Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

Stephanie Murg, Managing Editor, smurg@ioma.com

Vol. VII, No. 10/June 2007

CONTENTS

WASHINGTON G-2 REPORTS

Established 1979

Battle For Biosite Rages On As Beckman, Inverness Sweeten Offers

The battle to acquire Biosite (San Diego, CA) continues. After Inverness Medical Innovations trumped Beckman Coulter's March 24 offer of $1.55 billion, or $85 a share (a 50% premium to the company's trading price at the time), with a per-share offer of $90, Beckman amended its offer on May 2 to match it. Then, on May 9, Inverness raised its bid to $92.50 per share, a new offer that Inverness President and CEO Ron Zwanziger says he's "confident that Biosite will respond favorably to." As of press time, Beckman had not submitted a counter offer.

Biosite would have to pay a $50 million breakup fee if it decides not to accept Beckman's original offer, and speculation remains that Inverness's proposed financing for the deal is shaky. Beckman also has an ongoing relationship with Biosite to market the company's Triage test for B-type natriuretic peptide (BNP), a CLIA-waived test that is used in more than 70% of United States hospitals (see p. 12 for more about BNP testing). Beckman has said that it would keep Biosite's operations intact post-merger. In addition to a portfolio of rapid diagnostics, Biosite would help either bidder expand its pipeline in the promising field of proteomics-based diagnostics.

Kennedy's Lab Testing Bill Off The Fast Track

The bill to regulate laboratory-developed tests proposed by Sen. Ted Kennedy, S. 736, was not included in the recently approved legislative package (S. 1082) of reauthorization measures affecting pharmaceutical and medical device user fees and marketing. "We've told Kennedy's staff that we want to continue the dialogue [on this issue] and continue to talk with his staff," said American Clinical Laboratory Association (ACLA) President Alan Mertz at the organization's annual meeting in Washington, D.C.

Kennedy's bill, which is still alive, contains provisions that would designate most laboratory-developed tests (LDTs) as class II or III devices subject to the oversight of the Food and Drug Administration (FDA). Kennedy's staff had indicated that they aimed to get it passed quickly by attaching it to the FDA bill on the committee's "must-pass" list since the user-fee programs are set to expire on September 30 of this year.

Omitting S.736 from the reauthorization package provides more time for backers of the bipartisan bill, co-sponsored by Sen. Gordon Smith (R-OR), to obtain input from a variety of stakeholders. *Continued on p. 2*

▲ **Kennedy's Lab Testing Bill,** *from page 1*

The bill could be offered as an amendment later in the FDA user fee reauthorization process, but this looks unlikely.

Requiring premarket review for most LDTs would overwhelm both labs and the FDA, according to ACLA. LDTs, including in-house developed tests and modifications of FDA-approved test kits, encompass routine tests as well as complex molecular assays. Moreover, LDTs already are subject to the highest CLIA test performance standards.

An alternative approach to the issue of LDT regulation has been proposed by Senator Barack Obama. His bill, S.976, advocates a "go-slow" approach to federal oversight of genetic testing and genomics. Specifically, it calls for studies to advise Congress on further regulation of genetic testing and the impact on patient access, along with a decision matrix to help labs and test makers know which level of review is required and who is responsible.

Obama's bill, known as the Genomics and Personalized Medicine Act, would also expand research on genetic testing and genomics and the sharing of data, medical workforce training, and monitoring of direct-to-consumer marketing practices. It would also establish a CLIA specialty for genetic testing and direct the HHS secretary to increase payment for new genetic tests, where appropriate. Like S.736, Obama's bill has been referred to the Health, Education, Labor, and Pensions Committee.

FDA Clears Cepheid's MRSA Test

Over $2.5 billion in excess healthcare costs are attributable to MRSA infections.

The United States Food and Drug Administration (FDA) has cleared a new polymerase chain reaction (PCR)-based test for the rapid detection of methicillin-resistant Staphylococcus aureus (MRSA). Manufactured by Cepheid (Sunnyvale, CA) to run on the company's GeneXpert system, the Xpert MRSA test produces results in just over one hour. The FDA's announcement came only weeks after Cepheid received a regulatory nod for its PCR-based Xpert EV meningitis test (see May *DTTR*, p. 1). The company had previously received FDA clearance for molecular diagnostics for Group B Streptococcus.

MRSA infections, the leading cause of nosocomial infections, kill as many as 100,000 people in the United States every year. According to the Centers for Disease Control, MRSA now accounts for greater than 50% of hospital-acquired S. aureus infections and 63% of S. aureus infections acquired in intensive care units in the United States.

Cepheid's MRSA test now competes directly with the only other FDA-cleared MRSA test, the BD GeneOhm assay manufactured by GeneOhm Sciences, which is owned by Becton Dickinson (Franklin Lakes, NJ). Like Cepheid's Xpert MRSA test, the GeneOhm test uses real-time PCR to qualitatively detect colonization of MRSA by detecting a gene sequence that is unique to the drug-resistant strain of S. aureus. The BD GeneOhm MRSA assay provides results within two hours. Before the advent of these molecular methods, MRSA testing was conducted with traditional culture-based methods, which required growth on plated media for 24 to 72 hours.

Kimball Genetics Readies For Clinical Launch Of Warfarin Sensitivity DNA Test

In 2004, 23 million prescriptions for warfarin/ Coumadin were written in the United States (7 million for Coumadin and 16 million for warfarin).

Kimball Genetics (Denver, CO) is preparing to launch its warfarin sensitivity DNA test for clinical use. The test determines the presence of specific variations in the cytochrome P450 isozyme 2C9 (CYP2C9) and vitamin K epoxide reductase (VKORC1) genes, which confer sensitivity to warfarin and therefore significantly reduce the required maintenance dose. CYP2C9 is involved in warfarin metabolism, and VKORC1 influences warfarin's anticoagulation effect through vitamin K.

First developed as a rat poison by the Wisconsin Alumni Research Foundation (WARF), warfarin (sold by Bristol Meyers Squibb as Coumadin) is the most frequently prescribed oral anticoagulant, but it is difficult to manage due to its narrow therapeutic range and inconsistent patient response resulting from inter-individual variability. The dosing range is wide, from 5 mg/wk to 80 mg/wk, and depends on such covariates as age, weight, ethnicity, diet, and vitamin K intake in addition to genetic factors.

In November 2005, the FDA Clinical Pharmacology Subcommittee of the Advisory Committee for Pharmaceutical Sciences recommended testing for variations in the CYP2C9 and VKORC1 in patients requiring warfarin therapy based on evidence that lower doses are needed for patients with certain gene variants. The drug's label is expected to reflect this recommendation later this year. IVD companies are hotly anticipating the label change.

Warfarin testing has been hailed as the first pharmacogenomic test to enter widespread clinical practice. "This is the first really broadly used pharmacogenomic test that will become available to primary care practitioners or indeed to physicians broadly in the United States or for that matter in the world," says David Flockhart M.D., Ph.D., chief of the division of clinical pharmacology at the Indiana University School of Medicine, of warfarin sensitivity testing. "It's on the cutting edge of both laboratory medicine and clinical practice."

By informing the prescriber about the presence of genetic risk factors for overanticoagulation, warfarin testing can help clinicians achieve the correct maintenance dose faster. It is also likely to increase the safety and efficacy of warfarin treatment. The DNA tests identify patients who are sensitive to warfarin and who therefore require a lower dose to achieve a target international normalized ratio (INR), may be at an increased risk for bleeding complications, and without the DNA test, would require a longer period of time to achieve stable warfarin dosing.

Kimball's test, its first in the area of pharmacogenomics, has been available for research and investigational purposes since November 2006. Around the same time, TrimGen (Sparks, MD) launched its Mutector II Warfarin DNA test kit, also for research and investigational use only. The single tube test identifies three key variations in CYP2C9 and VKORC1, and the results can be analyzed with an ABI capillary sequencer.

Beginning in late 2005, PGXL Laboratories (Louisville, KY), which specializes in pharmacogenomic testing, has offered a combined CYP2C9 and VKORC1 genetic

test in partnership with Tm Bioscience, which is now part of Luminex Molecular Diagnostics (Toronto, Ontario). The test is priced at about $300. Direct-to-consumer genetic testing laboratory Genelex (Seattle, WA) also launched its warfarin dosing test in October of last year. It too is based on Tm Bioscience's Tag-It platform and costs $550. According to Genelex, private payors such as Anthem and Humana have covered costs for testing for the majority of its clients who submitted for coverage.

Warfarin Genotyping: What are the relevant CPT codes?*

- ❑ 83890 (Isolation)
- ❑ 83898 (Amplification)
- ❑ 83896 (Nucleic acid probes—multiple)
- ❑ 83912 (Interpretation and report)

*CPT coding will vary based on methodology used

PGxHealth (Morrisville, NC), a division of Clinical Data (Newton, MA), began offering its warfarin response test, PGxPredict:Warfarin, in October 2006. It is currently available in all states except New York, California, and Florida, where licensure is pending. PGxHealth's test methodology is similar to that of most laboratories offering this testing. After receiving a blood sample, genomic DNA is isolated and genotyping is performed by restriction length polymorphism (RFLP), which includes amplification of the gene regions containing the specific single nucleotide polymorphisms (SNPs) by PCR followed by restriction enzyme digestion and resolution of the restriction enzyme digestion fragments using gel electrophoresis and visualization.

In January of this year, ARUP Laboratories (Salt Lake City, UT) launched warfarin sensitivity by genotyping using PCR followed by fluorescent signal amplification. The Laboratory of Personalized Health (LPH), a division of Genomas (Hartford, CT), performs HILOmet Warfarin DNA Typing through Clinical Laboratory Partners (Newington, CT). The test result includes a recommended warfarin dose based upon CYP2C9 and VKORC1 DNA typing, age, height, and weight.

Kimball performs the test in its laboratory, and results are available within one day. The company plans to offer more pharmacogenomic tests this year and in years to come. The DNA testing laboratory's major areas of testing currently include inherited hypercoagulability, celiac disease, hemochromatosis, cystic fibrosis, and fragile X syndrome.

Chembio To Partner With Avago For Rapid POC Test Systems

Best known for its Sure Check and Stat-Pak tests for HIV, Chembio Diagnostics (Medford, NY) has agreed to partner with electronics company Avago Technologies (San Jose, CA) to develop rapid point-of-care (POC) testing systems that will integrate Chembio's Dual Path Platform (DPP), the lateral flow system that the company patented in March. The companies will focus first on developing rapid POC tests for HIV that are highly sensitive and accurate, cost-effective, and have data collection and storage capabilities. Formerly part of HP and Agilent Technologies, Avago's rapid diagnostics division helps partners move tests from the central laboratory or hospital to the point of care and to automate and improve the sensitivity of existing tests.

Novel Biomarkers Show Promise For Improved Cancer Screening

The American Cancer Society estimates that there will be approximately 218,890 new cases of prostate cancer in the United States in 2007, and 27,050 men will die of this disease.

Newly identified biomarkers may one day make cancer diagnosis as simple as a single laboratory test. In the meantime, they offer a new degree of precision and accuracy, along with the promise of earlier, more rapid detection of some of the world's most lethal and costly conditions.

Between 2000 and 2004, the costs of treating cancer rose 48%, from $42 billion to $62 billion, according to a study published earlier this year by the Agency for Healthcare Research and Quality (AHRQ). The study also found that of disease-related expenditures for the top five most costly conditions, spending on cancer patients increased the most, from an average of $4,577 to $5,727 per person.

EPCA-2 and Prostate Cancer

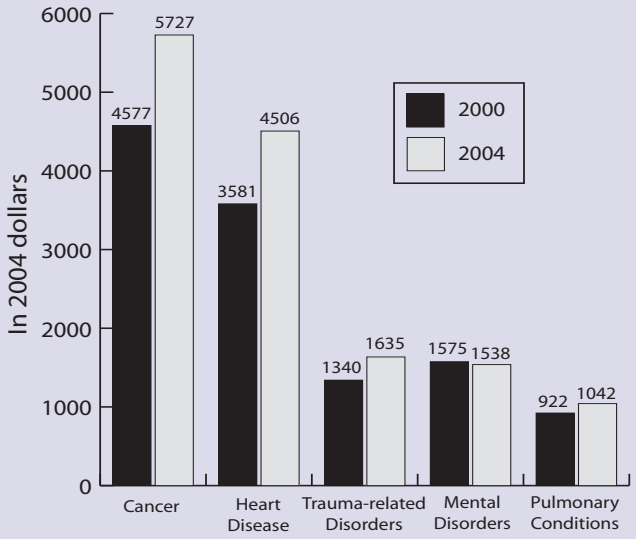
Two recently published studies present evidence of improved screening methods for the most common type of cancer in men (prostate cancer) and one of the disease's most lethal forms (pancreatic cancer). In a study published in the April issue of *Urology*, Robert H. Getzenberg, Ph.D., a professor at Johns Hopkins University, and colleagues provide evidence that testing for a newly identified blood protein known as early prostate cancer antigen-2 (EPCA-2) testing is a more accurate and precise way to identify prostate cancer.

Getzenberg and his team measured EPCA-2 levels in the blood of 330 patients of varying PSA levels, biopsy results, disease status, and tumor origins. Based on a pilot study, patients with an EPCA-2 cutoff level of 30 nanograms per milliliter or higher were considered to be at risk for prostate cancer.

Results showed that the EPCA-2 test was negative in 97% of the patients who did not have prostate cancer. Men with no evidence of disease (regardless of their PSA levels), as well as the control group of patients with other cancer types and benign conditions, all had EPCA-2 levels below the cutoff. In contrast, a 2003 study published in the *Journal of Urology* showed that PSA levels between four and 10 nanograms per milliliter were shown to be accurate in identifying patients without prostate cancer only 19% of the time.

In addition, 77% of the patients with benign prostatic hypertrophy (BPH), a common noncancerous prostate condition often associated with elevated PSA levels, had a level of EPCA-2 lower than the cutoff point. When it came to correctly identifying patients with prostate cancer, EPCA-2 levels at or above the cutoff were detected in 90% of the men with organ-confined prostate cancer and in 98% of the men with disease

Average Per Person Expenditures For Top Five Most Costly Conditions (2000 and 2004)



Source: Center for Financing, Access, and Cost Trends, Agency for Healthcare Research and Quality (AHRQ), Household Component of the Medical Expenditure Panel Survey (March 2007)

Notoriously difficult to diagnose at an early stage, pancreatic cancer is expected to strike 37,170 Americans and to kill 33,370 others this year, making it the fourth-leading cause of cancer death in both men and women.

outside the prostate. Overall, in this study, the EPCA-2 test detected 94% of the men with prostate cancer.

Results of the study also revealed that EPCA-2 levels were significantly higher in patients whose cancers had spread outside the prostate compared to those with disease confined to the gland. EPCA-2 was dramatically better at separating these groups than were PSA levels. Finally, the EPCA-2 test identified 78% of the men with prostate cancer in the group with PSA levels below the accepted cutoff level of 2.5 nanograms per milliliter. According to their PSA levels, these were all "healthy men," but EPCA-2 was able to show that they had prostate cancer.

Larger clinical trials for EPCA-2 are planned that could make this test available to the public in approximately 18 months. Onconome (Seattle, WA) has a licensing agreement with Johns Hopkins covering EPCA-2 and related technologies.

MicroRNA and Pancreatic Cancer

Diagnosing pancreatic cancer and predicting its course may one day be as easy as analyzing expression patterns of microRNAs (miRNAs), according to a study published in the May 2 issue of the *Journal of the American Medical Association* (*JAMA*). A team of researchers led by Mark Bloomston, M.D., of Ohio State University (Columbus, OH) found that miRNA may be useful not only in diagnosing the lethal disease but also in predicting survival time and differentiating between chronic pancreatitis and pancreatic cancer.

In humans, aberrant miRNA expression of miRNA, noncoding ribonucleic acids, contributes to carcinogenesis by promoting the expression of proto-oncogenes or by inhibiting the expression of tumor suppressor genes. While the role of miRNAs in pancreatic cancer is unclear, Bloomston and colleagues identified a global expression pattern of miRNAs that can differentiate pancreatic cancer from normal pancreas and chronic pancreatitis with 95% accuracy. Additionally, a subgroup of six miRNAs was able to distinguish long-term (greater than 24 months) survivors with node-positive disease from those dying within 24 months. Finally, high expression of a particular miRNA known as miR-196a-2 was found to predict poor survival.

The applications of this study are broad. For example, miRNA expression patterns could be used to direct therapy in patients with metastatic tumors of unknown origin or to help discriminate between benign and malignant tumors, something that routine histologic or immunohistochemical analysis could not do. The authors also note that "the ability of miRNAs to affect multiple genes in various pathways make them a logical target for investigation of novel antitumoral therapies."

Despite the great promise of biomarkers, they remain rare in clinical practice. In an editorial accompanying the *JAMA* paper, it is noted that this study "reflect(s) the beginning of the continuum integrating discovery, development, regulatory review, and the evidence basis of medicine required to translate advanced technology into clinical practice, a framework that has largely been ignored in the field of biomarkers."

House Passes Bill That Would Ban Genetic Discrimination

On April 25, the U.S. House of Representatives voted 420-3 to pass the Genetic Information Nondiscrimination Act (GINA). First introduced 12 years ago by New York Congresswoman Louise Slaughter, the bill will now go to the Senate floor, where it is expected to pass and ultimately be signed into law. The White House has already indicated that it supports the legislation.

GINA would prohibit discrimination by group health plans, health insurers, and employers based on individuals' genetic information, namely genetic predisposition to certain diseases. Previous versions of the bill were passed unanimously by the Senate in 2003 and 2005, but did not make it through the House.

Applied Microarrays Buys GE's CodeLink Business

Applied Microarrays (Tempe, AZ) has quietly acquired CodeLink, a range of pre-arrayed oligonucleotide bioarrays and processing tools previously owned by GE Healthcare (Chalfont St. Giles, United Kingdom). As of May 1, GE Healthcare's Web site stated that pre-arrayed CodeLink products would be available from Applied Microarrays. GE Healthcare will continue to sell CodeLink's non-arrayed activated slides and related reagents. Financial terms of the deal were not disclosed.

Unloading CodeLink is in keeping with the plan that GE announced last fall to discontinue that area of its biosciences business by April. GE Healthcare is a $17 billion unit of General Electric and employs more than 46,000 people worldwide.

Applied Microarrays, which specializes in contract manufacturing of custom microarrays and assay optimization, will be CodeLink's third owner. Motorola originally purchased the CodeLink technology from Surmodics and then sold the business to Amersham, which GE Healthcare acquired in 2003.

Sensing The Future Of Clinical Diagnostics

Forget mousetraps. These days everyone is trying to build a better electrochemical sensor, a so-called "lab-on-a-chip," in the hopes that a variety of industries will beat a path to their door. These small, rugged semiconductor microarray devices are shaping up to be the next generation of diagnostic testing. Two new sensors are differentiating themselves with novel detection chemistry, multiplex capacity, unprecedented sensitivity, and speed.

A team at Sandia National Laboratories (Albuquerque, NM) is developing a biosensor with a unique surface chemistry that is based on the electrodeposition of aryl diazonium salts. Compatible with many biomolecules, the chemistry enables the sensor to detect thousands of different biomolecules—including DNA, antibodies, enzymes, and peptides—on a one-inch by one-inch chip. Integrating multiple biomolecules on a single device could dramatically increase the platform's accuracy and precision while decreasing costs. For example, instead of a single antibody, the chip could test for several DNA sequences or both internal and external proteins unique to a virus or disease.

So far, the team has created sensor arrays that allow for the selective identification of nine biomolecules. Within two to five years, the team plans to integrate the array into a lab-on-a-chip format that will have an electronic readout identifying the biomolecules detected or wirelessly transmit the results to a computer. Sandia is partnering with array specialist CombiMatrix (Mukilteo, WA) to further develop the technology.

Raj Mutharasan, Ph.D., a professor of chemical engineering at Drexel University (Philadelphia, PA), is also making strides in biosensor technology. His millimeter-size biosensor can be used to detect minute amounts of protein in blood, urine, sputum, and spinal fluid within about 10 minutes. A study published in the April 1 issue of *Analytical Chemistry* using the sensor detected *E. coli* in ground beef at some of the lowest concentrations ever reported.

The sensor features a vibrating cantilever, supported at one end and coated with antibodies specific to the target of interest. When the target is present in a sample, it binds to the cantilever and alters the frequency of vibration so it can be read electronically. A voltage is applied to the ceramic layer, causing it to expand and contract, vibrating the glass sliver. The sensor detects changes in the glass sliver's resonance frequency and determines the presence and concentration of the target.

Results of a preliminary study using the device to noninvasively detect a prostate cancer biomarker in 15 minutes were recently presented by Drexel doctoral student David Maraldo at the most recent meeting of the United States and Canadian Academy of Pathology. A commercial prototype of the sensor is anticipated to be completed in July.

DiagnoCure Acquires Exclusive Rights For TDT's Colorectal Cancer Tests

Molecular diagnostics company DiagnoCure (Quebec City) has purchased exclusive worldwide rights for two molecular tests for colorectal cancer from Targeted Diagnostics & Therapeutics (TDT; Philadelphia), a biotechnology company developing molecular-based technologies for the detection, diagnosis, and treatment of gastrointestinal cancers and infectious diseases.

The agreement includes an option for DiagnoCure to commercialize molecular diagnostics for cancer with TDT's CLIA-certified reference laboratory. DiagnoCure, which made an initial payment to TDT of $2.2 million in stock for the testing rights, plans to use the company's lab to quickly bring to market "home-brew" molecular tests.

The tests, known as GCC-81 and GCC-N1, detect metastatic colorectal cancer in blood and lymph bodes, respectively. They are based on the detection of the guanylyl cyclase C (GCC) gene, which usually appears in the cells lining the intestinal track. In cases of metastasized colorectal cancer it is found outside of the intestine, making it a highly accurate biomarker for detecting the spread or recurrence of colon cancer.

Analyzing Test Ordering Patterns Helps Labs Cut Costs and Minimize Waste

The ATOP analysis focuses on four primary categories: order volumes compared to order volumes of related tests; order volumes compared to those of other clients; result distributions; and age, sex, and/or result distribution.

In recent decades, a number of studies and countless hard-nosed consultants have focused on inefficiencies and waste when it comes to such aspects of healthcare as hospital admissions and drug prescriptions, but little attention has been paid to lab tests. Can test ordering be optimized? ARUP Laboratories (Salt Lake City) answers with an emphatic "Yes!"

ARUP's new Analyzing Test Ordering Patterns (ATOP) program offers clinical laboratories the opportunity to take a closer look at their ordering patterns, with an eye to finding and eliminating inappropriate or inefficient ordering. Call it a diagnostics diagnostic.

The potential savings are vast. Brian Jackson, M.D., ARUP's medical director of informatics, cites a study published in *Health Affairs* that analyzed the variations in total expenses among various medical procedures. "Overall there were about 60% higher expenditures at the more expensive centers than at the less expensive, but more interesting to me was that the laboratory costs varied even more than the other areas."

The ATOP program assigns a team of ARUP pathologists and data analysts, as well as University of Utah School of Medicine faculty, to analyze a client's test ordering patterns looking for areas of potential over-, under-, and misuse. Costs and referral test volumes are compared and evaluated against ARUP's knowledge base of ordering issues, which draws on their database of more than eight years of archived test orders from hundreds of hospitals and laboratories nationwide.

"Simply by screening ordering volumes of different tests and looking at ratios of ordering volumes of different tests, it's possible to identify areas of inefficient testing," says Johnson. The program looks at about two dozen different disease topics. Typically, they focus on whatever the clients ask them to, rather than perform a complete analysis.

The process takes about a month. ARUP does not charge its largest clients for this service, although there is a fee schedule for other clients. Plans to offer the service outside the ARUP client base are not yet fully formed. "Historically we haven't [considered working with outside clients]," says Jackson. "We have all the data on our clients' esoteric testing. We've done some experiments on looking at our clients' internal ordering data as well, where the clients provided us with a spreadsheet of their test menu and annual volumes, and by doing that, we can do a more complete analysis."

Emory Medical Laboratory, part of Emory Healthcare (Atlanta), used the ATOP program as part of an effort to evaluate and optimize their laboratory's send-outs. When analyzing Emory's ordering patterns, ARUP discovered that the single largest test request was for serum drug screens. In fact, Emory was ARUP's largest single client using the test. "We looked at that and thought it was odd," says James

Ritchie, Ph.D., the lab's associate director. "We weren't a forensic drug lab. Why was that happening?"

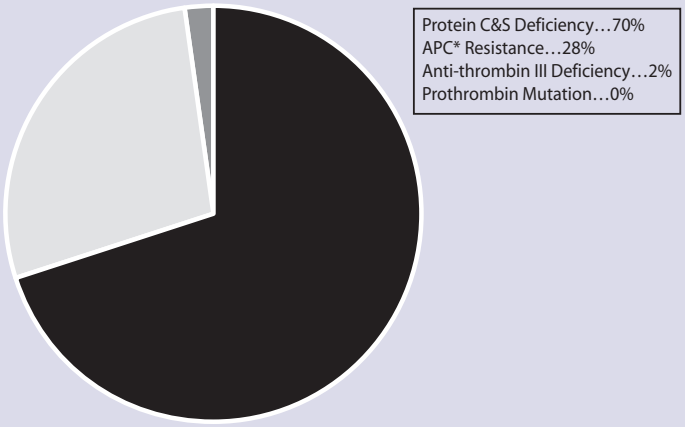
The answer was rooted in Emory's large organ transplant program, a major component of which is kidney transplants. "Often people who don't have functioning kidneys can't make urine, so they couldn't send urine samples," says Ritchie. "In those instances, they called down to the lab and asked if they could send a serum drug screen. I OK'd that." And what appears to have happened was the protocols for kidney transplants were cut-and-pasted into the protocols for all organ transplants. Every single transplant patient had a serum drug screen instead of the less expensive urine drug screen. Emory quickly amended the protocols.

The ATOP program detected other anomalies in Emory's test ordering, but the blood serum drug screen was the most significant change. How significant? According to Ritchie, the changes made as a result of the program saved Emory about $75,000 per year.

ARUP also provides the more specific example of a laboratory that was performing a number of tests for inherited thrombotic disorders. ATOP analysis demonstrated that while the prothrombin mutation, protein C and S deficiencies, and anti-thrombin III deficiency combined accounted for less than 10% of all inherited thrombotic disorders, the tests to diagnose these disorders represented 72% of the assays ordered by the laboratory in the period analyzed. By testing for APC resistance first, the analysis suggested, the laboratory's clinicians would greatly reduce the number and costs of subsequent tests.

"The role of ATOP analysis is very much a screening tool," says Jackson. "Because it's based on a limited dataset that we have, we're not linking that to clinical data or diagnoses or follow-up testing or anything like that. So we can't say with respect to any single order: that order is appropriate or not." What they can say, for example, is that this hospital is ordering five times more of a certain test than another hospital and there is no clear reason why, or that the ratio of Test A to Test B is much higher than you would expect if they were following national guidelines. "We're looking at the patterns of screening and then it's up to our client to decide which topics to choose to follow up further," he adds.

Testing for Inherited Thrombotic Disorders at Lab X



Source: ARUP
*Activated protein C

Ritchie, however, has found it so helpful he has asked for regularly scheduled reports. "What the whole process has pointed us toward is tracking our send-outs on a computerized system." Ritchie receives a quarterly report on what his laboratory is sending out and the laboratory's top 10 tests, which he then passes on to the rest of the staff broken down by lab sections. "That way we can say, 'Here are targets of opportunity to possibly bring things in-house.'"

IVD Stocks Rise 3%; Stratagene Climbs 27%

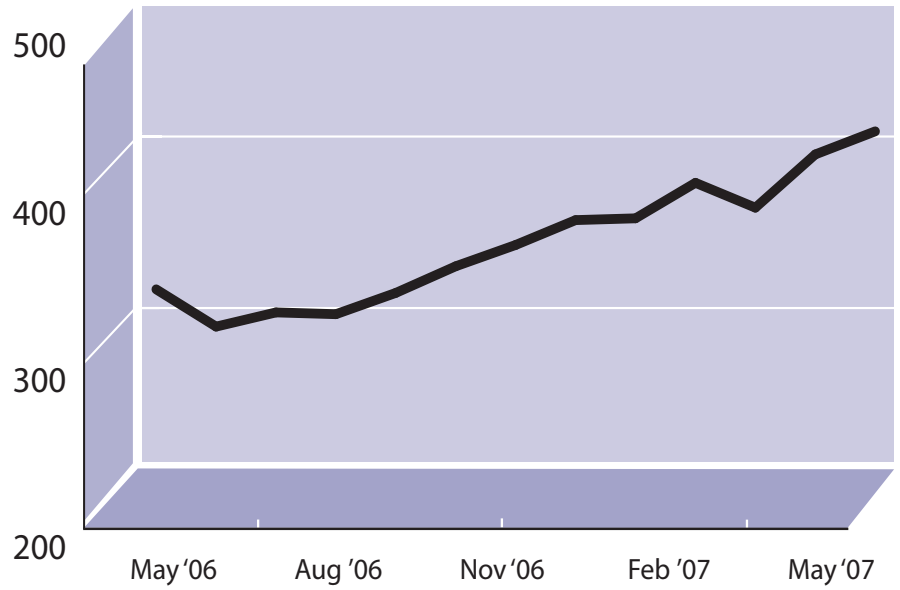
The 24 stocks in the G-2 Diagnostic Stock Index rose an average of 3% in the five weeks ended May 4, with 14 stocks up in price, eight down, and two unchanged. So far this year, the G-2 index is up 14%, while both the S&P 500 and the Nasdaq are up 6%.

Stratagene (La Jolla, CA) spiked 27% to $10.77 per share for a market capitalization of $242 million. In early April, Agilent Technologies (Santa Clara, CA) announced that it would acquire the life sciences company for $246.2 million (see May *DTTR*, p. 2) to strengthen its position in the diagnostic market. Agilent is paying $10.94 per share for the company, and heavy trading has pushed Stratagene shares toward that offer price, which represented a 29% premium to the April 5 closing price of $8.51.

Gen-Probe (San Diego) was up 10% to $52.76 per share for a market capitalization of $2.77 billion. The company recently announced that it will expand its collaboration with Millipore (Billerica, MA), which will market and sell Gen-Probe's mycoplasma tissue culture non-isotopic (MTC-NI) test, a DNA-based probe system, to its biopharmaceutical customers. The companies were already partnering on MilliPROBE, a new line of nucleic acid tests for the biopharma market.

Meanwhile, **Digene** (Gaithersburg, MD) rose 5% to $45.97 per share for a market capitalization of $1.04 billion. On May 8, the gene-based test maker reported that its third-quarter earnings soared to $5.3 million, up from $1.1 million a year ago, on strong sales in the United States of its flagship human papilloma virus (HPV) test. Revenue rose 34% to $52.5 million from $42.2 million. According to Digene, HPV test sales were up 41% to $48.3 million. The company also recently raised its guidance, predicting revenue of $202 million for the fiscal year ending June 30.

G-2 Diagnostic Stock Index



Source: The G-2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 24 IVD companies.

Up	Price	% Chg
Abbott Labs	$58.30	2%
Becton Dickinson	79.28	1
Biosite	93.92	1
Cholestech	17.75	3
Cytyc	35.14	1
Dade	50.76	11
Digene	45.97	5
Gen-Probe	52.76	10
Johnson & Johnson	64.48	5
Meridian	30.61	8
Nanogen	1.77	11
Quidel	14.11	13
Stratagene	10.77	27
Ventana	50.81	18
Unchanged		
Beckman Coulter	63.33	0
Clinical Data	22.23	0
Down		
Abaxis	23.13	-7
Affymetrix	26.42	-15
Bio-Rad	70.25	-1
Immucor	33.21	-2
Inverness Medical	39.65	-5
Luminex	13.97	-1
OraSure	7.54	-1
Third Wave	5.16	-6

G-2 Insider

BNP Test Predicts Mortality In Heart Failure Patients… A study published in the May 15 issue of the *Journal of the American College of Cardiology* is the first to demonstrate a connection between B-type natriuretic peptide (BNP), a hormone released by the heart when it is stressed or damaged, and in-hospital mortality for heart failure patients. BNP levels at admission were found to be predictive of higher in-hospital mortality rates.

According to lead investigator Gregg C. Fonarow, M.D., a professor of cardiology at UCLA and director of the Ahmanson-UCLA Cardiomyopathy Center, the researchers were surprised that the BNP test was so highly predictive of mortality across a broad population of heart failure patients and a range of BNP levels. The researchers used data collected in 2003 and 2004 at 191 American hospitals on 48,629 heart failure patients whose BNP levels were taken within 24 hours of hospital admission. Fonarow calls the project "the largest biomarker study in heart failure ever conducted."

The relationship between levels of BNP and in-hospital mortality persisted independent of other factors and held true even after adjustment for age, gender, systolic blood pressure, pulse, and other lab tests, such as blood urea nitrogen, creatinine, and sodium. Higher BNP levels were also predictive of other clinical outcomes, such as the need for mechanical ventilation, the length of the hospital stay, and the amount of time spent in the intensive care unit.

According to Fonarow, BNP levels may be a useful addition to routine assessment and can help guide care and treatment of patients hospitalized with acute heart failure. The next step will be further research to demonstrate that patients with higher BNP levels at admission benefit from more intensive monitoring and treatment.

Company References

ACLA 202-637-9466
AHRQ 301-427-1364
Applied Microarrays 480-229-4245
ARUP Labs 800-522-2787
Avago Technologies 619-318-0303
Biosite 858-805-4808
Cepheid 408-541-4191
Chembio 631-924-1135
Clinical Laboratory Partners 860 696-8020
CombiMatrix 425-493-2000
Digene 301-944-7000
Emory Medical Lab 404-712-5227
Genelex 800-523-3080
Genomas 860-545-4574
Gen-Probe 858-410-8000
Kimball Genetics 800-320-1807
Luminex 512-219-8020
PGxHealth 203-786-3400
PGXL Labs 502-569-1584
Stratagene 858-373-6300
TrimGen 888-825-6005

Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by Washington G-2 Reports, 3 Park Avenue, 30th Floor, New York, NY 10016-5902. Tel: 212-244-0360. Fax: 212-564-0465. Order line: 212-629-3679. Web site: www.g2reports.com.

Stephanie Murg, Managing Editor; Dennis Weissman, Executive Editor; Janice Prescott, Sr. Production Editor; Perry Patterson, Vice President and Publisher; Joe Bremner, President.

Receiving duplicate issues? Have a billing question? Need to have your renewal dates coordinated? We'd be glad to help you. Call customer service at 212-244-0360, ext. 2.