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From the Desk of R. Lewis Dark...

THE DARK REPORT

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

Restricted information, see page 2

Commentary & Opinion by...

R. Lewis Dark

Founder & Publisher

PCR Celebrates Its Twentieth Anniversary in 2005

IT'S BEEN A BUSY YEAR AND I HOPE NO ONE THINKS we've been remiss by not mentioning a milestone anniversary until now. On the other hand, I personally can't recall reading about this anniversary elsewhere in the lab industry press during 2005. So maybe I am among the few to call attention to the fact that, on March 28, 2005, a number of foundational PCR (polymerase chain reaction) patents expired in the United States. These patents have been held by **Roche**, which was bold in its original decision to acquire these patents.

PCR was developed in 1985 by biochemist and surfer Kary Mullis, Ph.D. while he worked for **Cetus Corporation** of Emeryville, California. Cetus paid Mullis a $10,000 bonus for this invention. It was in 1998 that Cetus, in collaboration with **Perkin-Elmer Corporation**, introduced the "DNA Thermal Cycler" to automate the PCR process.

By early 1989, Cetus had agreed to collaborate with **Hoffman-LaRoche** to develop and commercialize IVD diagnostic products that incorporated PCR technology. In 1991, Hoffman-LaRoche paid $300 million to Cetus and acquired the rights to PCR. Mullis was honored by a Nobel Prize in Chemistry (for PCR) in 1993, just eight years after publication of his work.

Today, with full hindsight, that bold decision to pay $300 million to license PCR technology is widely viewed as a savvy business decision. Roche has enjoyed substantial revenue from licensing fees and royalties paid by companies and laboratories using this technology. Over 100 companies and 600 laboratories worldwide have such arrangements with Roche.

Moreover, the expiration of the first PCR patents on March 28, 2005 may be characterized as "The King is Dead! Long Live the King!" That's because Roche states that "continuing patents and patent applications number approximately 300 in the U.S. and approximately 900 outside the U.S." It has built this patent estate with an eye toward maintaining PCR licensing and royalty fees for some time into the future.

Because of the contribution that PCR has made in accelerating the genetic revolution—including the mapping of the human genome—I certainly think it is appropriate to remind all laboratorians that PCR is officially 20 years old in 2005! TDR

Innovative AP Reports Created by Path Group

Great example of responding to market, clinicians like customized path reports

CEO SUMMARY: Too often local pathology groups fail to react to intensified sales competition for the biopsy referrals of clinicians in their community. In Torrance, California, the 30 pathologists of Pathology, Inc. decided it was time to invest capital and resources into developing their own flavor of "value-added" pathology services. These custom-tailored pathology reports are now pulling in new client accounts.

IT'S NOT OFTEN that a private pathology group practice is willing to spend capital and resources to develop customer-friendly, value-added services. That's what makes the state-of-the-art prostate biopsy reporting system developed at **Pathology, Inc.** particularly interesting.

In recent years, the 30 pathologists associated with Pathology, Inc., located in Torrance, California, have offered report formats to physician-clients that can be highly-customized to the personal preferences of individual clinicians.

"To support our outreach program, we wanted to add images and other improvements to our existing reporting system," stated Eric Glassy, M.D., Pathologist and Principal at Pathology, Inc. "We were responding to physician-client demand in our market. This demand was triggered by competition from larger lab companies which were offering color digital photographs in their reports."

Glassy is the inventor of the new reporting system. "I'm a frustrated graphic designer," he admitted, "and I knew there were ways to improve reporting that would add value for physicians and patients.

"Our reports are customizable for each physician-client and for each patient," stated Glassy. "Physicians can add their own logo—which is visible on the printed laboratory report they receive from us. They can select from seven formats, depending on the test-results scenario. The software also has flexible client mapping options. This

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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 $11.90 per week in the US, $12.50 per week in Canada, $13.65 per week elsewhere (billed semi-annually).

allows physicians to describe cancer sites according to their preference.

"Some pathologists want to use the report as the 'whole report,' meaning both gross and micro," he noted. "Others want to use it as a preliminary report. For some of our clients, the ability to transmit the report by fax is important. The software system we created has the capability to meet these types of specific client needs.

Ease of Use Is Important

"Some lab companies claim they can put images on reports," Glassy continued. "But ease of use remains a factor with their offerings. Those companies use systems built on **Microsoft** Word templates. Some of the features—such as headers and labels—are difficult to use. The choice of MS Word as software to pull in images means that it is not a seamless process to produce an integrated printed report. Our reporting software is simple to use, so training is minimal.

"From the outset of this design project we had two goals," stated Glassy. "First, we wanted to upgrade existing reporting systems in ways that would add value for our urologist clients and improve patient care. Second, we wanted to differentiate our pathology laboratory's services from the competition.

Desktop Workstations

"We designed the stand-alone software to fit standard pathology systems that run on MacIntosh or PC workstations," he explained. "The system can run on a server, so different users can access a report at the same time. Pathologists can generate monthly and quarterly summary reports and more detailed individual reports that precisely indicate the length and percentage of cancer in each core. This information can be useful for research studies.

"Our system evolved in four stages," explained Glassy. "First we introduced color images into the reports. Urologists want color, so this was an important competitive response to larger laboratories. Second, we incorporated urology-focused statistics, such as Partin Tables. Third, we designed the patient information segment. Fourth, we added a treatment planning sheet. Of course, we keep adding improvements. We're now implementing our third major update of the software.

"For me, the most satisfying outcome of this project is the ability to position the pathologists at that important educational moment between a physician and his patient. That is the critical consultation when the physician and the patient discuss the results of the laboratory information provided in the reports.

"Our customized report is a useful tool for both sides during a very difficult time for the patient," observed Glassy. "It can't substitute for the handholding that often is a part of these consultations, but we have feedback from physicians that it does make things go easier.

Innovation By Local Paths

What sets the pathologists in this private medical group apart from many of their peers is the sensitivity to changes in the healthcare marketplace and the willingness to counter the sales strategies of national labs sending sales reps into Pathology, Inc.'s local community. "We realized that, as pathologists, we had to do more than just give accurate results in order to compete effectively," recalled Glassy. "We recognized that developing an improved reporting system would give us a significant competitive edge. That spurred our pathology group and its business arm, **Pathology Business Services**, to commit the necessary dollars to fund this project.

"Customized reports have proved quite effective at expanding our client base," Glassy noted. "It now allows us to make inroads into large clients, who pre-

viously would have gone with lab firms like **DIANON Systems** or **USLabs**.

"In addition to attracting new business, it has proved useful in retention of our existing client base," he added. "As hospital-based pathologists, our hospital relationships do help to capture new business. But, relationships break down if our pathology group does not introduce innovations and offer new value-added services to sustain them.

"Customized reports have proved quite effective at expanding our client base," Glassy noted. "It now allows us to make inroads into large clients, who previously would have gone with lab firms like DIANON Systems or USLabs."

"Two top selling points are the patient information page and the FAQ (frequently asked questions) page," Glassy noted. "In addition to diagnostic information, the reports provide extensive educational material for the patient, including where to go on the Web for additional information.

"Often patients are too emotionally shut down to absorb information during the physician consultation about test results," Glassy stated. "Now they can take home the detailed, personalized information they need to make difficult treatment-related decisions. This information can be studied at a later time.

Reduces Consultation Time

"One benefit from the patient education presentation we make is that it dramatically reduces the consultation time required with the physician, as well as the time required for the follow up visit," observed Glassy. "It also allows treatment to begin sooner to the benefit of the patient. The ability to quickly provide essential, highly-customized information to patients streamlines the urologists' practice. They recognize we've helped them realize greater efficiency and higher productivity. This is something that we do not see being done by the bigger lab companies in our market."

Pathology, Inc. has designed the system to be transportable into other private pathology group practices. "We sold a number of systems to labs that contacted us, primarily through our Website, eVirchow.com," Glassy noted. "The cost is in the range of $10,000, based on which modules are incorporated. For example, within the breast module, reports can be provided with or without graphic representations of Nottingham scores. However, selling software is not our core business. That is why we do not have an active marketing program for this product."

Invested In Sales Team

This unique pathology reporting system is not the only proactive business strategy implemented at Pathology, Inc. The group has also invested in a professional sales and marketing team. The pathologists understand that, to increase revenues and partner compensation, they must invest in a sales program that will add new clients and bring in growing numbers of specimens.

Pathologists and their group practice admininstrators should recognize that, by investing in their own business, the pathologists at Pathology, Inc. are taking the necessary step to protect and enhance the financial stability of their group practice—while also generating an ever-growing flow of additional revenue—the source of increased profits. TDR

Contact Eric Glassy at 310-225-3221.

—By Pamela Scherer McLeod

California Pathology Group Goes Innovative with System That Allows Docs to Customize Their Pathology Reports

Here are samples of reports produced from the innovative software system developed by Pathology, Inc. of Torrance, California. From right, clockwise:

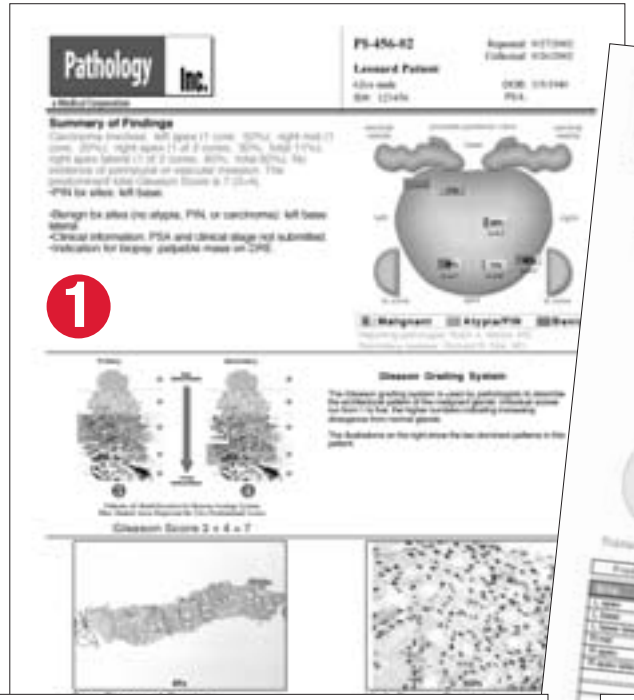
1: Summary page of a 7-page prostate cancer report with picture of biopsy core and micro section

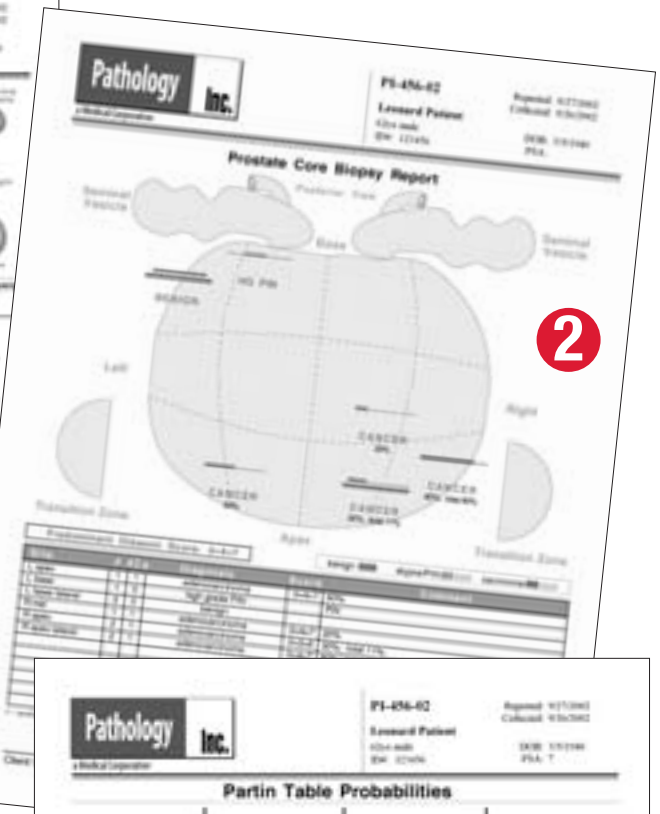
2: Detail page of prostate core biopsy report

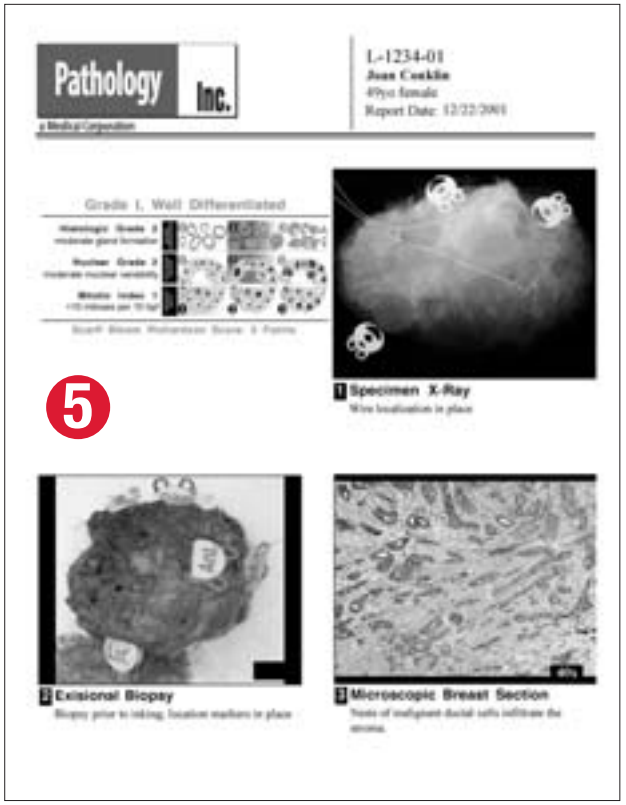
3: Partin Table information page in the 7-page prostate cancer report

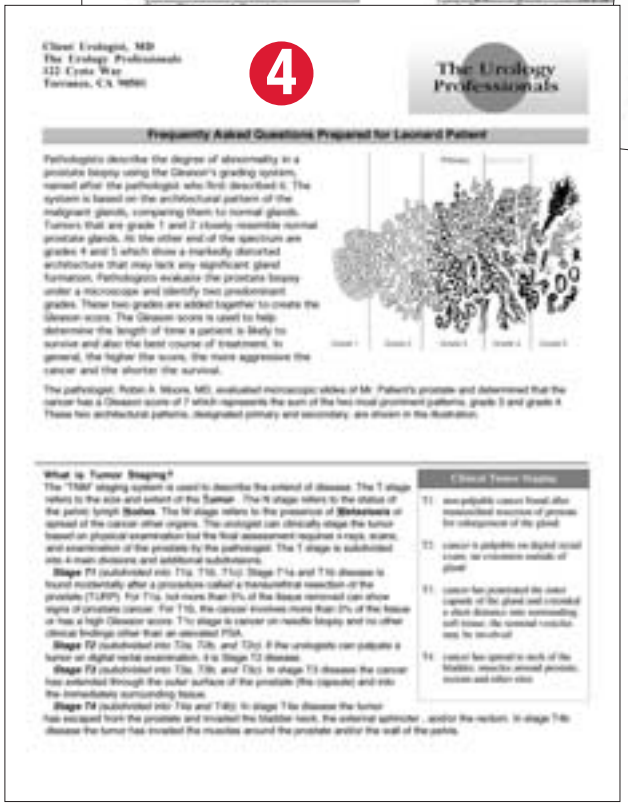
4: Patient-specific "Frequently Asked Questions" page in 7-page prostate biopsy report

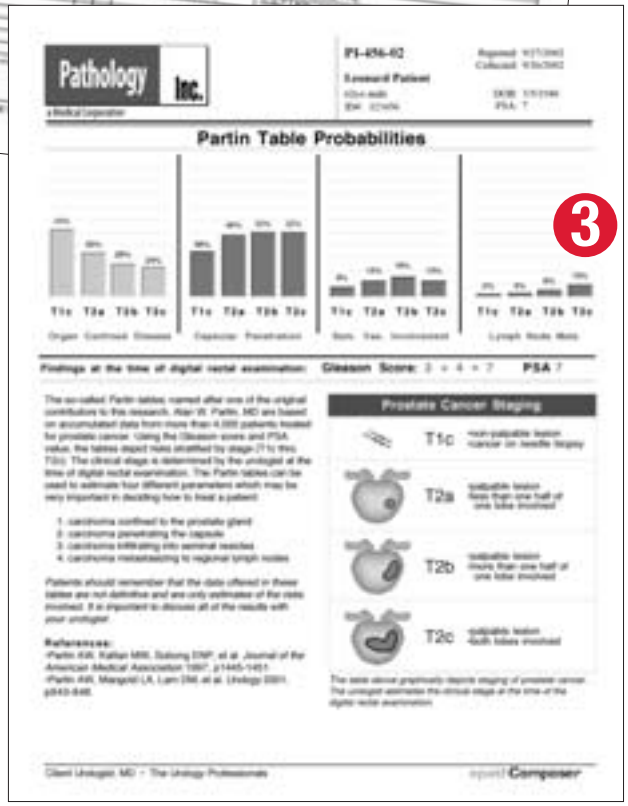
5: Sample of breast cancer report











Quest Pays $934 Million In Acquisition of Lab*One*

Quest Diagnostics came a' courting... and LabOne decided to say "yes!"

***CEO SUMMARY:** In many ways, this acquisition would appear to be the "same old story" of lab consolidation that has marked the lab industry for almost 20 years. Yet, beneath the surface is an unexpected dimension: a motive to use the resources of both companies to better position Quest Diagnostics Incorporated to compete in the rapidly-evolving national market for wellness services.*

WITH AN AGREEMENT TO PAY almost $1 billion to buy **Lab*One*, Inc.**, laboratory industry giant **Quest Diagnostics Incorporated** is back in the lab acquisition game.

The deal was announced on August 9, 2005 and is expected to close during fourth quarter. Lab*One*, based in Lenexa, Kansas, is on track to post revenues in excess of $500 million during 2005. By contrast, Quest Diagnostics' revenue in 2004 was $5.12 billion.

Lab*One* was not actively looking for a buyer. Earlier this year, the company was approached by Quest Diagnostics. Negotiations over recent months led to the agreement announced on August 9.

In buying Lab*One*, Quest Diagnostics is continuing the pattern of the two blood brothers acquiring those smaller laboratory companies which achieve critical mass. Along with an adequate revenue base, these smaller companies usually enjoy a strong share in some local markets, or they have a significant market position in specific segments of the laboratory testing marketplace.

Quest Diagnostics' interest in Lab*One* was for both of these reasons, along with a third: Lab*One* represents an interesting springboard to develop laboratory testing services that serve the evolving wellness market. It is this dimension of the acquisition which indicates how Quest Diagnostics wants to position itself in coming years.

Kansas City & Cincinnati

In terms of geography, Lab*One* has two particular assets which Quest Diagnostics considers quite valuable. One is Lab*One*'s clinical testing business in Kansas City, Missouri. The other is Lab*One*'s **HealthAlliance** laboratory operation in Cincinnati, Ohio.

These are both markets where Quest Diagnostics does not already have a strong presence. Further, each of these markets is supported by a state-of-the-art laboratory facility. In fact, Lab*One* only recently moved into its new, 138,000 square foot laboratory in Cincinnati.

Looking at lab testing market segments, Lab*One* has a modest and growing business in drugs of abuse. But the most attractive segment play for Quest Diagnostics is Lab*One*'s solid business in providing "risk assessment services to the life insurance industry," including blood testing. In recent years, it has also expanded into health screening for employers.

Wellness Strategy

Here is the key to understanding one important reason why Quest Diagnostics paid such a strong price to acquire Lab*One*. It wants to become a major player in the growing market for wellness services. Lab*One* already has an established presence in this market segment, along with management experience and important business relationships.

Both laboratory companies understand how employers, health insurers, and the life insurance industry are devoting more resources to help their employees and beneficiaries live a healthier life. Laboratory testing plays a key role in this effort.

Hoping For Synergies

There are interesting synergies in this market segment. For example, Lab*One* operates a network of mobile paramedics. These professionals travel to the customer to provide relevant health services.

By contrast, Quest Diagnostics has an extensive national network of patient service centers, rapid response labs, regional lab testing centers—all supported by client and field service personnel. This opens up new opportunities with Lab*One*'s existing clients, since the local Quest patient service center would be in a position to serve those Lab*One* clients following the pending merger.

THE DARK REPORT observes that the expressed interest by Quest Diagnostics in the wellness marketplace is a noteworthy development. It is a major motive behind Quest Diagnostics' agreement to approach Lab*One* and negotiate the pending acquisition.

Lab administrators and pathologists should take this as a cue to pay closer attention to new health and wellness initiatives being introduced in their region by local employers and health plans. This is consistent with THE DARK REPORT'S prediction that consumer-directed health plans (CDHPs) will be a focal point for reform of the American healthcare system. As this happens, laboratory testing services will cease to be considered a "commodity." Instead, consumers will opt for value when selecting their laboratory. TDR

Quest's Strategy Shifting With New CEO

SINCE THE ARRIVAL OF SURYA N. MOHAPATRA, PH.D., as Chairman and CEO of Quest Diagnostics Incorporated, there has been a subtle shift in the company's laboratory acquisition strategy.

Knowledgeable sources say that, because Mohapatra has an engineering and a science background, he has a keen interest in developing product and raising the value of services Quest Diagnostics provides in the marketplace. For that reason, the company is primarily seeking acquisitions that have an intrinsic and clear value to support that strategy.

This contrasts somewhat from the acquisition strategy of former CEO Kenneth Freeman. Freeman's long career in finance and business development gave him a different perspective on growth by acquisition. During Freeman's tenure, Quest Diagnostics was a regular and aggressive bidder for most lab acquisition opportunities. Under Mohapatra's leadership, Quest Diagnostics is showing more selectivity when it negotiates and bids for lab acquisitions.

CEO SUMMARY: In the 15 years it has operated a molecular diagnostics testing program, Beaumont Reference Laboratory (BRL) has learned important lessons on how to evaluate which specific molecular assays are ready for clinical introduction. It has also learned effective ways to anticipate the clinical and financial success of such assays. Part II of this two-part series details some of the management strategies and methods BRL uses to sustain its financially-viable molecular testing program.

EXPERIENCE TEACHES VALUABLE LESSONS AT BEAUMONT

Picking Winners and Losers For the Molecular Test Menu

SUCCESS WITH A MOLECULAR TESTING PROGRAM requires skill at determining which specific tests will be clinical and financial winners and which will be losers.

Part II of this two-part series on molecular testing at **William Beaumont Hospital** (WBH) in Royal Oak, Michigan provides insights on identifying molecular assay "winners" and losers." This series is based on a presentation by Frederick L. Kiechle, M.D., Ph.D., Chairman of the Department of Clinical Pathology at William Beaumont Hospital and Medical Director of Beaumont Reference Laboratory, at the *Executive War College*, held last May in New Orleans.

Part I, published in the August 1, 2005 issue of THE DARK REPORT, dealt with how WBH's Department of Clinical Pathology and BRL developed its molecular laboratory and expanded both the test menu and specimen volume over the past 11 years. It identified the key objectives and management strategies employed at WHB and BRL to grow a successful molecular program. Part II focuses on how BRL identifies the most promising molecular tests, evaluates market demand, determines which clinicians are likely to order such tests, and maximizes the revenue potential of such molecular assays.

"In the 11 years since we started our clinical molecular testing program, we've gained plenty of experience in how to evaluate the potential of different molecular assays," noted Kiechle. "There's an interesting tightrope to be walked, because the laboratory must meet the needs of clinicians by offering some tests which are not adequately reimbursed, while supporting the program with other molecular assays which can be considered financial "winners."

As most pathologists and lab managers know, certain molecular assays are rapidly displacing conventional testing methods as the clinical standard of practice. As molecular assays based on new technologies enter the clinical marketplace, more laboratories will be establishing a molecular diagnostics testing program. The WBH/BRL experience provides valuable lessons about the timing for moving from an existing assay to a molecular version.

"Currently, our molecular testing menu is organized around five areas of clinical opportunity," observed Kiechle. "They are: 1) inherited disorders; 2) genetic risk factors; 3) infectious diseases; 4) hematology; and 5) pharmacogenomics—studying the genetic factors of drug response.

At BRL, the process of evaluating a new molecular assay always begins with a market study. "One way to identify molecular tests in high demand in your market is by looking at the test utilization patterns of the physicians practicing in the community," stated Kiechle. "Some subspecialties use a higher volume of molecular tests than others. It's essential to know what these subspecialties are, what tests they order, and how many tests are ordered per physician.

"To do this properly, a laboratory must think externally. It must get into the local physician community and spend time visiting client-physicians, gathering relevant information, and learning which physicians are adopting new clinical procedures that will require molecular tests to help in diagnosis and monitoring the patient," noted Kiechle. "This is a listening, learning, and data-gathering exercise. It takes time and resources, but the resulting information allows the laboratory to make sound decisions about which molecular assays have the best potential and when the timing is right to add them to the test menu.

Table 1: Average number of specific molecular tests ordered per physician per month during 2002.

Internal Medicine (135 MDs)		Ob-gyn (68 MDs)	
C. tracho	0.38	C. tracho	4.90
N. gonorrhea	0.35	N. gonorrhea	4.90
		HPV	1.20
		Factor V Leiden	0.03

"For example, there is a significant difference in how internal medicine physicians and ob-gyns utilize molecular tests for *Chlamydia trachomatis* and *Neisseria gonorrhea*," he continued. "In our market area, we identified and surveyed 135 internal medicine doctors and 68 ob-gyns. Utilization of these tests, when calculated as an average number of tests ordered per physician per month, was significantly different.

"As the table shows *(see sidebar above)*, internal medicine physicians only order, per month, an average of about one-third of one test each for *Chlamydia* and *Neisseria*," observed Kiechle. "In contrast, each month, ob-gyns are ordering, on average, almost five tests each for *Chlamydia* and *Neisseria*. HPV, combined with the liquid preparation Pap smear, is often ordered by ob-gyns, as is Factor V Leiden.

"This information helped us develop a market strategy when we were ready to introduce these tests," added Kiechle. "It allowed us to concentrate on those physicians expected to regularly utilize these tests because of their patient populations and practice patterns. Further, the ordering patterns for the tests shown in this table has remained fairly constant.

Medical Specialties

"During the early years of our outreach testing program, our focus was on the specialties of family practice, pediatrics, internal medicine, cardiology, endocrinology, gastroenterology, nursing homes, ob-gyn, and urology," said Kiechle. "In 2002, our eleventh year in the outreach business, our outreach lab did a total of 2,976,494 procedures, with 2,806 ordering physicians. Among the different medical specialties, the big winners for us were internal medicine and family practice, accounting for two-thirds of the total procedures.

"Nursing homes came in third, with 13% of the volume," he added. "Pediatrics accounted for 4%, while cardiology, endocrinology, and gastroenterology came in at less than 3% each. Urology was the big surprise, with less than 1% of total volume.

Test Ordering Patterns

"Once we have looked at the practice and lab test ordering patterns of physicians, we next study the patient numbers," Kiechle said. "It is important to monitor these numbers against any anomalies that may appear.

"An example involving cytology illustrates this point," he continued. "The next table shows the changes in cytology procedures between 2000 and 2004. Even as the number of clients referring tests has increased, the total numbers of cytology procedures has flattened out in the past two years. We attribute this anomaly to the change in the frequency of Pap smear revisits as a result of HPV testing.

Table 2: BRL Cervical Cytology Volume

Year	Conventional Papanicolaou test	Liquid-Based Cytology	Annual Total
2000	54,524	14,359	68,883
2001	39,375	33,795	73,170
2002	17,009	63,973	80,982
2003	7,836	81,860	89,696
2004	4,098	86,319	90,417

Table 3: Molecular Tests 2004 Examples/Totals

Location	Factor V Leiden	HPV	C.tracho	N. gonorrhea	Total all molecular tests
Royal Oak	797	52	1,881	1,613	8,624
Troy	453	33	709	184	2,181
BRL	304	2,663	13,514	13,226	33,019
Totals	**1,554**	**2,748**	**16,104**	**15,023**	**43,824**

"The clinical setting also affects physician test ordering patterns. Beaumont Health System operates two hospitals. The biggest is 1,061-bed William Beaumont Hospital in Royal Oak, a tertiary care hospital. The second is **Beaumont Troy Hospital,** a 254-bed community and teaching hospital. BRL is the outreach laboratory within our health system," explained Kiechle.

"That gives us two inpatient environments and an outreach setting where clinicians can order molecular tests," he noted. "As Table 3 illustrates, Factor V Leiden is more popular in the inpatient setting than it is in the outreach program at BRL. It's the reverse with HPV, which is extremely popular in the outreach business.

Two Things Needed

"The lesson here is that it is important to know two things about a specific molecular test," said Kiechle. "First, will it be more popular in the inpatient/outpatient arena or in the outreach community? Second, is the patient population large enough to generate the specimen volume needed to support the economics of offering this specific assay? Table 3 demonstrates how HPV specimens originate primarily from the outreach marketplace."

Once BRL has evaluated physician ordering patterns and the patient population available to support a specific molecular assay, its next analysis involves the economics of individual molecular tests. Here is where the financial winners and losers are identified.

"We looked at 26 tests from the year 2003," Kiechle stated. "It is important to look at those loss leaders—what I call

Table 4: Molecular Pathology Estimated Revenue/Profit

- 26 tests studied from 2003
- 6 tests lost $200,368
- 20 tests made $1,950,662
- Extended net: $1,750,294
- Percent margin = 58.5%

Table 5: Impact of reimbursement on winners/losers

Comparison example

	"Loser": CMV	"Winner": C. trachomatis
Annual Volume	192	17,812
Cost/test	$347.50	$11.02
Average reimburse/test	$41.16	$41.16
Extended net	-$58,817.28	+$536,854.00

the molecular losers. Table 4 summarizes this study and shows that six molecular tests lost $200,368 while 20 tests made $1,950,662.

"As these numbers imply, there are often good clinical reasons why a hospital laboratory would offer a test in-house that might not be fully reimbursed," he explained. "From a clinical, as well as financial, perspective, it is vital for the laboratory to stay abreast of which assays are available and what types of assays are moving through the development pipeline.

Offering Clinical Value

"We added an assay—FLT3 gene mutation—to our hematology section because our medical director was impressed with its clinical value," noted Kiechle. "Everyone recognized how the results of this test carry enormous weight in swaying diagnosis.

"What may at first appear to be a molecular test winner, could in fact be a loser when all the numbers are factored in," stated Kiechle. "It is critical to know how much the major payers are reimbursing for a specific test *before* deciding to bring it on board.

"Generous reimbursement for some higher-volume molecular tests can be used to offset the losses that accrue to molecular tests brought on for important clinical reasons," he commented. "The laboratory needs to diligently collect and maintain accurate data on the financial performance of each molecular test. This is important because it is how the laboratory can monitor and sustain its financial viability.

"In the case of CMV, its loser status is partially attributable to the fact that we do this test STAT because of our transplant program. If we didn't do these tests STAT, the numbers would not be so bad. This is one more example of a non-economic reason that justifies bringing on a test," said Kiechle.

"In fact, Table 6 and Table 7 show lists of molecular 'winners and losers' in our molecular testing program," he explained. "On the losers list, we lose money on HIV and HCV because of third-party payer contracts. We are reimbursed $12.78 for each HIV viral, which has a Medicare reimbursement rate of $118.00. **Blue Cross/Blue Shield** reimburses HCV viral load at $12.48, while Medicare reimburses at $59.00. This variation among payers is the reason why it is vital to know precisely what your laboratory will be paid for the tests it performs.

Best Margins On Tests

"It is the opposite for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhea* (NG)," offered Kiechle. "These two tests are our best margin drivers. It was the introduction of CT and NG that pushed the financial performance of our molecular laboratory program from red ink to black ink back in 1994-5. These are very popular tests in this community.

BRL's Specific List of Winners & Losers

Table 6: Molecular "Losers"

Test	Annual Volume	Estimated Annual Loss ($)
Hep C Viral Load	1,130	$60,478
HIV Viral Load	1,596	$33,404
Hep C Qualitative	870	$26,909
Hep B Viral Load	458	$13,484
Mycobacterium TB	258	$7,276
CMV		$58,817

Table 7: Molecular "Winners"

Test	Annual Volume	Est. Annual Gain ($)
N. gonorrhea	16,732	$688,689
C. trachomatis	17,812	$536,854
Cystic fibrosis	1,822	$261,366
MTHFR genotype	1,276	$208,856
HPV	2,930	$144,446
Factor V Leiden	1,582	$136,796
Prothrombin F II genotype	1,064	$92,004

BRL has learned valuable lessons about monitoring annual growth in its molecular program. "To project the impact of growth on the individual sections of the laboratory, it's important to have hard data," Kiechle stated. "On a daily basis, BRL tracks the number of requisitions received from each of the two major client bases—physician offices and nursing homes.

Daily Test Volumes

"We also track our Monday-to-Friday cycle. The greatest total volume of requisitions is received on Monday, with the lowest number of requisitions from physician offices on Wednesday. Many of these offices close Wednesday afternoons. Using these data as a global baseline, we monitor for fluctuations in volume," noted Kiechle.

"We also monitor the volume generated by our target specialty practices," he continued. "Every year we calculate the number of requisitions per physician and the number of procedures per requisition. This information is useful for our sales team in targeting areas for growth. The information is also used to project equipment and personnel needs."

A consistent management theme at BRL is the collection of good information prior to making decisions. BRL has taken the time to evaluate and understand how physicians within its regional market order and use molecular tests. It has estimated the potential size of the market and developed a business plan that allows it to generate enough specimens to ensure both financial and clinical success with individual molecular assays.

It should be also noted that a portion of the increased revenues from BRL's molecular testing program are invested back into the laboratory. This allows BRL to hire and retain the management talent it needs to collect information and evaluate the performance of these molecular tests.

It is no accident that the molecular testing program at William Beaumont Hospital and Beaumont Reference Laboratory is financially-sustainable. The leadership team at BRL is diligent about execution of its business strategies. It is a reminder to all laboratories that "doing the homework" provides the detailed information needed to drive effective decisions. TDR

Contact Frederick L. Kiechle at 248-646-2724.

—By Pamela Scherer McLeod

Proteomic Tests Poised For Clinical Market

Potential for earlier detection, higher sensitivity and specificity

CEO SUMMARY: Proteomics-based technology is developing rapidly. The strategic collaboration announced last month between Ciphergen Biosystems and Quest Diagnostics Incorporated is potentially worth $25 million. It is an expensive bet that next-generation proteomics tests soon to enter the clinical marketplace will provide high clinical utility and give physicians new diagnostic tools.

NEW PROTEOMIC-BASED TECHNOLOGIES ARE MOVING STEADILY toward the clinical diagnostics marketplace. The promise of proteomics is highly sensitive, multi-analyte assays capable of early detection of disease.

Competition to establish market advantage in proteomics-based diagnostic testing is intensifying. One example is the $25 million deal between **Quest Diagnostics Incorporated** and **Ciphergen Biosystems, Inc.** to commercialize selected assays from Ciphergen's proteomics pipeline. *(See TDR, August 1, 2005.)*

Prime Time For Proteomics?

The high level of interest in novel proteomics assays by major players is one sign that a market shift is under way. For that reason, it is timely for pathologists and lab executives to look at why Quest Diagnostics and Ciphergen think their $25 million deal makes economic sense—and whether this particular technology has the potential to shift the testing paradigm within the clinical laboratory industry.

The diagnostic potential of proteomics is huge. That's because of ongoing discoveries involving the role of proteins in disease. Many proteins undergo post-translational biochemical changes. These changes create enzymes which modify or cleave the proteins in a specific way. Proteomic techniques now under development permit large-scale quantitative comparisons between normal and diseased cells in these post-translational protein expressions. Ciphergen, along with serveral other biotech firms, is targeting this area of diagnostic potential.

"Proteomics technologies used today permit large-scale quantitative comparisons between disease and disease-free clinical samples," observed Eric T. Fung, M.D., Ph.D., Vice President of Clinical Affairs at Ciphergen, based in Fremont, California. "The goal of today's translational proteomics is to discover novel biomarkers and combinations of biomarkers to determine which such markers are indicative of distinct disease conditions."

Ciphergen's technology is called SELDI, for "Surface-Enhanced Laser Desorption/Ionization." It is a proprietary proteomics system which uses proprietary ProteinChip® arrays. These arrays are specifically designed to discover, validate, and analyze different biomarkers.

"Many people think we 'discover' with SELDI and 'validate' on ELISA (Enzyme-Linked Immunosorbent Assay)," observed Fung. "However, SELDI allows researchers to go directly from discovery to assay. Not only does this speed up the process, but it allows measurements in real time.

Multi-analyte Assays

"SELDI also allows us to simultaneously analyze multiple analytes," explained Fung. "This is a needed capability in pharmacogenomics, or personalized medicine."

Ciphergen is using SELDI-based processes and associated bioinformatics tools to generate multi-marker assays. It is working on tests to better classify four different types of cancers—breast, ovarian, colon, and prostate. "The SELDI platform uses the body's host response as an amplified signal," noted Fung. "This allows detection of even very small tumors. We have termed this response 'host response protein amplification cascade,' or HRPAC."

High-throughput System

"The key to proteomics is separation," stated Gail Page, Ciphergen's President and Chief Operating Officer. "We have developed systems and processes that provide for high throughput, parallel-fashion protein separation. It marries robotics and automated liquid handling in a 96-well format. Knowing that the eventual market for this product will be clinical laboratories, it is designed with throughput and reproducibility of outcomes in mind."

"SELDI affords Ciphergen the unique capability of creating a strong pipeline of research assays," explained Page. "Most small diagnostic companies typically enter the market based on their development of a single clinical assay. We are not constrained by that limitation.

Research Versus Clinical

"What gives our technology a special advantage is that the entire process of discovery and analysis can be performed on the same platform," observed Page. "We believe this will accelerate the time from assay discovery and validation to clinical use."

As an example, it took a year or more for new generations of gel technology to move from research labs to clinical labs. Ciphergen believes its sophisticated software will allow its proteomics-based assays to make the transition from research into clinical use in a matter of months.

"Now, with our sophisticated software, we believe these proteomics-based assays can make the transition from research into clinical use in a matter of months."

"Biomarker tests are quantitative measurements of biological activity that signal the presence of disease," said Fung. "Multi-marker assays are the basis for the clinical diagnostic tests that Ciphergen is preparing." In the pipeline are proteomic-based tests being developed for use by the physician in the management of ovarian, breast, liver and prostate cancers.

"Researchers are identifying biomarkers for cardiovascular disease, Alzheimer's disease, and other neurodegenerative diseases," he added.

"Other areas of current research for Ciphergen include infectious diseases and blood bank testing."

Ciphergen has strategic alliances with two key players in clinical diagnostics. In June 2005 Ciphergen entered into a research collaboration with **Bayer Pharmaceuticals Corporation** to identify biomarkers predictive of response to cancer therapy, and to develop assays for cancer clinical trials.

A month later, in July, Ciphergen signed an agreement with Quest Diagnostics. "We see a philosophical alignment between our two companies," commented Page. "There is a shared vision of growth through new technology and novel assays.

Access To Clinical Market

"In particular, we see Quest as an innovator, backed by good marketing and focused on good science," she explained. "Over the years they have demonstrated experience in launching new clinical assays. As we move our assays from the development stage to the commercialization stage, this alliance with Quest Diagnostics gives us access to the clinical marketplace. Such access to the clinical market also supports our efforts to penetrate research and pharmaceutical markets."

"In parallel, our agreement with Bayer is part of our strategy to expand collaborations with drug companies," stated Page. "The goal is to accelerate and streamline clinical development of new drugs through the identification of important drug response biomarkers." Other collaborations for Ciphergen include deals with the **National Cancer Institute** and **Johns Hopkins University School of Medicine**.

"Additionally," Page stated, "we have programs overseas. Over 500 of our proteomics chip systems have seeded the research markets in locations all over the world."

Ciphergen is one of several companies rapidly developing diagnostic capabilities in proteomics. As these efforts mature, pathologists and laboratory directors can expect to see a steady acceleration in the number of proteomics-based assays moving from the R&D pipeline into clinical use.

Proteomics Race Is On

On the positive side, many of these new lab tests will allow for earlier detection of disease, or provide enhanced sensitivity and specificity over existing methods. On the cautious side, it is unclear that most payers will move swiftly to provide coverage for these tests and reimburse them at adequate levels.

Lab managers and pathologists should take note of another dimension of Ciphergen's business strategy. Its instrument system is designed to be used, with modifications, in both research labs and clinical laboratories. Ciphergen hopes this will compress what has been a rather lengthy period of time between a discovery and relevant research-grade assay to commercialization.

Two Testing Environments

Historically, the research assay is often limited by old platforms—trying to fit the new technology "square peg" to an existing instrument "round hole." Ciphergen's strategy is to design a state-of-the-art instrument system which can support the research lab while also performing the high volumes of tests needed by clinical labs.

Because Ciphergen has focused on four types of cancer—breast, ovarian, colon, and prostate—it is likely that the first assays to emerge in the Ciphergen/Quest collaboration will involve these diseases. TDR

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—By Pamela Scherer McLeod

INTELLIGENCE LATE & LATENT

Items too late to print, too early to report

In California, some physicians continue to seek illegal kickbacks from clinical laboratories. The problem is widespread enough that the FBI has conducted several "sting operations." In a jury trial related to the long-running "Durascam" healthcare fraud investigation, a married pair of doctors, Adelina Vorperian, M.D. and Kevork Vorperian, M.D., were convicted on charges of accepting kickbacks in exchange for referring laboratory specimens. The pair admitted receiving nearly $6,800 in payoffs from a lab representative who was cooperating with federal investigators. Mrs. Vorperian faces 10 to 16 months in prison, while her hubby faces 6 to 12 months for his lessor role in the fraud.

MORE ON: Lab–MD sting

Launched in California in 1998, Durascam became the largest undercover medical fraud inquiry in U.S. history. With FBI agents posing as doctors and patients at a fake medical clinic in Los Angeles, the investigation uncovered illegal kickbacks or false insurance billing for HME (Home Medical Equipment). Over 400 people were arrested in connection with this investigation, which also triggered a rash of legislation in California and Florida requiring accreditation for HME providers.

MORE CONSUMERS GET EXPERTS TO CHALLENGE ERRORS IN MED BILLS

Now days more and more consumers are paying a billing expert to verify and challenge their healthcare bills. Media sources are now writing stories about the growing demand for "medical billing advocates." These are individuals who help consumers analyze medical bills and negotiate with providers in the event of discrepancies. Consumers are motivated to retain these services for two reasons. First, consumers know that an estimated nine of every ten medical bills contain significant errors. Second, facing higher co-pays, deductibles, and out-of-pockets, consumers are paying closer attention to the cost of health services provided to them by hospitals, physicians, and laboratories.

ADD TO: "Bad Bills"

This trend is already visible in the laboratory industry. Labs are telling THE DARK REPORT that growing numbers of consumers are calling to "negotiate" their lab testing bill. Lab directors and pathologists may want to study this issue and prepare written guidelines for their billing and collections staff.

"HIGH RISK" CONCERNS AT AP LAB CONDO CO.?

When the CEO of your anatomic pathology laboratory condominium company has his resume posted on a Web site, it might be a sign that things are less than great with either this business model or company...or both. Recently seen posted on the Web site of the **American College of Healthcare Executives** (ACHE) was the resume of one Ken Flowers, MBA, CHE. Current position: CEO of **Uropath, LLC** in Dallas, Texas. He'll relocate to any of 15 states, including Alaska. By the way, Mr. Flowers lists as "personal interests" wildlife video and classic vehicle restoration.

That's all the insider intelligence for this report. Look for the next briefing on Monday, September 12, 2005.