLES CAN TURN UP IN ANY BARREL, a fact that's true in every profession—including pathology. New York City police charged a former pathology department head at **Staten Island University Hospital** (SIUH) with stealing nearly \$19,000 worth of insurance payments by tampering with his hospital's computer system.

Karl W. Lanks, M.D., 65, of Brooklyn, the former chairman of the hospital's department of pathology and laboratory medicine, surrendered to police on October 7 and faces felony charges of computer trespass, computer tampering, and grand larceny, the *Staten Island Advance* reported.

Lanks worked for the hospital as a contractor and was not an employee. He chaired the pathology and laboratory

medicine department for 14 years. Last year, Lanks left the hospital and became Medical Director at **Enzo Biochem Inc.**, a clinical lab in Farmingdale, New York.

Court papers document how, from May 15 to 22 of 2007, before he left the hospital, Lanks gained access to the hospital network and changed billing codes so that insurance payments meant for SIUH went to him instead. An investigation by the district attorney's office and NYPD's Computer Crimes Squad led to Lanks' arrest.

Lanks was arraigned in court October 8 and released on his own recognizance. He is scheduled to returned to court on November 24. He refused to comment on the case when contacted by the *Staten Island Advance*.

►► CLARIENT ENGAGES UNIV. OF PENN FOR TRAINING IN FLOW CYTOMETRY

IN AN UNUSUAL ARRANGEMENT between a public laboratory company and a university medical school, **Clariant, Inc.** has engaged **University of Pennsylvania** School of Medicine's Flow Cytometry and Cell Sorting Resource Laboratory to develop a multilevel educational and technical training program for Clariant employees and staff.

In the first phase of this agreement, Clariant staff undergo quarterly on-site training by Flow Cytometry Lab personnel. The training is designed to teach Clariant staff how: 1) to evaluate current procedures and education in specific processes; 2) to develop guidelines for clinical evaluation of hematologic malignancies, quality control and quality assurance procedures; and, 3) to develop programs to ensure compliance. In phase two of the agreement, UPenn's professionals will provide ongoing, on-demand consulting and technical guidance regarding equipment and educational and process issues for Clariant.

It is likely that this formal consulting relationship between Clariant and the

UPenn flow cytometry lab is a response to the swift advances in the science and technology of flow cytometry and related diagnostic procedures. By linking up with an advanced academic center like UPenn, Clariant makes it easier for its scientists and technical staff to stay well trained on the state-of-the-art in flow cytometry. Another benefit is that Clariant will likely stay informed on key research and similar technology improvements that it can quickly incorporate into its laboratory and business as a way to gain competitive advantage.

►► MAYO CLINIC USES RFID SYSTEM TO REDUCE TISSUE SPECIMEN LABELING ERRORS

OVER THE PAST 18 MONTHS, clients and readers of THE DARK REPORT have followed the progress of Mayo Clinic's use of RFID (radio-frequency identification) chips to dramatically cut specimen labeling errors in its high-volume gastrointestinal endoscopy center and the histology laboratory. (See TDR, January 29, 2007.)

At the upcoming 2008 **American College of Gastroenterology** (ACG) annual meeting, Mayo will report the results of this groundbreaking use of RFID technology in a laboratory setting. In the pre-RFID period, when Mayo's endoscopy unit sent 8,231 specimen bottles to the pathology laboratory for evaluation during the first three months of 2007, there were 765 errors.

After implementing RFID labeling, the endoscopy unit sent 8,539 specimen bottles for evaluation in the first three months of this year, with only 47 errors, a reduction of 94%!

Schuyler Sanderson, M.D., a pathologist involved in the study, shared the operational aspects of this project at the 2007 *Executive War College* and again at the 2008 *Lab Quality Confab* held last month in Atlanta, Georgia. Mayo has implemented the RFID system in all its gastroenterology surgery suites. **TDR**

Pathology Boot Camp To Address Three Trends

➤ **Challenges for anatomic pathology groups include pricing, competition, and technology**

➤➤ **CEO SUMMARY:** *Anatomic pathology groups across the nation must develop effective strategies to address challenges in pricing, intensifying competition, and expensive new technologies. That's the assertion of three pathology practice administrators who have organized a boot camp in Dallas next month specifically to train other practice administrators and managers. This event will provide administrators from any size pathology group with useful skills and insights.*

AS A PROFESSION, anatomic pathology (AP) is under siege. The nation's 3,300 independent pathology group practices face challenges on several fronts—each of which eats away at the financial viability of the private practice model.

To answer these threats, next month a special training session for pathology practice administrators will provide knowledge and expertise on how to respond to these trends, so that pathology groups can prosper in tough times. The event is the “APF Pathology Practice Managers’ Boot Camp 101: Elements of a Successful Practice.” It will be conducted on November 6-7 in Dallas, Texas. This event is organized by the **American Pathology Foundation (APF)**.

Intrigued, THE DARK REPORT contacted the event organizers to learn more about current trends threatening pathology groups and what types of business strategies will be discussed at the upcoming boot camp. Sessions will be led by three accomplished pathology practice administrators. They are Krista Crews, Executive Director, of **ProPath** in Dallas,

Texas; Tricia Hughey, CEO, of **UniPath, LLC**, in Denver, Colorado, the largest pathology practice in the Rocky Mountain region; and Lance Beard, Administrator, **Pathology Associates of Corpus Christi, LLP**, and **HistoPath, Inc.**, in Corpus Christi, Texas.

➤ **Fierce Competition In AP**

“Competition is fierce in pathology,” noted Crews. “Referring physicians want pathologists to deliver greater service, higher quality, and faster turnaround times. It is incumbent on every pathology group practice to understand three marketplace trends. First is pricing and how it supports a profitable pathology practice. Second is the arrival of new technology and how it is transforming work flow and clinical services in anatomic pathology. Third is how to respond to ever more intense competition for AP specimens

“Many pathology groups today lack sufficient resources on the business side,” added Crews. “Too often, a pathology group addresses business issues by assigning the most business-savvy pathologist in

the group to handle those tasks. But if that pathologist doesn't have adequate time to devote to the business concerns of the practice, then his or her pathology group will lose ground in the marketplace.

► Pathologists Need To Invest

"Pathologists must be willing to invest in the business side of their practices," she continued. "Doing so allows them to compete with aggressively-priced competitors, even as they deploy new technology to make their group a tougher competitor.

"To me, the most important trends today are pricing, technology, and competition, as I noted earlier," noted Crews. "On pricing, pathology groups are squeezed every time they renegotiate a contract, especially from the bigger healthcare payers.

"There are fewer payers because of consolidation and each payer asks the same question: 'Why should I pay your pathology group more for this particular test when I can get it for less from **LabCorp** or **Quest Diagnostics**?' asked Crews. "That's a tough question to answer, meaning the challenge for pathologists is to justify rational reimbursement.

► Emphasize Important Codes

"In negotiating managed care contracts, pathologists need to work to get away from tying all pricing for pathology services to a government price schedule, such as from Medicare," she explained. "You can work against that trend by carving out the eight, ten, or more codes that are most meaningful to your individual situation. Negotiate those codes at specific rates with each of your payers. Then get whatever reimbursement you can on the remainder of the codes. Put the 80/20 rule to work on your behalf by getting 80% of your revenue from those 20% of codes that are the most important ones to your group.

"To make this strategy successful, your pathology group must know its workload," noted Crews. "The information you need

comes from your billing system. If it is done right, then you know the specific codes worth fighting over, such as 88304, 88305, and 88342, and codes for immunostains. Every pathology group has this information. It's time to use it.

"The second trend is technology, particularly the use of information systems," Crews said. "To be successful in today's market, a pathology group must deliver results quickly and accurately. This requires the pathology practice to have the proper electronic links with its referring physicians, and that costs money. Maintaining a high level of service and offering current technology are the cornerstones of your group's successful response to competitors.

► A Relationship Business

"Historically, pathology was a relationship business. But it is now much less of a business built on personal relationships because of the growth of managed care, the development of national labs, and the commoditization of lab tests," she added. "Your pathology group's referring physicians may love you because of your quality results and great turnaround time (TAT), but that still may not be enough to maintain the relationship when competitors' sales reps call on your client physicians.

"Your competitors' TAT may be slower than your group's TAT," she explained. "But even if they are slower, they'll win if they deliver test results directly into the clinician's electronic medical record (EMR) system and make the process easier for the referring physicians' office.

"The third trend is competition," observed Crews. "Pathologists today have all kinds of non-traditional competitors, both regionally and nationally. This change in the competitive landscape occurred because overnight delivery services and electronic reporting now allow any pathology group to receive specimens from all 50 states and efficiently deliver test reports back to the referring physicians.

Pathology Practice Administrators To Learn Business Strategies at APF's "Boot Camp"

IT WAS FRUSTRATION at the lack of opportunities for pathology practice administrators to get practical, effective knowledge and training that inspired the upcoming American Pathology Foundation's "Pathology Practice Management Boot Camp 101: Elements of a Successful Practice," to be held in Dallas, Texas, on November 6-7, 2008.

"Our goal is get back to the basics," stated Lance Beard, Administrator at Pathology Associates of Corpus Christi, LLP, and HistoPath, Inc., in Corpus Christi, Texas. "Administrators will acquire a detailed understanding of national, regional, and local trends. They will then develop effective strategies and action plans that are appropriate to their pathology groups' particular needs and situations.

"We saw the need for a forum designed expressly for pathology practice administrators," added Tricia Hughey, CEO of UniPath, LLC, in Denver, Colorado. "We all have similar concerns, confusions, chal-

lenges, and complexities in our respective groups. The boot camp gives us a chance to learn from within and then return to our practices better armed and fully engaged in a bi-directional network of peer mentorship.

"Those attending the boot camp will leave with specific knowledge about what is required to run a successful practice, how to assess their situation, and how to develop a plan," observed Krista Crews, Executive Director, of ProPath in Dallas, Texas. "It can't give every attendee answers to all questions because each market is different. But this boot camp will give them: 1) the tools to know where to look for answers; 2) what it takes in their market to be successful; and, 3) how to develop a plan that helps their group achieve financial and clinical goals."

For registration information and to download a brochure on the APF Boot Camp visit the APF's Web site at www.apfconnect.org.

"There is also competition from those physicians who are not pathologists, such as urologists, gastroenterologists and dermatologists," continued Crews. "Many of these specialists are developing anatomic pathology as an in-office ancillary service.

"In recent years, these physicians have banded together into bigger groups with many more doctors. That gives these consolidated regional 'super practices' large volumes of patients, more tools, and more business resources than local pathologists. In these situations, long-term relationships and the pathologist's quality won't be sufficient to allow local pathologists to retain the business.

"Let's face it, many labs have sales people moving into our territories, but it's not simply the presence of sales people that should cause the worry," she explained. "You have to worry when they offer services that you don't offer. If you're in a large market where there is good transportation, be prepared for regional and national competition. Transporting specimens is easy in anatomic pathology.

"So, your group must focus on the service and convenience of delivering your results," she continued. "You may be the best in scientific quality and have fast TAT, but if an out-of-area competitor can match

you on quality, can also get close on TAT, and delivers automated results with an easier-to-digest report, you will probably lose that account.

“Another aspect of technology relates to rapid advances in the digitization of pathology images and the move toward fully digital systems in anatomic pathology,” advised Crews. “Pathologists need to stay in the driver’s seat about how and when to deploy this new technology.

“Further, it is important to understand the inherent competitive downside of not using these new technologies,” observed Crews. “If a pathology group can understand how an investment in these systems will pay off by making their pathology group a more effective competitor in the market, then that group will be well ahead of the curve.

► Embrace New Technology

“The pathology profession needs to embrace technology and constantly look for ways to use new innovations to improve processes and cut costs,” she explained. “For example, bar code technology can streamline and automate lab processes and help eliminate errors. In the traditional histology laboratory, much of the work processes are manual. Our lab implemented bar codes in histology and that has helped us to achieve greater throughput without adding more staff or other resources.

“In fact, ProPath grew its business 30% to 40% directly as a result of these operational improvements,” observed Crews. “Throughput was made better and more reliable by automating processes and replacing our manual reading of labels with automated reading of labels.”

At the upcoming pathology administrator’s boot camp, each of these three topics: pricing, technology, and competition, will be addressed during the two day conference. Organizers of this special training note that there is swift and ongoing transformation taking place in the anatomic pathology market. Competitive forces set in

motion during the 1990s have accelerated during this decade. For example, during the 1990s, such companies as **Dianon Systems, Inc.**; **UroCor, Inc.**; and **Impath, Inc.** established themselves as national laboratory companies and began sending sales reps into local communities across the country to solicit specimens and case referrals.

► More Competitors

During that decade, these three companies posted rapid growth rates in specimen volume, revenue, and net profit. Watching from the sidelines were the two blood brothers and Wall Street. By the end of the decade, both **Laboratory Corporation of America** and **Quest Diagnostics Incorporated** had developed primary strategies to expand their presence in the anatomic pathology marketplace and investors were funding new companies specifically to compete for anatomic pathology specimens.

Since 2000, the anatomic pathology marketplace has become crowded with a host of new and different competitors. This has placed many private pathology practices under great financial stress, as competitors siphoned away specimens referred by physicians who had been loyal to their local pathology group for decades.

► An Unusual Opportunity

THE DARK REPORT observes that it is both unusual and overdue for pathology practice administrators from three thriving pathology “supergroups” to share their insights, knowledge, and experiences in a conference such as the Boot Camp 101. Their perspectives on how to turn the pricing tables on payers, ways to use technology to expand market share, and how to meet and beat APF competitors are likely to make this APF practice administrators’ boot camp a unique learning opportunity. **TDR**

Contact APF at 877-993-9935, ext. 202, or info@apfconnect.org; Krista Crews at 214-237-1655 or krista.crews@propath.com; Tricia Hughey, at 303-512-2202 or thughey@unipathllc.com; Lance Beard at lancebeard01@yahoo.com or 361-992-4211.

INTELLIGENCE

LATE & LATENT

Items too late to print,
too early to report



Once again, laboratory test unbundling is on the radar screen of federal regulators. Included in the 2009 work plan for the federal **Office of Inspector General** (OIG) is a review of laboratory test unbundling and a review of the extent of variation in laboratory test payment rates among Medicare contractors. OIG will determine if clinical laboratories have unbundled profile or panel tests by submitting claims for multiple dates of service or by drawing specimens on consecutive days. It also will examine the extent to which the Medicare carriers have controls to detect inappropriate payments for laboratory tests.



LAB IN FLORIDA OFFERS HOME DRAWS

Hoping to increase market share, build patient loyalty, and fend off national lab competitors, **Premiere Clinical Lab** of Lady Lake and Leesburg, Florida, is offering its patients the choice of having specimens drawn at home or at a patient service center (PSC). According

to Premiere's President, Susan Rendon, M.D., although the home collection service adds to the lab's costs, patients and physicians like it. Plus, the home service generated a favorable story for the lab in *The Villages Daily Sun*, a local newspaper.



CONSUMER ACTIONS FOCUS OF NEW GENETIC STUDY

Genetic profiling is being offered at a discounted price to as many as 10,000 employees, family members, and friends of the **Scripps Health** system in San Diego, California. Researchers will assess changes in the behavior of the participating individuals over the next 20 years. Four companies are collaborating to offer this research to assess the behavioral effects of personal genetic testing on patients. **Scripps Translational Science Institute** (STSI), a research division of Scripps, wants to know if personal genomic testing will motivate participants to exercise, eat well, quit smoking, and pursue illness prevention. The study co-

sponsors are **Navigenics Inc.** of Redwood Shores, California; **Affymetrix Inc.** of Santa Clara, California; and **Microsoft Corporation** of Redmond, Washington. Study participants age 18 and older can get a scan of their genome and a detailed analysis of their genetic risks. Participants will get guidance on how to use the results from Navigenics and be able to store information in Microsoft's electronic health record, called HealthVault.



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*That's all the insider intelligence for this report.
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