Volume XIV, Number 3 Monday, February 19, 2007

From the Desk of R. Lewis Dark...

THE DARK REPORT

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

R. Lewis Dark:
New Technologies Bring New Issues for Laboratories.....Page 2

Quest Diagnostics Acknowledges
Loss of UnitedHealth Business.....Page 3

New Competitive Forces
Alter Market Status Quo.....Page 5

LabCorp Uses United Contract
As a "Growth Driver".....Page 7

UK Laboratories Pushed
To Serve Primary Care.....Page 9

LIS as Productivity Tool
Throughout the Laboratory.....Page 11

Whooping Cough Cases
Reveal Test Deficiencies.....Page 15

New Guidelines to Boost
Cancer Test Accuracy.....Page 17

Intelligence: Late-Breaking Lab News.....Page 19

Restricted information, see page 3

COMMENTARY & OPINION by...

R. Lewis Dark
Founder & Publisher

New Technologies Bring New Issues for Pathologists

TECHNOLOGICAL IMPROVEMENTS ARE MOVING through the lab industry like a buzz saw through balsa. Three briefings in this issue provide examples. In two briefings, we address the topic of false positive results generated in part because of innovations in molecular testing. In the third briefing, we explain how more sophisticated automation and complex new diagnostic technologies are outrunning the ability of legacy laboratory information systems (LIS) to keep pace.

Another factor that can outdate legacy lab information systems is a dynamic, fast-growing hospital laboratory outreach program. As you will read on pages 11-14, Gilbert Hakim, CEO of **SCC Soft Computer** in Clearwater, Florida, explains how the newest generation of technologies in automation, analyzers, molecular diagnostics, and informatics integration is pushing laboratories to adopt increasingly sophisticated computer software solutions.

Newly recognized problems with false positives in certain types of molecular assays are tackled in two briefings. The first, on pages 15-16, deals with whooping cough outbreaks in several hospitals in recent months that received wide media attention. Our expert pathologist comments on the challenges of improving the sensitivity and specificity of molecular assays for *Bordetella pertussis*, along with insights on how individual laboratories can improve the performance of these assays.

Our second briefing on this subject, on pages 17-18, deals with concerns about variation in sensitivity and specificity in testing for the HER2/neu gene across different laboratories performing this test. To improve this situation, the **American Society of Clinical Oncology** (ASCO) and the **College of American Pathologists** (CAP) made news in December when they jointly recommended practice guidelines for HER2 testing for breast cancer.

Each of these developments illustrates how the pace of technology change is accelerating, not just in laboratory medicine and laboratory operations, but across the entire American healthcare system. Lab administrators and pathologists will be challenged to keep up with this knowledge explosion. On the other hand, effective deployment of new technology is something that proactive laboratory organizations can use to stay ahead of their competitors. TDR

Quest Acknowledges Loss of United Business

Company tells investors that, during January, it lost 50% of its existing UnitedHealth business

CEO SUMMARY: In the boxing world, prize fights between heavyweight contenders always grab the world's attention. The same is true in the lab industry, where the current fight between the industry's two heavyweights has the potential to reshape several important aspects of the national market for lab testing services. This boxing match started on January 1, when the exclusive national contract between UnitedHealth and LabCorp became effective.

ROUND ONE IN THE CURRENT FIGHT for the heavyweight championship of the laboratory testing marketplace appears to have gone to **Laboratory Corporation of America**.

At the end of January, executives of **Quest Diagnostics Incorporated** acknowledged that their company has already lost 50% of its **UnitedHealth** lab testing business. Further, they told Wall Street investors that, by year's end, they are likely to lose all the UnitedHealth business.

These statements translate into some remarkable numbers. At the end of 2006, revenue from UnitedHealth comprised 7% of Quest Diagnostics' $6.3 billion in annual revenue. Thus, in the first four weeks after LabCorp's exclusive national lab testing contract with UnitedHealth took effect (beginning January 1, 2007), Quest Diagnostics has lost the equivalent of approximately $220 million in annual revenue!

This is a significant development for the entire laboratory industry. The switch of $220 million per year in lab business from one laboratory to competitors in the space of just 30 to 60 days is, to the knowledge of THE DARK REPORT, without precedent in the laboratory industry over the past 20 years.

The primary beneficiary of this situation is LabCorp. It has a favored contract position with UnitedHealth and is believed to be gaining most of the business that is leaving Quest Diagnostics. Also benefiting from this situation are local laboratories that hold regional contracts with UnitedHealth. They tell THE DARK REPORT that they are adding a substantial volume of UnitedHealth business.

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

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SUBSCRIPTION TO THE DARK REPORT INTELLIGENCE SERVICE, which includes THE DARK REPORT plus timely briefings and private teleconferences, is $13.10 per week in the US, $13.70 per week in Canada, $14.85 per week elsewhere (billed semi-annually).

It is likely that the laboratory industry has embarked on a cycle of change that will take several years to unfold. There are at least four ways in which the status quo will change.

Managed Care Contracting

The biggest effect will be seen in managed care contracting. LabCorp's unprecedented, 10-year exclusive contract with UnitedHealth is likely to be just the first. It is believed to have negotiated a similar, exclusive contract with **Horizon Blue Cross Blue Shield of New Jersey**. If it is willing to trade low prices and a large financial guarantee that it will move leakage back into the network, it may win other exclusive contracts with the nation's largest health insurance companies.

Of course, Quest Diagnostics will have a competitive response to LabCorp. It can be expected to become an aggressive bidder against LabCorp for these same contracts. It will not concede this business without a tough fight.

Which brings up the second way that the status quo will change. Should Quest Diagnostics and LabCorp end up in a slugfest over big managed care contracts, payers can be expected to win lower prices. If they do, it will put regional laboratories in a financial squeeze, assuming that they are able to maintain network status with these payers.

Entry Into New Cities

Third, by intent, LabCorp is using the UnitedHealth contract to expand in communities and regions where it historically has had little or no presence. Such expansion will make LabCorp a tough, new competitor in these communities. It plans to build an extensive, nationwide network of laboratories and patient service centers.

Fourth, the UnitedHealth contract is already triggering new growth strategies between the two blood brothers. For example, Quest Diagnostics announced that it is looking to expand in the Pacific and in South America. It also announced plans to enter the point-of-care testing business and then, within days, acquired **HemoCue** of Ängelholm, Sweden.

It is important for lab directors and pathologists to understand that the UnitedHealth contract sets forces into motion that will change the status quo for years. LabCorp took a bold step with its willingness to accept lower pricing and to offer UnitedHealth a $200 million incentive that it could bring leakage under contract.

Should LabCorp be willing to extend similar terms to other large health insurers, such as **WellPoint**, **Aetna**, **Cigna**, and **Humana**, Quest Diagnostics will certainly respond competitively. After all, Quest is now in a position in which it must defend its existing managed care contracts. It will also be motivated to strip managed care contracts away from LabCorp as a way to regain market share.

Unruly And Unpredictable

That's why the competitive market for lab testing services will be unruly and unpredictable in the near future. Regional laboratories and pathology group practices will need to stay alert for threats to their existing sources of specimens.

To provide understanding of how Quest Diagnostics and LabCorp view the current situation, THE DARK REPORT offers an analysis of each company's public comments and strategies on the pages that follow. Keep in mind, also, that UnitedHealth has been an active participant in this market upheaval. It is willing to require patients to pay out-of-pocket when the physician sends lab tests out of network. It is also willing to take punitive action against physicians who fail to cooperate by using network laboratories.

Finally, consider this: if Quest Diagnostics and LabCorp are in the midst of a 15-round championship fight, then round one goes to LabCorp. But, with 14 rounds to go, it is too early to judge the outcome. TDR

New Competive Forces Alter Market Status Quo

Quest Diagnostics announces plans to expand internationally and enter POCT

CEO SUMMARY: January was not kind to Quest Diagnostics, as the company disclosed that it was likely to lose all its UnitedHealth business by year end. It also found itself excluded from the Horizon Blue Cross Blue Shield of New Jersey program. By February 1, however, Quest Diagnostics had acquired HemoCue, a point-of-care testing company with international distribution and annual revenue of $90 million.

EXPECT AN INTENSE CONTRACTING WAR TO BREAK OUT between **Quest Diagnostics Incorporated** and **Laboratory Corporation of America**. As this war develops, it is likely to affect the entire laboratory industry.

But that's just for starters. When LabCorp negotiated its exclusive national lab services contract with **UnitedHealth Group, Inc.**, it set in motion a number of forces that will disrupt the status quo of laboratory testing in the United States. In public statements and presentations at financial conferences, executives at Quest Diagnostics and LabCorp have begun to provide clues as to how they believe the laboratory testing marketplace will evolve.

In managed care contracting, LabCorp has already stung Quest Diagnostics twice. First was the UnitedHealth contract. *(See TDR, October 14, 2006.)* Second, in January, **Horizon Blue Cross Blue Shield of New Jersey** excluded Quest Diagnostics (and **Bio-Reference Laboratories, Inc.**) from its PPO program.

LabCorp was already the exclusive statewide laboratory provider for Horizon's HMO. It is believed that LabCorp offered Horizon an improved contract to become the exclusive provider for its PPO and other plans.

That strategy would be predictable for LabCorp. The more it can exclude competing labs in the New York/New Jersey area from regional managed care contracts, the easier it is for LabCorp to persuade local physicians to use its services. Based on this strategy, it would not be surprising to see additional announcements from regional players that they are excluding Quest Diagnostics and other regional laboratories in favor of LabCop.

Looking For Opportunities

Quest Diagnostics recognizes this development. On January 25, CEO Surya N. Mohapatra told financial analysts, "We are monitoring the competitive environment. We expect to see competitive pressure play out for the next six to 12 months.

"We are seeing a competitor [LabCorp] use lower price for exclusivity over the long term," continued Mohapatra, "and, more importantly, guaranteeing leakage. And we have a payer that's protected itself by having $200 million in transaction costs, but has gone out of its way to take choice away from physicians

and their patients—basically turning PPO products into [closed panel] HMOs."

Mohapatra called attention to the relationship between low price and service. "These contracts are not profitable [to our competitor] and service will be affected," he said. "We will continue to provide service and remain competitive with our pricing."

Quest Diagnostics believes that its competitor will continue to use a similar pricing strategy with other managed care contracts. This process will play out over the next year. By implication, Quest Diagnostics is indicating that, if the pricing that LabCorp offered to UnitedHealth and other health insurers is truly below the cost of providing services, then LabCorp's financial performance will reflect this situation at some point.

On the other hand, it may be that LabCorp has developed an operational cost advantage that allows it to offer lower prices to managed care companies and still earn an acceptable margin. Over time, LabCorp's quarterly financial reports will reflect these facts.

Buying Labs Overseas

Faced with the rapid erosion of 7% of its annual revenues, Quest Diagnostics is adding to its business plan. "There are two new areas for us," Mohapatra explained. "One is international expansion. We have narrowed down our prospects. We will go to selected countries in the Pacific and South America. The second area is point-of-care testing (POCT). This is a market segment where growth is averaging 8% to 10% per year."

Quest Diagnostics wasted no time acting on this second business strategy. Several days later, on February 1, it announced that it would pay $420 million to acquire **HemoCue AB**. This company is based in Sweden and sells a line of point-of-care testing (POCT) products.

In practical terms, Quest Diagnostics faces a simple problem. During the course of 2007, it projects it will lose 8% of its revenue base (7% from the UnitedHealth contract and 1% from the Horizon PPO contract), or about $500 million. It must replace that revenue. One way to accomplish this goal is to acquire other companies. HemoCue is a start.

Quest Diagnostics will be looking for laboratories to acquire in the United States as well as specific countries around the Pacific Rim and in South America. There are laboratories available to be acquired. For the most part, however, these are smaller lab companies that serve healthcare systems for which growth prospects are modest.

The most interesting wild card over the next year will be the managed care contracting strategy Quest Diagnostics implements in response to LabCorp's coup with UnitedHealth. Over the next 12 to 24 months, there is likely to be intense competition between the two blood brothers as existing managed care contracts come up for renewal. TDR

Quest Buys HemoCue, Enters POC Testing

With the acquisition of HemoCue AB, Quest Diagnostics Incorporated is now a worldwide player in point-of-care testing (POCT).

HemoCue, based in Ängelholm, Sweden, generates about $90 million in annual revenue and distributes its products in 120 countries. It says it has installed "more than 200,000 analysers and photometers globally."

Among HemoCue's primary products are the HemoCue B-Hemoglobin system, which it has sold since the early 1980s. It launched the HemoCue B-Glucose system in the early 1990s and a urine albumin system in the early 2000s. Last year, it introduced HemoCue WBC, for total white blood cell count.

LabCorp Uses United As a "Growth Driver"

Company reports positive progress from the first six weeks of its United Contract

CEO SUMMARY: In the first six weeks since its exclusive national contract with UnitedHealth became effective, Laboratory Corporation of America has made major gains in several key markets. It has also begun to share the details of its three-phase strategic plan to maximize the leverage it gets from its 10-year pact with UnitedHealth.

IN JUST A FEW SHORT WEEKS, **Laboratory Corporation of America** has radically destabilized the status quo between itself and **Quest Diagnostics Incorporated**.

On January 25, Quest Diagnostics told financial analysts that, by December, it expected to lose literally all its UnitedHealth business (7% of revenues) and all the business it had with **Horizon Blue Cross and Blue Shield of New Jersey** (1% of revenues). Collectively, these two lost contracts represented $500 million of revenues for Quest Diagnostics in 2006.

Seizing The Opportunity

LabCorp expects to pick up the lion's share of this business. If it does, then it will have triggered one of the largest shifts in market share seen in the laboratory industry in the past 20 years—and it will have accomplished this feat in a relatively short period of time.

If there is a downside to LabCorp's managed care contract strategy, it is likely to be linked to the level of pricing LabCorp accepted in exchange for exclusivity and a 10-year contract with UnitedHealth. As noted on pages 5-6, Quest Diagnostics' CEO has publicly questioned his competitor's ability to provide satisfactory service at a contract price which Quest Diagnostics considered unacceptable during its negotiations with UnitedHealth.

LabCorp recognizes this challenge. "We are in a very tough pricing environment," stated LabCorp CEO David P. King at an investor conference in January. "The UnitedHealth contract presented us with a singular opportunity. It gave us an exclusive relationship with the nation's largest health insurer, when measured by revenues, and the nation's second largest, when measured by covered lives."

On the other hand, LabCorp's CEO has consistently stated that LabCorp expects to maintain adequate profit margins on the pricing it agreed to accept from UnitedHealth. It has even provided a measurement tool, stating it will sustain its current level of EBITDA (Earnings Before Interest, Taxes, Depreciation, and Amortization.) The truth of that assertion will be demonstrated during the next 18 months, each time LabCorp reports its quarterly financial performance.

LabCorp also faces the challenge of converting this short-term shift in market share into long-term gains. Linchpin to this

strategy is its exclusive national laboratory services contract with UnitedHealth. LabCorp's strategy is to use this contract as the "growth driver" for expansion into new regional markets and to increase market share in existing markets.

Contract Has Three Stages

LabCorp intends the UnitedHealth contract to be a growth driver in three stages. In stage one, LabCorp considers that it has gained exclusivity with UnitedHealth in the markets served by **Oxford Health Plans**, **Pacificare Colorado**, **Neighborhood Health Partnership** in Florida, and **Mid Atlantic Medical Services, LLC** (MAMSI) in Maryland and Virginia, along with its status as the sole national laboratory for UnitedHealth.

In stage two, LabCorp intends to establish additional regional networks of laboratories to serve UnitedHealth patients. "Over time, we will broaden the networks to bring more and more UnitedHealth providers into network status," explained LabCorp CEO David P. King at a recent investor conference. These networks are likely to follow the business model of the Oxford network. This would place LabCorp in a primary position.

New Laboratory Networks

It is also a clever way, in coming years, for UnitedHealth and LabCorp to bring regional laboratories into provider networks with reimbursement arrangements that are more favorable to UnitedHealth. Over the long term, this factor could further disrupt existing managed care contract practices for laboratory services, particularly if UnitedHealth gains substantial benefits from expanding the Oxford laboratory network concept to other regions and other national payers take steps to implement similar arrangements.

In stage three, LabCorp hopes to use the networks and standardized laboratory data to develop ways for laboratory testing to contribute to enhanced healthcare outcomes. LabCorp hopes it can work with UnitedHealth to use the principles of evidence-based medicine to develop more effective treatment plans.

The scale and scope of LabCorp's business strategy and ambitions are revealed by its remarkable accomplishment. Between October 3, 2006, and January 1, 2007, it opened 400 new patient service centers (PSCs) across the United States. It also hired 1,200 new employees. This new staff is involved in sales, provides phlebotomy services in PSCs and other locations, handles expanded courier routes, and processes the increased volume of specimens arriving in its laboratories.

Seizing The Opportunity

Laboratory administrators and pathologists should note that LabCorp's primary objective is to leverage the infrastructure it is now creating to serve UnitedHealth. It wants to expand throughout the country.

"Our greatest strength [from the UnitedHealth contract] has been in New York and Florida," stated King to a gathering of financial analysts and investors. "We view this [UnitedHealth] as not just opportunities in the Northeast, but as a national opportunity—an opportunity for which we intend to take full advantage."

LabCorp can certainly create that opportunity if LabCorp, in the second stage of its UnitedHealth contract strategy, succeeds in creating Oxford-like lab networks in other parts of the country. That would give it powerful leverage in those regions.

Viewed from the first six weeks of the UnitedHealth contract, LabCorp has certainly surprised many critics. Its success also recalls one of the most famous advertising campaigns of the 1960s, when **Avis Company's** "We're Number Two—We Try Harder" drew lots of attention away from industry leader **Hertz Corporation**. At this point, LabCorp has shifted attention away from its larger rival. It may still be number two in size, but it has certainly served notice that it won't be a passive competitor. TDR

UK Laboratories Pushed To Serve Primary Care

National Health Service shifts emphasis to early detection and active intervention

CEO SUMMARY: At the fifth annual Frontiers in Laboratory Medicine (FiLM) meeting in Birmingham, England, lab administrators and pathologists from the United Kingdom and the United States gathered to share knowledge about innovations in the management of clinical laboratories. The event sold out for the second consecutive year, demonstrating the keen interest in the United Kingdom for improving laboratory testing services.

CLINICAL LABORATORIES in the United Kingdom are responding to significant changes in their nation's health system.

These issues were a primary theme at the fifth annual *Frontiers in Laboratory Medicine* (FiLM) meeting, held in Birmingham, England, on January 30-31, 2007. FiLM is a co-production of THE DARK REPORT and the UK's **Association for Clinical Biochemistry** and, like the *Executive War College*, provides information and case studies about management innovations in clinical laboratory and anatomic pathology.

"Our healthcare system is placing a new emphasis on several aspects of care," noted Michael Hallworth, Ph.D., Consultant Biochemist at **Royal Shrewsbury Hospital** in Shrewsbury, England. "First, there is an effort to increase early detection and active intervention in primary care settings. As this occurs, providers are seeking to implement the principles of evidence-based medicine.

"Second, programs to improve access and to support patient-centered care are being launched," he continued. "Laboratories must respond to the evolving needs of primary care clinics and patients.

"Third, efforts have commenced to give both primary care physicians and patients more choices of providers, particularly when it comes to hospital care," observed Hallworth. "The **National Health Service** (NHS) is instituting new procedures that make it easier for a patient to select the hospital they prefer—and for the money which pays for that care to follow the patient.

"Payment By Results"

"Fourth, programs to provide 'payment by results' are giving providers extra incentive to improve patient safety and to improve clinical outcomes," observed Hallworth. "Funding for these 'payment by results' programs is substantial and having positive effects.

"Fifth, the NHS plans to create opportunities for private sector participation in our healthcare system," he added. "The thinking is that private providers can add additional capacity and create competition that will spur everyone to improve."

Hallworth believes that laboratories in his country will be challenged to adopt

and support these system-wide initiatives. "In our country, laboratories are based, for the most part, in hospitals," he explained. "Currently, these hospital laboratories are the main source of testing for the primary care clinics.

"In recent years, primary care physicians have increased their utilization of lab tests as they respond to incentives for early detection and active intervention," said Hallworth. "However, hospital laboratories haven't seen a proportional increase in their funding to cover the cost of this additional testing. That's one example of why changes must come to laboratory medicine in this country."

Lab Test Utilization

At FiLM, these developments were discussed. One session paired Priscillla Cherry, now President of Laboratory Services at **Fairview Health** in Minneapolis, Minnesota, with Bob Dredge, Senior Fellow, Financial Management at the **University of Keele**, in Keele, England. Both speakers explained how laboratory organizations were evaluating ways in which increased testing could support a measurable improvement in clinical outcomes, while simultaneously lowering the overall cost per healthcare encounter.

"However, a key problem we have in the United Kingdom is that the financial accounting systems in use by laboratories and their parent health trusts makes it difficult to get the information needed to accurately assess the cost of care and the associated clinical improvements that result from better use of laboratory testing," stated Dredge. He is working to develop the accounting systems that could be used by laboratories to do such analyses.

At the same time that the United Kingdom's healthcare system is pushing for progress in the five areas noted above, a parallel effort is under way in the pathology sector. As used in the U.K., pathology refers to all of laboratory medicine, including clinical laboratory testing and anatomic pathology services.

During the past 18 months, the NHS tasked Lord Carter of Coles to lead an "Independent Pathology Service Review Panel." This panel issued its report and recommendations in August 2006. (At *http://www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4137606&chk=J4*). At FiLM, members of the Pathology Service Review Panel provided insights and updates to the pilot projects now in the implementation stage.

"One of the important elements of the Review was a recommendation that pathology be funded through its own independent organization," stated Professor Chris Price, a Panel member. "With the emphasis on primary care, the current funding arrangements for pathology services—usually through the parent hospital—have lacked the flexibility required for laboratories to respond to the evolving needs of primary care clinics.

"Another recommendation was to create pilot projects to demonstrate the effectiveness of different operational models of pathology," continued Price. "For example, some pilot projects will create consolidated laboratory organizations that integrate laboratory services across several hospitals in an area."

Lab Test Reimbursement

"However the biggest challenge will be the process of commissioning lab tests [establishing reimbursement levels], as most of the commissioners know little about lab testing," observed Hallworth. "They are focused on commissioning patient episodes and care pathways. Lab testing is part of those pathways—and often have an important bearing on the ways those care pathways are managed." TDR

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LIS As Productivity Tool Throughout the Laboratory

Laboratories are becoming sophisticated in their approach to lab information systems

CEO SUMMARY: Is the classic laboratory information system (LIS) morphing into a different information technology product? That's the observation of one laboratory IT expert, who says that "best of breed" LIS products are becoming productivity tools that support improved clinical performance and give lab managers the comprehensive, real time information they need to closely manage laboratory work flow, including genetic and molecular testing.

PERFORMANCE DEMANDS on laboratory information systems (LIS) are intensifying, yet many products currently in the marketplace lack the full range of capabilities needed to help laboratories keep pace with unfolding healthcare trends.

"Legacy lab information systems are caught within the two jaws of an ever-tightening vice," observed Gilbert Hakim, CEO of **SCC Soft Computer** (SCC), in Clearwater, Florida. "On one side is the constant flow of new technology in molecular and cytogenetics testing. This places more demands on existing laboratory information systems than in past years.

"On the other side, operational pressures and the unique needs of hospital laboratory outreach programs are putting equally powerful demands on the existing LIS," continued Hakim. "Lab administrators need detailed flows of real time data to more tightly manage the laboratory. They also need an informatics solution to drive automation and provide the expanded range of functions required to support an outreach testing program."

Just two years ago, Hakim made many of the same points in an interview with THE DARK REPORT *(see "LIS Market Evolving to Serve New Needs," May 30,* 2005). "However, several key differences between the lab industry in May 2005 and the lab industry today are startling," declared Hakim. "For example, the menu of tests offered by laboratories continues to increase and become more complex.

Sophisticated Lab Operations

"At the same time, lab managers are becoming more sophisticated in how they operate their laboratories," he added. "Automation in the laboratory, along with the growing use of quality management methods like Lean and Six Sigma, require more sophisticated information technology.

"One reason so many laboratories are automating work processes and asking more of their laboratory information system is the shortage of skilled labor," said Hakim. "To remain competitive, and to handle the constantly increasing volume of specimens moving through their labo-

ratory, lab directors must find ways to make their laboratories more productive.

"Automation is one way to achieve that," he explained. "Information technology can also be used to enhance specific work processes in the pre-analytical, analytical, and post-analytical stages.

"However, in many ways, laboratories are moving faster than their suppliers," he stated. "LIS vendors are struggling to keep pace with the demand by their laboratory customers for more functionality, more reliability, and better integration of the LIS with the information systems used in their parent hospital or by their office-based physician clients."

Supporting Lab Outreach

"Laboratory information systems grew out of the need to create a single data base to collect, store, and report lab test data being produced by the host of instruments and analyzers finding their way into laboratories during the 1980s and 1990s," explained Hakim. "But most of these LIS products were never designed to support a hospital laboratory outreach program or act as laboratory automation software.

"Thus, during this decade, as more laboratories launched outreach programs, installed automated systems to boost productivity, and began to manage laboratory work processes in a more proactive way, their legacy LIS lacked the needed functionality," he said. "Add to this the steady growth in molecular testing, genetics, flow cytometry, and anatomic pathology—all of which generate substantial quantities of data. The LIS industry has been challenged to keep pace with all the demands of their laboratory customers."

Watching the changes unfolding in the laboratories of his customers, Hakim has come to view the design and function of LIS in a different way. "In today's intensely-managed laboratory environment, laboratory informatics has become a productivity tool," he said. "However, for any laboratory information system to succeed as a sophisticated, robust productivity tool, it needs to be capable of accepting and consolidating data from all the laboratory's activities.

"This means accepting data from all different types of testing, from routine to molecular testing, genetics, flow cytometry, and anatomic pathology," explained Hakim. "It also means having the capability to track the work processes in the laboratory, from pre-analytical to post-analytical, including storage and reporting."

The business strategy at SCC has been to deliver a unified, comprehensive laboratory information system that can support all the lab's IT needs. "Our goal has been to eliminate the need for a laboratory to go to an outside middleware vendor to get functions and performance that it needs, because its legacy LIS cannot deliver.

"All lab managers are familiar with the challenges," he continued. "First is the shortage of medical technologists. Without adequate staffing, some labs must send out work to reference labs.

"Additionally, the shortage of technicians causes labor costs to rise, and because the genetics market is booming, some bench technicians are jumping into clinical and research settings for better jobs in genetics and molecular testing, cytogenetics, and flow cytometry," added Hakim.

Shortage Of Skilled Labor

"As labs lose staff, they are forced to adopt automation and introduce robotics," Hakim said. "Robotics becomes financially attractive when labs can't hire enough technicians or processing people.

"Another factor in the acceptance of automation is that sophisticated laboratory information systems are using rules engines to verify results," he continued. "In the past, every result had to be manually reviewed. Now, 60% to 80% of results that are normal can come from instruments and be posted without staff review because the rules engine validates and releases normal results.

"Robotics and rules engines allow labs to cut the volume of data they need to review," Hakim noted. "But robotics and rules engines are also forms of automation, which are good for LIS companies. We connect robotics directly and we have a very robust rules engine. What's more, all errors originating within instruments and robotics, along with patient diagnosis and history, is in one system. Therefore, our rules engine has direct access

"For labs doing molecular testing and cytogenetics, the big issue is productivity," he added. "These labs are desperate for automation because they already operating at capacity and yet the volume of specimens continues to increase. The right LIS can allow them to process more specimens, which means more income. And these tests don't generate $5 or $10 per test. Some genetic tests start at $1,000 and it goes up from there. Genetic tests can be enormously profitable for laboratories.

Outreach Testing Needs

"Over the past few years, hospitals have added to the volume of outreach work they do," Hakim said. "As volume increases, labs often find that their legacy LIS can't support many outreach functions. About 90% of large hospitals today have outreach programs. But 10 years ago, only about 20% of large hospitals had outreach programs. They have added commercial outreach testing because they had extra capacity and they had high fixed costs for labor, instruments, and real estate. When they brought in outreach work, the incremental cost they had was for reagents, and that's peanuts compared with their fixed costs. So, the profit on this outreach work is often more than 50% to 60% on every sample.

"However, with the larger scale of testing comes the need to more closely track and monitor that work as it flows through the laboratory," observed Hakim. "If the lab's LIS is inefficient, there is the risk of service breakdowns that could negatively impact inpatient testing and outreach clients.

Is the Traditional LIS On Path to Extinction?

WITHIN THE LIS MARKET, consolidation has been ongoing for several years. "The result is that some smaller LIS vendors are not making many new sales and are really in an almost dormant stage," said Gilbert Hakim, CEO of SCC Soft Computer.

"It also means that the number of companies developing and supporting laboratory information systems is declining steadily," he stated. "With fewer hospitals spending money to upgrade or purchase a new LIS, it is tougher for the smaller companies to have the cash flow needed to support their installed base of systems while putting money into developing the next generation of LIS products.

"Many LIS vendors are just trying not to lose accounts," observed Hakim. "They aren't adding new ones. In fact, last year, one consultant suggested that the LIS market is dead.

"I don't know if that's true, but I do believe the market is moving beyond the traditional LIS," he explained. "Across the healthcare system, the trend is to integrate systems and unify the collection of information and access to that information. That's one reason why we advise hospitals to invest in more sophisticated systems that can consolidate data across all laboratory systems."

"That is why any laboratory with a growing, successful outreach program needs a sophisticated and efficient informatics capability," he said. "Continued growth from outreach specimens frequently motivates hospitals to upgrade their legacy lab information systems. Since the majority of LIS vendors do not produce the software needed to handle the most sophisticated work being done in labs today, that is one reason labs have often turned to middleware sources.

"At the same time that laboratories have become more complex and sophisticated users of laboratory information systems, the

LIS product pipeline has failed to keep pace," observed Hakim. "For instance, some LIS vendors have left the market and have gone into more lucrative areas such as hospital information systems. In other cases, LIS vendors have been acquired.

"These trends have been good for us," he added. "The strong demand has allowed us to pioneer the development of the sophisticated modules that the market needs.

"For example, during the past three years, the market for molecular testing and cytogenetics has grown steadily," explained Hakim. "Today, these tests are being done in tertiary care hospitals, in teaching hospitals, larger hospitals, and integrated delivery systems.

"In addition to doing cytogenetics and molecular testing, all of these large hospitals also have anatomic pathology, blood banks, and flow cytometry," Hakim said. "The scientists in these large labs need a single database that can consolidate information from all of these different systems. Of course, they want everything at hand from the reporting side and from the diagnosis side. To render a diagnosis, they need all results from the same specimen across multiple departments.

Increasing Productivity

"When the laboratory has an information system that consolidates data from all the different systems and sources, this increases the productivity of the scientists reviewing the information," he added. "It means that the pathologists don't need to jump back and forth among the different systems to determine the diagnosis.

"We have examples of well-known hospitals that selected our LIS solutions because our systems eliminate the need to go through separate systems (in pathology, molecular testing, and in hematology, for example) just to assemble the result to render the diagnosis. Our system makes everything available in one view.

"This can have a dramatic impact on productivity, since the most expensive labor is for those top scientists who use information from several systems to make the diagnosis," stated Hakim. "An LIS that collects all the requisite information can save enormous amounts of time and labor costs.

"But, here's another important aspect about these systems that is often overlooked in the outreach market," Hakim added. "Systems that consolidate all the necessary data are saving a lot of time for outreach physicians too. These doctors don't want to get five different reports for the same patient. They want everything consolidated into one report. They want integrated report modules, and that's what our system does.

Turning Away Work

"Another dimension to using LIS as a productivity tool is the fact that many hospitals don't have enough pathologists to handle the steady increase in cases," Hakim continued. "I've seen laboratories turning away work because their pathology department was already at capacity. They have no choice because most molecular and cytogenetics labs are manual.

"In these situations, our integrated LIS can increase capacity because our software consolidates information from all the various departments, including cytogenetics, molecular, and flow cytometry," he said. "This produces increased productivity at the same time that service to referring clinicians improves.

"I believe the market will be huge for laboratory information systems that can handle all the informatics needs of hospital laboratories, particularly where there is an extensive molecular pathology program and a thriving outreach business," predicted Hakim. "Labs will see LIS products that collect data across all departments of the clinical and anatomic pathology laboratories."

THE DARK REPORT observes that Hakim's description of LIS as a productivity tool accurately reflects the changes taking place in hospital laboratories across the United States today. It marks another step in the evolution of LIS products. TDR

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Whooping Cough Cases Reveal Test Deficiencies

Molecular tests called into question as hospitals research outbreaks of Bordetella pertussis

CEO SUMMARY: Doctors rely on labs for the definitive diagnosis of the bacterium that causes whooping cough. Yet in several recent cases, the use of a molecular test for a definitive diagnosis led to questions about the effectiveness of the test. Molecular pathologists recommend labs may need to do a second test to confirm initial findings and labs may need to be diligent about any equivocal findings to avoid reporting false positive results.

IN RECENT MONTHS, SEVERAL HOSPITALS made headlines as they coped with outbreaks of *Bordetella pertussis* (whooping cough). In some cases, the news was not the identification of *Bordetella pertussis* within the institution, but the fact that laboratory testing appeared to be generating a high rate of false positives.

As more cases of *Bordetella pertussis* surface, health officials are facing difficult questions about how to diagnosis this infection. The issue is important to pathologists and lab directors because they will increasingly be asked to identify pertussis and other conditions using molecular diagnostics. "To do so accurately, definitive protocols need to be developed that may require labs to perform additional testing," said Michael Mihalov, M.D., Chair of Pathology and Director of the Diagnostic Molecular Pathology Lab at **Resurrection Medical Center**, in Chicago.

Mihalov is uniquely qualified to comment on this topic because he is an expert in molecular pathology and he trained as a pediatric resident at Chicago's **Cook County Hospital** before going into pathology. As a result, he has clinical experience with whooping cough patients.

Last year, infectious disease specialists at the **Dartmouth-Hitchcock Medical Center** in New Hampshire identified what they thought was an outbreak of pertussis. Over the course of the outbreak, about 1,000 health care workers were tested, 142 were told they had the condition, and more than 4,500 hospital workers got the acellular pertussis vaccine.

A Case of Misplaced Faith?

Last month, a number of newspapers reported that epidemiologists and infectious disease specialists had decided that healthcare experts had placed too much faith in the new, molecular test for pertussis. "In fact, the issue is not so much that experts placed too much faith in molecular testing, but rather health systems have not yet developed a clinically relevant algorithm for interpreting molecular results," observed Mihalov.

"Recent articles on this outbreak focused only on the molecular test and didn't elucidate the difficulties of identifying the specimen with a culture and using a molecular test," Mihalov said. "Growing a culture is just as difficult, if not more difficult, as doing the molecular test. Yet, these

reports said the molecular test failed. They didn't say that the test it is replacing is also fraught with problems.

"For cases of pertussis and other similar infections, we're in a transition period where the medical field is still attempting to define what constitutes a clinical infection. Culture is probably not the gold standard any longer because it is too insensitive. If the clinician obtains an adequate specimen and has a lab nearby that is proficient in doing cultures, then you could do it by culture," Mihalov said. "But in most cases, we don't have that, which is why molecular technology is replacing the growing of cultures. The **Illinois Department of Health** does molecular testing almost exclusively for pertussis, for example.

Molecular Testing Caveats

"But there are caveats to molecular testing which we have to understand," he added. "Every test has a positive range, an equivocal range, and a negative range. If the original tests are in the equivocal range, then pathologists and clinicians should think carefully before assuming that the specimens are clinically diagnostic of a disease. In the Dartmouth-Hitchcock case, clinicians made an assumption that the result was positive, meaning there was an outbreak. Those assumptions may need some reworking, particularly if any of the initial results were in the equivocal range. In fact, the data from Dartmouth-Hitchcock is still being analyzed, I believe, and it remains to be seen if pertussis organisms were present or if there was some cross reactivity with other nucleic acid that was present during the original testing.

"Molecular testing has inherent limitations that must be taken into account," Mihalov continued. "Many of these tests are developed by individual labs, and not every lab uses the same algorithm to confirm positive results.

"As we move forward, and more of these situations occur in which clinicians use lab data to define outbreaks, the tests and the clinical expertise will both improve," he said. "First, many labs will employ a second molecular test to confirm the initial result. And second, over time, the FDA is likely to approve methods for testing such specimens. When the FDA approves a specific test, it is likely to have undergone rigorous testing to define the specificity of the test.

"What's happening today is that many labs are using analyte specific reagents (ASRs), or home brews, for the molecular test they use to identify pertussis," Mihalov explained. "These home brews are not FDA approved tests but the FDA has allowed labs to develop in-house procedures using these ASRs. When labs use them, they also need to validate the test in their own labs. The problem is that in most labs, we are limited in the number of organisms against which we can test our new reagents. Furthermore, most labs don't have enough experience to know the exact specificity of the test when using a home brew assay.

Specificity Required

"As more labs use molecular tests," Mihalov said, "they will need to more rigorously determine the specificity of their tests. In addition, every lab will need to ensure that the result is unequivocally positive before it labels something a definite infection, especially with an organism like *Bordetella pertussis*.

"To confirm a diagnosis, it may be necessary to perform additional testing," he said. "There are two ways to do that. First, you can ask the clinician for another sample, particularly when the first result is equivocal. Or, second, you could get a confirmation of an initial positive result with a second molecular test. Ideally the second test would target a different region of the organism's nucleic acid than the initial test. Then, only if both of those tests are positive would we call it a positive result." TDR

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New Rules to Boost Cancer Test Accuracy

Breaking new ground, oncodiagnostics are changing how pathologists test for breast cancer

CEO SUMMARY: Recent developments in breast cancer testing are leading to changes in pathology. Oncologists and pathologists have issued new guidelines regarding HER2 testing and new research suggests changes may be coming for estrogen-receptor testing as well. For the first time, the new guidelines require a certain level of testing and new procedures for pre-analytical processing.

CONCERN THAT CERTAIN WIDELY USED BREAST CANCER TESTS may underestimate the number of patients who test positive for breast cancer has fostered three recent developments regarding laboratory testing that may affect the patient's ability to receive hormone therapy.

Each of these developments signals a shift in acceptance for molecular testing. Further, each represents recognition that the quality of molecular tests results can vary, leading to false negatives and a call for more definitive testing.

First, the **American Society of Clinical Oncology** (ASCO) and **College of American Pathologists** (CAP) made news in December when they jointly recommended practice guidelines for HER2 testing for breast cancer. The issue was the subject of a cover story in *CAP Today*. Second, **UnitedHealthcare** followed the CAP-ASCO announcement with a decision to cover members who had earlier tested for breast cancer, and wanted retesting due to concern that the earlier test was inaccurate. UnitedHealthcare encouraged its members to discuss the issue with their oncologists to determine if retesting was appropriate.

Third was the publication of a study in the December 20, 2006, issue of the *Journal of Clinical Oncology*. Researchers determined that a new anti-estrogen receptor antibody reagent for identifying estrogen receptors (ER) in breast cancer specimens is significantly more sensitive and specific than current reagents. Participating in the study were several laboratories, including **PhenoPath Laboratories** in Seattle, Washington.

Deficiencies In Gene Testing

Research shows that 14% to 16% of patients are incorrectly labeled with overexpression of HER2/neu gene and 18% to 22% are incorrectly reported with gene underexpression. These deficiencies in HER2 testing led to the new guidelines.

"The new guidelines are significant for two reasons," said Allen M. Gown, M.D., Medical Director and Chief Pathologist at PhenoPath. "First, pathologists and oncologists developed them jointly. Researchers know that such tests require close collabo-

ration between the two specialists. These new guidelines reflect that knowledge. Second, the guidelines address the issue of fixation time in specimen processing, a first in pathology."

Similar error rates are occurring in HER2 and ER testing and inadequate fixation may cause false negatives in both HER2 and ER testing, Gown said. A minimum fixation of six hours is needed for ER testing, he added.

"One significant factor that affects the accuracy of such testing is pre-analytical variables, and the most critical is fixation time," Gown said. "The new guidelines require six to 24 hours of fixation."

In an interview with THE DARK REPORT, Gown said, "These developments are a reminder that lab testing for anything is a work in progress. Our latest research shows, for example, that we may not necessarily be using the best reagents for estrogen receptors. Laboratorians should study these developments and determine if they are using optimal tests. If they are not using optimal tests, they could be failing to identify cancer cases.

"The new ASCO-CAP guidelines do not actually tell labs what reagents to use, but they do specify a certain way to conduct testing to achieve a level of accuracy that equals 90%," Gown said. "Now that standards for HER2 testing have been announced, we can assume that ASCO and CAP will consider guidelines for ER testing, based on the new research.

"For example, here at PhenoPath, in our most recent research, we evaluated a new anti-ER antibody called SP1 and compared its performance with that of the older 1D5 antibody," Gown explained. "We found the new SP1 antibody was more sensitive than the older 1D5 antibody. About 8% of the patients were characterized as ER-negative with the older 1D5 reagent. But, these patients were positive with the new SP1 antibody, and this group of patients clearly demonstrated improved survival.

"When you do the math, it's clear that 8% of patients could be 15,000 to 20,000 casts of cases of cancer that are missed each year," Gown explained.

"For this reason alone, it is important for laboratorians to take notice that this research was published in an oncology journal, the *Journal of Clinical Oncology*," Gown said. "This type of research gets published in oncology journals because it has important implications for tumor treatment. For this reason, pathologists should be reading oncology journals. This is where the field is going, and it's where all the new developments in oncodiagnostics are reported."

From Research to Action

THE DARK REPORT has several observations on this issue. First, research into the lack of consistency and accuracy in performing the HER2 and ER testing demonstrates how the healthcare system is moving quickly to measure outcomes, identify areas for improvement, and then implement those improvements in the form of published guidelines. Second, the collaboration between oncologists and pathologists to improve HER2 and ER testing shows how molecular diagnostics require pathologists to have a more active ongoing role with clinicians.

Third, as Gown noted, pathologists seeking to stay informed about the latest developments in oncology, infectious disease, and other fields need to be aware of the literature in other specialties. This development is another sign of growing clinical collaboration between pathology and most medical specialties.

In the coming years, the most effective pathologists will be those who reach outside the walls of the laboratory to interact with and support clinicians in getting the right answer at diagnosis, and then consulting with these specialists so that they provide the most appropriate therapies for patients. TDR

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INTELLIGENCE

LATE & LATENT

Items too late to print, too early to report

Recently **Quest Diagnostics Incorporated** disclosed that it was planning to acquire laboratories in other countries, particularly in South America and the Pacific Region. *(See pages 5-6.)* One potential acquisition candidate is **Diagnósticos da América** (DASA), a public laboratory company with lab facilities in several major cities in Brazil. With annual revenues in excess of US$260 million, it has existing scale to be attractive to Quest Diagnostics. Also, Brazil's healthcare system offers further growth potential in laboratory testing. As a public company, Diagnósticos da América has regularly come to the United States to participate in investment conferences.

Cytyc Acquires Adeza

Last week, **Cytyc Corporation** announced that it would pay approximately $450 million to acquire **Adeza Biomedical Corp.** of Sunnyvale, California. Adeza's primary product is a patented FDA-approved diagnostic test for fetal fibronectin, used to assess the risk of preterm birth.

KAISER PERMANENTE TO CREATE DATABASE WITH GENETIC INFO

Last week, a research division of **Kaiser Permanente** began contacting two million of its adult members in the Northern California Kaiser program. It is asking these members to support the creation of a database that will include genetic information by volunteering to provide blood or saliva samples that can be used to determine their personal genetic profile. Kaiser expects that 500,000 people will eventually contribute genetic material. This puts the size of Kaiser's effort on par with the United Kingdom's **BioBank**, and the gene bank in Iceland that has data on 275,000 individuals. The name of this project is the Kaiser Permanente Research Program on Genes, Environment and Health (RPGEH).

ADD TO: Genetic Database

In recent years, **Geisinger Health System** in Danville, Pennsylvania, launched a similar project to create a medical database that includes personal genetic profiles of its beneficiaries. Organizers of the Geisinger and Kaiser data repositories expect to use the information to identify the genetic and environmental factors that influence common diseases. Priorities for researchers are heart disease, cancer, diabetes, high blood pressure, Alzheimer's disease, and asthma. Kaiser's clinical laboratory will participate in the collection of the blood and saliva specimens for the RPGEH data repository.

GENETIC DISCRIMINATION LAW MOVES TO VOTE

With relatively little publicity, Congress has been debating a bill that would bar discrimination by employers and insurers based on genetic information. Last week, the bill passed the House Committee on Education and Labor and now moves to the full House, where it is likely to be approved. The Senate has already twice passed a version of this bill, so it is expected that a final version of the bill will be passed and become law.

That's all the insider intelligence for this report. Look for the next briefing on Monday, March 12, 2007.

Preview #3

Executive War College

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LabCorp CEO David P. King on...
Managed Care Contracting for Lab Services: Important Changes Lie Ahead

In this special presentation, LabCorp's new Chief Executive Officer will provide insights about the managed care industry, the American healthcare system, and what changes are likely to occur in payer contracts for lab testing services. It's an *Executive War College* exclusive and Mr. King has been asked to speak plainly and candidly about important issues which can prove beneficial or financially corrosive to the entire laboratory industry. It's an opportunity to meet LabCorp's new leader and hear how this multi-billion-dollar lab company expects the lab testing marketplace may evolve in coming years.

For full agenda and program details, visit darkreport.com

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