Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Issue 09-01/January 2009

CONTENTS

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Genentech Files Petition with FDA Urging Regulation of Lab-Developed Tests

As the diagnostic and clinical laboratory industries await the United States Food and Drug Administration (FDA)'s final guidance on the regulation of in vitro diagnostic multivariate index assays (IVDMIAs), Genentech (South San Francisco, Calif.) has filed a citizen petition urging the government regulatory agency to hold in vitro diagnostic tests developed by clinical laboratories for in-house testing to the same standards as those tests developed and sold as test kits. FDA currently regulates tests sold in kit form but not laboratory-developed tests (LDTs).

In a copy of the 32-page document obtained by *DTTR* shortly after its December 5 filing date, Genentech requests that FDA "initiate rulemaking to exercise regulatory jurisdiction over all LDTs and use its current risk-based classification system to determine the level of regulatory oversight and review that is necessary and appropriate for these tests."

The biopharmaceutical company also calls for FDA to simultaneously begin enforcement action against "any clinical laboratory or any other company that is selling an LDT or making claims about its potential indication for use, effectiveness, or value, or that otherwise impacts patient safety without having sufficient analytical and clinical evidence to support such claims."

Continued on p. 10

Rosetta Genomics Launches First Test

On December 11, Rosetta Genomics (Rehovot, Israel; Jersey City, N.J.; Philadelphia) announced the commercial launch of its first diagnostic test. Known as miRview squamous, the test uses a single microRNA (miRNA) to differentiate non-small-cell lung cancer (NSCLC) patients with squamous cell carcinoma from those with non-squamous carcinomas.

The test is available through Rosetta Genomics's CLIA-certified lab in Philadelphia. It has a list price of $3,170, a company representative tells *DTTR*. Results are available within 10 days.

"miRview squamous offers physicians a standardized, quantitative diagnostic tool which may assist in determining the appropriate targeted therapy for NSCLC," said Amir Avniel, president and CEO of Rosetta Genomics, which was founded in 2000 to develop miRNA-based molecular diagnostics.

Continued on p. 2

▲ **Rosetta Genomics,** *from page 1*

Squamous patients have been found to respond differently to targeted therapies than non-squamous patients. "The difference in response can range from potential fatal bleeding to poor response," explained Dalia Cohen, M.D., chief scientific officer of Rosetta Genomics. "Given the varying outcomes of targeted therapies for NSCLC, we view every NSCLC patient who is a candidate for targeted therapy as a potential end user for this test."

Current methods for differentiating squamous from non-squamous NSCLC lack standardization, are difficult to reproduce, and have low accuracy. Studies that reviewed the accuracy and reproducibility of histopathological classification of lung cancer found that as many as 40 percent of samples had been misclassified.

Invitrogen, Applied Biosystems Close on $6.7 Billion Merger Deal

Invitrogen (Carlsbad, Calif.) and Applied Biosystems (Norwalk, Conn.) have completed the $6.7 billion strategic merger announced in June. Headquartered in Carlsbad, the new company is called Life Technologies Corporation and began trading on the NASDAQ on November 24.

The combined company's newly launched Web site describes Life Technologies as "a global biotechnology tools company dedicated to improving the human condition." With deep offerings in reagents, systems, and services, the combined company has historical sales of approximately $3.5 billion, 9,500 employees, and a presence in more than 100 countries.

In recent months, Invitrogen and Applied Biosystems emphasized that they did not expect the ongoing upheaval in the capital markets to have any impact on financing for the merger deal.

On an October 21 conference call, Invitrogen management noted that the merger integration plan remained on track, with planned cost synergies for the first year estimated at $80 million.

HHS Report Examines Potential of Molecular Medicine

On November 14, Health and Human Services Secretary Michael Leavitt released the second report from his Initiative on Personalized Health Care, which examines the potential of a molecular-based understanding of health and disease to improve the quality and cost-effectiveness of health care.

The new report, *Personalized Health Care: Pioneers, Partnerships, Progress*, includes reports from 10 institutions where personalized health care techniques are beginning to be used. It also includes seven papers examining the opportunities and challenges for personalized health care from the perspective of different stakeholders in the health care sector.

Included in the report, which Leavitt released while speaking at a conference on personalized health care at the Harvard Medical School, is a prologue written by the HHS secretary that includes six tests to help conceptualize what personalized

health care might look like and how individuals may judge how personalized their care really is.

"The 'person' in personalized health care is at the core of the change I anticipate," writes Leavitt. "Clinicians will indeed be able to diagnose and treat with ever greater precision. But, at the same time, a growing role for the patient as decisionmaker, supported by new information tools, will be a prominent feature marking a new age of personalized medicine."

The tests include whether a patient has an electronic health record and whether or not the individual's physician offers him or her a strategic plan for health maintenance based on that person's biology, family history, and individual factors.

The third test asks whether that person's physicians and other health care providers, as well as the patient, have access to decision support tools and use those tools. The HHS secretary said that guidance provided by such tools should increasingly be based on the patient's personal health care information.

A fourth test is the expectation that whenever possible, treatments will be recommended to the patient based on his or her own biology and preferences—not merely on the basis of best guesses and population averages.

The final two tests ask if the patient's personal genomic or other molecular-level information is available for clinical use and if the individual has the opportunity, if he or she wishes, to contribute to new health knowledge by making his or her own clinical information available for research.

LabCorp, National Jewish Health to Collaborate on Molecular Diagnostics

The nation's second largest provider of laboratory testing will partner with National Jewish Health (NJH; Denver) to develop, market, and commercialize a range of molecular diagnostic tests, LabCorp (Burlington, N.C.) announced on December 10.

In response to queries from *DTTR*, Gary Smith, Ph.D., executive director of the Advanced Diagnostics Laboratory at NJH, characterized the agreement as "multi-year" but would not disclose the financial terms or specific duration of the deal. According to Smith, the tests under consideration for development include rapid molecular diagnostic tests, prognostic tests, and genetic tests.

Among the companion diagnostic tests being considered are CYP2C9 and VKORC1 for warfarin dosage, CD20 for rituximab (used to treat rheumatoid arthritis and non-Hodgkins lymphoma), and LTE4 for asthma treatment stratification.

News of the agreement comes only months after Smith, a former LabCorp executive, was named executive director of National Jewish Health's outreach lab businesses, known collectively as the Advanced Diagnostic Laboratory. Smith was with LabCorp for 14 years, most recently as senior vice president of managed care, Western operations and senior vice president of operations, Midwest division.

American College of Physicians Releases Guidance on HIV Screening

On December 2, the American College of Physicians (ACP; Philadelphia) released guidelines urging physicians to begin routine HIV screening among patients at age 13, regardless of whether they engage in risky behaviors. The recommendations did not include an upper age limit because 20 percent of people living with HIV are older than age 50. The guidelines will be published in the January 20 issue of the *Annals of Internal Medicine*.

Based upon an evaluation of the HIV screening guidelines developed by the U.S. Preventive Services Task Force (USPSTF) and the Centers for Disease Control and Prevention (CDC), ACP's guidelines differ from that of USPSTF, which urges routine screening only for patients at high risk of the virus. However, many patients do not inform their physicians about their risky behaviors.

"Although risk-based screening has been recommended for more than 15 years, evidence from the CDC and Veterans Affairs indicate that almost half of patients are identified late in the course of disease, when they will no longer receive the maximum benefit from antiretroviral therapy," conclude the authors of the ACP guidelines.

The ACP guidance also differs from the CDC guideline on routine HIV testing, which recommends routine screening until age 64 unless the HIV prevalence in the patient population is known to be less than 0.1 percent. While the authors of the ACP guidelines affirm the cost-effectiveness of this approach, they note the difficulty of knowing HIV prevalence in certain patient populations.

According to the Centers for Disease Control and Prevention (CDC), an estimated 1.1 million people are living with HIV/AIDS in the United States. Of these, approximately 25 percent have undiagnosed disease and are unaware of their HIV infection.

Hospitals and clinics have been slow to implement the CDC's 2006 recommendations on routine HIV screening. Many experts point to the lack of funding necessary to implement routine HIV testing in settings such as emergency rooms.

On the issue of rapid versus traditional testing, the ACP guidelines note that traditional testing (enzyme immunoassay followed by Western blot) has very high sensitivity and specificity, and therefore, false-positive results are rare. However, results from traditional testing are not rapidly available, while rapid tests provide results within one hour.

The guidelines also note the recently published study that found relatively high false-positive rates with an oral rapid test and other similar reports. "Patients and clinicians should be aware that any positive rapid test result must be confirmed with traditional testing," advises ACP.

Finally, ACP recommends that clinicians determine the need for repeat screening on an individual basis. The USPSTF does not make recommendations about the frequency of screening, while the CDC guideline recommends that providers screen patients at high risk for HIV at least annually.

New Study Findings May Aid in Breast Cancer Diagnosis, Treatment Selection

The results of several new scientific studies have significant implications for the diagnosis and treatment of breast cancer. The findings include the discovery of a protein that appears to be responsible for causing breast cancer to spread, a new link between HER2 status and treatment response, and insight into how to improve tools for calculating risk of mortality and disease recurrence.

Protein Linked to Invasive Breast Cancer

In a study published online in *Developmental Cell* on December 8, researchers at Albert Einstein College of Medicine of Yeshiva University (New York City) and the Massachusetts Institute of Technology (Cambridge, Mass.) identified a protein that appears to be responsible for causing breast cancer to spread.

The new study identifies a protein known as Menainv as a potential early marker for metastatic breast cancer. Present on invasive cells within a breast tumor, Menainv is found in those cells that move into surrounding tissue and eventually to blood vessels but not on resident cells, which do not travel to other tissues.

The study marks the first time that a protein has been shown to contribute to the invasive and metastatic ability of tumor cells, strengthening the potential use of this protein as a marker. Six out of 10 newly diagnosed breast cancer patients have cancer that is still in its primary location.

Directed by Einstein professor John S. Condeelis, Ph.D., the research involved developing an in vivo invasion assay used to isolate metastatic tumor cells from breast tumors. The researchers found that that Menainv forces tumor cells in mammary tumors of mice to become invasive and eventually to metastasize to the lung.

The American Cancer Society estimates that 184,450 Americans will be diagnosed with breast cancer this year and 40,930 will die from the disease.

Additional results of the study have important implications for patient treatment. The tumor cells that contained Menainv were found to be less likely to respond to newer breast cancer treatments that inhibit receptors for epidermal growth factor (EGF), which has been shown to increase a breast cancer cell's invasive potential. The researchers believe that drugs that inhibit EGF may lack effectiveness on tumor cells containing Menainv.

If Menainv behaves similarly in humans as it does in mice, it would be an especially attractive marker for metastatic breast cancer because its structure would allow an antibody or a PCR assay to be developed to identify it. Such an assay could be used to detect the presence of Menainv in biopsies and blood samples, allowing doctors to

identify breast cancer patients who are more likely to have progressive disease and recommend the appropriate treatment.

HER2 Levels May Aid in Treatment Selection for Metastatic Breast Cancer

In another study, researchers at the University of Southern California / Norris Comprehensive Cancer Center (Los Angeles) examined how a patient's HER2 status affects her response to the oral chemotherapy agent lapatinib and found that the drug benefits women with HER2-positive breast cancer, while women with HER2-negative breast cancer or those who express EGRF alone derive no incremental benefit.

Published in the Dec. 1, 2008, issue of *Clinical Cancer Research*, the study also found that approximately 10 percent of metastatic breast cancer patients are misclassified, preventing some from receiving optimal therapy.

Lapatinib is approved by the FDA for use only in women who have HER2-positive metastatic breast cancer and who were previously treated with anthracyclines, trastuzumab, and taxane. Lapatinib inhibits both HER2 and EGRF receptors.

Researchers found that HER2 amplification, but not EGRF expression is correlated with responsiveness to the drug. Women with both high and low levels of HER2 amplification respond to lapatinib. However, women with HER2-negative metastatic breast cancers do not respond.

Women with HER2-positive metastatic breast cancer who receive lapatinib and chemotherapy have shown an improvement of approximately 50 percent in progression-free survival when compared to chemotherapy alone. Unfortunately, high-volume laboratories using laboratory technicians instead of pathologists to score gene amplification misclassify approximately 10 percent of HER2 amplified breast cancers as not amplified, preventing these patients from being candidates for lapatinib.

Improving Tools for Mortality and Recurrence Risk Assessment

Finally, a study published in the December 15 issue of *Cancer* examined the effectiveness of online tools that provide individually tailored estimates of breast cancer mortality and risk of disease recurrence. The researchers focused on how the tools, such as Adjuvant! (www.adjuvantonline.com), displayed their results and found that the relevant risk statistics could be better conveyed with graphics that are simpler than the existing set of four stacked horizontal bars.

The researchers presented 1,619 women, aged 40 to 74 years, with one of four risk graphics, including the current Adjuvant! report format and three simplified versions. Based upon measurement of the survey participants' comprehension of key statistics, time required to complete the task, and graph-perception ratings, the researchers found that simplifying the results—by expressing them through a pictograph rather than a bar graph, for example—significantly improved comprehension. "Although most patients will only view risk calculators such as Adjuvant! in consultation with their clinicians, simplifying design graphics could significantly improve patients' comprehension of statistics essential for informed decisionmaking about adjuvant therapies," concluded the authors.

Gene Networks May Predict Leukemia Growth Rate

Groups of genes may be more reliable than individual markers in determining the clinical course of chronic lymphocytic leukemia (CLL), according to findings presented on December 8 at the annual meeting of the American Society of Hematology in San Francisco.

Selecting a therapy for a CLL patient is complicated by the difficulty in determining the clinical course of the disease: whether a patient has a form of CLL that progresses slowly and with few initial symptoms or a more aggressive form. Previous studies have used microarrays to highlight differences in messenger RNA (mRNA) levels found between CLL patients with different rates of disease progression. Researchers at the University of California San Diego hypothesized that "a repertoire of transcriptional activity" was contributing to or resulting from the dynamic changes of CLL cells and could therefore be useful in determining disease prognosis.

Using mRNA expression microarrays, the researchers analyzed the activity and patterns of gene expression in cancer cells from 126 patients with aggressive or slow-growing CLL. They then used algorithms to match these gene activity profiles with a database of 50,000 known protein complexes and signaling pathways among nearly 10,000 genes and proteins, searching for "subnetworks" of aggregate gene expression patterns that separated groups of patients. They found 30 such gene subnetworks that, they say, were better in predicting whether a disease is aggressive or slow-growing than current techniques that are based on gene expression alone.

"When you are analyzing just the gene expression, you are analyzing it in isolation," explained Han-Yu Chuang, lead author of the study. "We are looking for new markers—no longer individual genes—but a set of co-functional, interconnected genes," she said. The researchers have previously shown the potential of this method in predicting breast cancer metastasis risk.

Clinical trials are needed to validate whether specific gene subnetworks can predict disease CLL progression in patients. Chuang thinks that the subnetworks can be used to provide "small-scale biological models of disease progression," allowing researchers to better understand the process. Eventually, she said, a microarray-based diagnostic could be used to test blood samples for such genetic subnetworks that indicate the likely course of CLL.

BD Receives FDA Approval for Cervical Cancer Screening System

BD Diagnostics, a segment of Becton, Dickinson and Company (BD; Burlington, N.C.) has received U.S. Food and Drug Administration (FDA) premarket approval for its BD FocalPoint GS Imaging System. This new system is designed to enhance cervical cancer screening for cytology laboratories, using the BD SurePath

Pap test slides to detect evidence of squamous carcinoma, adenocarcinoma, and their usual precursor conditions.

The BD FocalPoint GS Imaging System is intended to address the problem of Pap smear false negatives through guided screening (GS) technology that helps rapidly relocate the fields of view that the system has identified as the most likely to contain cells of interest.

BD Executive Vice President Vincent A. Forlenza called the system a "milestone" in BD's efforts to expand its presence in cancer diagnostics. The product is the first in a series of products for cancer detection and management that are the result of BD's 2006 acquisition of TriPath.

Protein Levels Indicate Risk of Death in Colorectal Cancer Patients

A study published online in the Journal of Clinical Oncology on December 8 found that in people who have undergone surgery for colorectal cancer, the levels of two insulin-related proteins predicted their chances of dying from the cancer or from other conditions.

Patients with high prediagnosis levels of insulin-like growth factor binding protein-1 (IGFBP-1) were more than half as likely to die from the disease; while those with high levels of C-peptide, a marker of insulin secretion, were nearly twice as likely to die.

The prospective observational study was designed to explore why lifestyle factors such as obesity, inactivity, and unhealthy diet are associated with an increased risk of colon cancer, cancer recurrence, and death. Such lifestyle factors can lead to elevated levels of circulating insulin, a hormone that may influence cancer cell growth by binding directly to colon cancer cells or by altering other blood proteins.

"We don't know yet whether the two proteins identified in this study are part of the actual mechanism that promotes colon cancer recurrence or whether they are simply 'markers' for risk of colon cancer recurrence and death," says the study's lead author, Brian Wolpin, M.D., of Dana-Farber and Brigham and Women's Hospital (Boston, Mass.). "But the results underscore the growing evidence that lifestyle choices can have an impact on the risk of recurrence in patients with surgically removed colorectal cancer."

Using data from the Nurses' Health Study and the Health Professionals Follow-up Study, investigators examined prediagnosis levels of four insulin-related proteins in 373 people diagnosed with nonmetastatic colorectal cancer between 1991 and 2004. All four proteins are known to increase or decrease in response to lifestyle factors such as obesity, physical inactivity, and poor nutrition.

Levels of two of the proteins (insulin-like growth factor-I and IGFBP-3) were unrelated to colon cancer recurrence or death. However, the connection between IGFBP-1, C-peptide, and mortality was strong.

Patients with the highest levels of IGFBP-1 had a 56 percent lower risk of death during the study period and a 57 percent lower risk of dying from colorectal cancer. Researchers speculate that the protein may exert a protective effect by blocking other growth factors that contribute to colon cancer cell proliferation.

High levels of C-peptide, by contrast, doubled the risk of overall death in people with cancer but were not significantly associated with death from colorectal cancer itself. This may be because of an even stronger link between high insulin levels of other potentially fatal diseases, such as heart disease and stroke, or because C-peptide is not as accurate a measure of insulin-related hormonal changes as other proteins, the study authors speculate.

Clarient Introduces Second Genetic Test for Colorectal Cancer

Anatomic pathology and molecular diagnostics company Clarient (Aliso Viejo, Calif.) has launched its new BRAF gene mutation test. The laboratory-developed test is for use as a predictive molecular biomarker for patients with colorectal cancer (CRC).

In July of 2008, Clarient launched its first predictive CRC biomarker, which detects mutations in the KRAS gene. The KRAS test has a current revenue run rate of over $5 million per year. Mutations in BRAF, a downstream target of KRAS, are also associated with sporadic colorectal carcinomas.

"In conjunction with KRAS, BRAF could help explain why an additional subset of patients may not respond to anti-EGFR therapies," said Clarient CEO Ron Andrews, referring to cancer treatments such as cetuximab (sold by ImClone as Erbitux) that block the activation of receptors for epidermal growth factor.

"The field of colon cancer testing is now taking the same approach that we've been using for many years in breast cancer testing with HER2 and estrogen receptors."

According to the American Cancer Society, approximately 155,000 patients were diagnosed with CRC in 2007, many of who must decide whether anti-EGFR treatments will be used to manage their disease. KRAS mutations explain about 30 percent to 40 percent of cases in which patients fail to respond to these treatments. BRAF may account for approximately 12 percent to 15 percent of CRC patients who do not have a KRAS mutation but also show no response to these drugs.

"The field of colon cancer testing is now taking the same approach that we've been using for many years in breast cancer testing with HER2 and estrogen receptors," said Ken Bloom, M.D., chief medical officer at Clarient. "The recent inclusion of KRAS to the NCCN guidelines clearly indicates that these tests are becoming increasingly important in identifying whether a patient is a candidate for a particular set of therapies."

▲ **Genentech Files Petition with FDA,** *from page 1*

Genentech's petition is particularly concerned with LDTs that are used to guide clinical treatment decisions. The company is the maker of Herceptin, the breast cancer therapy that targets tumors that express the HER2 protein and therefore requires that patients be tested for this genetic characteristic before receiving the drug. FDA-approved LDTs for determining HER2 status include the HercepTest (Dako), PathVysion (Abbott Molecular), and HER2 FISH pharmDx kit (Dako).

The petition points out that while the Herceptin label does not provide information on HER2 LDTs that have not been approved by FDA, some clinical laboratories market and perform nonapproved tests for the purpose of selecting patients for Herceptin therapy. The petition points to HER2 tests developed and marketed by CombiMatrix Molecular Diagnostics (HerScan) and Monogram Biosciences (HERmark). Other nonapproved companion diagnostics (for use with drugs other than Herceptin) mentioned in the petition include those offered by Rosetta Genomics, Clinical Data, and Genzyme.

In cases such as these, Genentech urges FDA to "take immediate enforcement action to remove the test from the market until the clinical laboratory conducts the necessary studies to demonstrate, to FDA's satisfaction, the analytical and clinical validity of the test's intended use."

With regard to the frequently cited lack of resources that would hamper FDA's ability to exercise full-scale regulatory control over LDTs, Genentech's petition points out the staff increases at the FDA Center for Devices and Radiological Health that were made possible by the passage of the Medical Device Amendments of 2002. "Additional 510(k) or PMA submissions would be accompanied by user fees, helping to offset the additional resources FDA would need to devote to this effort," notes Genentech.

The FDA Office of In Vitro Diagnostic Devices (OIVD)'s recent efforts to step up its oversight have focused on IVDMIAs, a subset of LDTs or manufactured test kits that a) combine the values of multiple variables using an interpretation function to yield a single, patient-specific result that is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, and b) provide a result whose derivation is nontransparent and cannot be independently derived or verified by the end-user.

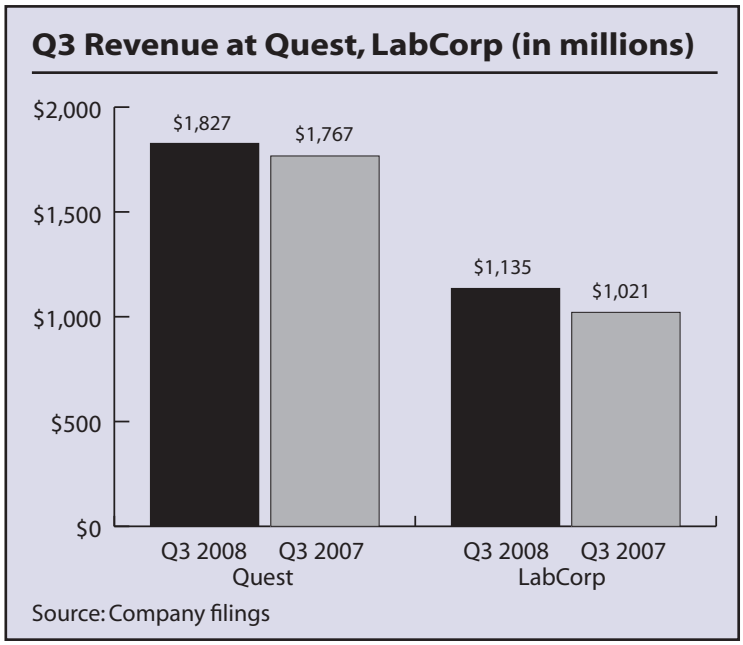
In revised draft guidance issued in July 2007, the FDA clarified that LDTs or test kits that meet the definition of an IVDMIA will soon require OIVD premarket submissions. "FDA intends to enforce regulatory requirements for all currently marketed laboratory-developed IVDMIAs that do not receive marketing clearance or approval within 18 months of publication of the final guidance document," noted the draft guidance document.

Esoteric Testing Fuels 11% Q3 Revenue Growth at LabCorp

In the economically challenging third quarter of 2008, esoteric testing helped LabCorp (Burlington, N.C.) to outpace Quest Diagnostics (Madison, N.J.) in revenue and volume growth. LabCorp saw revenues grow by 11.2 percent to $1.1 billion, and volumes increase 10.6 percent. Quest, the nation's lab testing leader, saw smaller gains, with revenue growth of 3.4 percent to $1.8 billion and volumes up by 0.7 percent.

According to William Blair & Company (WB&C; Chicago) analysts Amanda Murphy and John Kreger, the difference in the growth rates of the two laboratory companies is largely due to LabCorp's strategy of driving utilization within specialty physician offices. "Esoteric utilization was up 8.4 percent for the quarter (versus core testing, which was up 1.5% in the United States," wrote Murphy and Kreger in a research note. "In our view, this provides further support for our belief that LabCorp is the stronger esoteric franchise of the two national labs, as Quest continues to have difficulty driving synergies out of its AmeriPath acquisition."

At both Quest and LabCorp, increased demand for vitamin D and HPV testing are driving growth in esoteric testing. At LabCorp, vitamin D testing grew an estimated 80 percent to 100 percent in the second quarter of 2008, although that growth came off of a very low base. HPV testing at the company is now growing an estimated 6 percent to 7 percent above the company's 5 percent esoteric testing growth rate.



Amidst strong growth, however, LabCorp is grappling with regulatory challenges to its genomic and esoteric businesses. In October of 2008, the company voluntarily withdrew from the market its OvaSure cancer test in response to a warning letter from the FDA questioning the test's clinical validity.

Meanwhile, Quest's former test kit manufacturing subsidiary, Nichols Institute Diagnostics, continues to be a drag on the company's bottom line. On a recent earnings call with analysts and reporters, Quest's senior vice president and chief financial officer Robert Hagemann announced that the company had reached a settlement agreement with the government, which includes entering a guilty plea to single count of felony misbranding. He added that a record pretax charge of $73 million was made during the quarter and added to the reserve fund, now totaling $314 million, which will go toward settling the suit and related issues.

Looking ahead, Quest revised its revenue growth guidance from 9 percent to 8 percent. "The change is principally due to the impact of hurricanes in the third quarter, a delay obtaining approval for one our point-of-care products, and not seeing the acceleration in volume we had anticipated in our clinical testing business," said Hagemann.

LabCorp has reaffirmed its revenue-growth guidance of 11 percent and issued preliminary guidance for 2009, stating an expected revenue-growth rate of between 3.5 percent and 5.5 percent. Quest has not issued any preliminary guidance for 2009.

Roche Gets CE Mark for New HIV, HBV Viral Load Tests

Roche Molecular Diagnostics (Pleasanton, Calif.) has received CE Mark certification for its new viral load tests for HIV and hepatitis B virus (HBV), allowing the tests to be sold for clinical use in the European Union. Both tests are for use on the COBAS AmpliPrep / COBAS TaqMan system, Roche's fully automated, real-time PCR platform that was CE Mark certified in 2005.

The newly CE Mark certified HIV test quantifies the amount of HIV-1 RNA in a blood sample. It is the second version of Roche's COBAS AmpliPrep/COBAS TaqMan HIV-1 test and offers a broader dynamic range than the test's initial version, which was approved by the United States Food and Drug Administration in 2007 and rapidly accepted by the market.

Using a "dual-target" approach, the new test simultaneously amplifies and detects two separate regions of the HIV-1 genome. This method provides reliable test results even when mutations are present. The new HIV-1 test is the first dual-target test to be offered on the COBAS AmpliPrep / COBAS TaqMan System.

"HIV mutations are a serious problem. Because it is impossible to predict when these mutations will occur, we have designed this test to detect all HIV-1 (Group M and O) strains," said Daniel O'Day, president and CEO of Roche Molecular Diagnostics.

Also receiving CE Mark certification was the new version of the COBAS AmpliPrep / COBAS TaqMan HBV test, which detects and quantifies HBV DNA in patient plasma and serum. Monitoring an HBV patient's viral load allows clinicians to select patients for treatment as well as predict and assess individual responses to therapy.

Like the new HIV test, "version 2.0" of Roche's HBV viral load test offers an expanded dynamic range It is available in kits of up to 72 tests and packaged in ready-to-use reagent cassettes.

Tom Daschle Nominated for HHS Secretary

President-Elect Barack Obama has formally nominated former Senate majority leader Tom Daschle to the position of Secretary of Health and Human Services. Daschle has also been tapped to serve as director of the new White House Office of Health Care Reform. "He will be responsible not just for implementing our health care plan, he will also be the lead architect of that plan," said Obama, at a December 11 press conference announcing his decision.

Since losing re-election to the Senate in 2004, Daschle has been a public policy adviser and member of the legislative and public policy group at the law firm Alston & Bird. He is also a senior fellow at the Center for American Progress (CAP) and a member of a member of the Council on Foreign Relations.

Jeanne Lambrew, also a senior fellow at CAP, will serve as deputy director of the White House Office of Health Care Reform.

Abaxis Gets CLIA Waiver for Point-of-Care Test Panels

The U.S. Food and Drug Administration (FDA) has granted waived status under CLIA regulations for two additional analytes, creatine kinase (CK) and phosphorus (Phos), used with the Piccolo and Piccolo Xpress point-of-care analyzers manufactured by Abaxis (Union City, Calif.). The waivers affect Abaxis's Renal Function and MetLyte 8 test panels.

The Renal Function Panel is a standard panel mostly used for determination of renal function status. The MetLyte 8 is commonly used to assess a variety of metabolic conditions across several specialties, including pediatrics and cardiology. With the waiver of these two panels, 11 of the company's 13 medical test panels have CLIA-waived status. These include lipid, liver, kidney, and general chemistry panels.

After its first quarter of 2009 (ended June 30, 2008) was adversely affected by economic conditions, Abaxis reported record revenues and operating income in its second quarter, which ended September 30. Medical reagent disc sales were up 28 percent to 434,000 units compared to the same period of the previous year. "The question now is with the distributors we have, can they pay their bills on time?" said Clint Severson, chairman and CEO of Abaxis, at the Piper Jaffray Health Care Conference on December 3 in New York City.

"We see more relationship to the economy with the price of gasoline," added Severson. "If the price of gasoline goes above five dollars a gallon, business tends to go down. If gasoline drops below two dollars, it tends to go up. That's what we've seen."

Gene Express, BioTrove to Co-Market Lung Cancer Test

Gene Express Inc. (Wilmington, N.C.) and BioTrove Inc. (Woburn, Mass.) will team up to test market a genetic profiling test for lung cancer risk. The test will be marketed to reference laboratories and independent laboratories as well as community hospitals.

Announced on December 2, the exclusive agreement provides for the co-marketing of the Standardized NanoArray PCR (SNAP) gene expression profiling system, which uses BioTrove's OpenArray nanofluidic polymerase chain reaction (PCR) technology platform and Gene Express' PCR standards. The development of the test is supported by a two-year National Institutes of Health grant, which was awarded earlier this year.

Designed to accelerate and control PCR analysis of biomarkers associated with lung cancer risk, the SNAP system combines several high complexity, multi-gene diagnostic tests into a single tool that offers simplified workflow and reduced sample requirements relative to currently available tests.

According to BioTrove, the OpenArray system allows users to conduct up to 3,072 independent PCR analyses simultaneously on up to 144 samples in a plate the size of a microscope slide.

Diagnoplex, Generation Health Close on Funding Rounds

Two startup companies focused on molecular diagnostics have managed to raise capital in difficult economic conditions. Diagnoplex (Epalinges, Switzerland), a developer of molecular diagnostics for cancer, has raised CHF10 million (approximately $8.6 million at current exchange rates) in a Series A round led by Novartis Venture Fund and NeoMed, with Initiative Capital Romandie acting as co-investor. Generation Health (Saddle River, N.J.), a genetic testing benefit management company, raised nearly $5 million in Series A funding. Its backers include Highland Capital Partners, Correlagen Diagnostics, D2Hawkeye, and company management.

Diagnoplex develops blood-based cancer diagnostics for use on its proprietary molecular diagnostics platform, which was developed by Stavros Therianos, Ph.D., the company's founder and chief executive officer, during his tenure at the University of Rochester (Rochester, N.Y.).

Employing single-channel quantitative multiplex reverse transcriptase-polymerase chain reaction (scqmRT-PCR) technology, the platform allows for quantification of the copy number obtained with real-time PCR and the quantification of up to 60 genes simultaneously. The scqmRT-PCR platform could be used to determine multi-gene "signatures" of different cancers.

Diagnoplex plans to use the proceeds from the financing to support the further clinical development of Colox, a noninvasive test for the early detection of colon cancer, which will be made available in kit form. An early-stage study of 140 patients has shown that Colox can detect adenoma, even in its precancerous stage.

Meanwhile, Generation Health is focused on helping employers and other health care payors address the rapidly evolving field of genetic testing by achieving improved medical outcomes while controlling medical costs. "All health care payors will eventually have to address the area of genetic testing," said Per G.H. Lofberg, chairman, CEO, and co-founder of the company. "Our goal is to offer payors an organized approach to this exciting new field and to help them manage the administration of this health benefit in a cost-effective manner."

Lofberg was one of the creators and leaders of Medco Health Solutions, the pharmacy benefit management company. "We see some clear parallels between the evolution of pharmacy benefit management and what is occurring in the field of genetic testing," said Lofberg. "Payors will need to put in place benefit designs that encourage the use of medically important and cost-effective genetic tests, while limiting their exposure to run-away medical expense from diagnostic testing of marginal clinical utility."

In addition to Lofberg, the co-founders of Generation Health include Richard K. Schatzberg, chief marketing officer of Generation Health; J. Christian Kryder, M.D., chairman and CEO of D2Hawkeye; and David Margulies, M.D., chairman and CEO of Correlagen Diagnostics, a genetic testing and analysis company.

IVD Stocks Down 12%; Affymetrix Falls 30%

The 17 stocks in the G-2 Diagnostic Stock Index fell an average of 12 percent in the five weeks ended December 5, with 15 stocks down in price and two up. The G-2 index is down 40 percent for the year, while the S&P 500 and the Nasdaq have plummeted 39 percent and 42 percent, respectively.

Shares in GeneChip maker **Affymetrix** (Santa Clara, Calif.) were down 30 percent, ending the period with a share price of $2.67 and a market capitalization of $176 million. On December 8, the company announced that it had completed its $73 million acquisition of privately held Panomics (Fremont, Calif.), a manufacturer of assay products for a variety of genetic, protein, and cellular analysis applications.

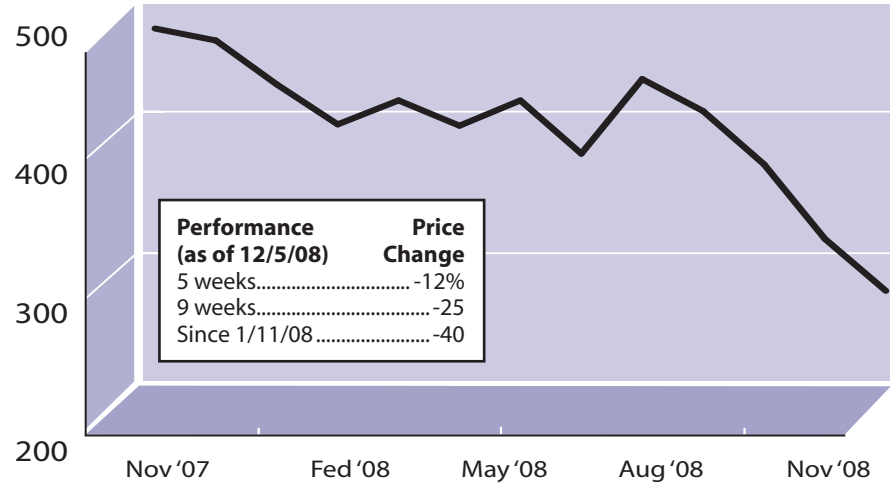
One of only two gainers in recent weeks was **OraSure Technologies** (Bethlehem, Penn.), which was up 3 percent to close at $3.45 per share and a market capitalization of $142 million. Although the company's third quarter revenues of $16.9 million were down 21 percent compared to the same period in 2007, sales of the company's OraQuick Advance rapid HIV-1/2 antibody test increased 18 percent during the quarter. The company attributed the drop in revenues to an expected decrease in sales of over-the-counter cryosurgical products.

OraSure recently announced the termination of its distribution agreement with Abbott Laboratories, which has exclusively distributed the OraQuick Advance HIV test to U.S. hospitals and reference laboratories, and on a nonexclusive basis, to the U.S. physician office market. Beginning in 2009, OraSure will distribute OraQuick HIV directly to both U.S. hospitals and reference laboratories, while physicians' offices will continue to be served through distributors.

"We believe taking this business direct will help us maximize sales by taking greater control of an important market, U.S. hospitals," said Doug Michels, president and CEO of OraSure, in a conference call with analysts. "It will also lay a foundation to sell future products into the same channel and, in particular, our OraQuick rapid HCV [hepatitis C virus] test once FDA approval is obtained."

For up to the minute laboratory and diagnostic firm data, financial news, and company podcasts—go to **www.g2reports.com**

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 17 IVD companies.

UP	PRICE	% CHG
Bio-Rad	$73.21	5%
OraSure	3.45	3
DOWN		
Abaxis	14.37	-4
Abbott Labs	52.75	-5
Affymetrix	2.67	-30
Beckman Coulter	40.57	-20
Becton Dickinson	64.91	-8
Clinical Data	9.27	-16
Gen-Probe	40.45	-11
Immucor	22.51	-17
Inverness Medical	16.42	-25
Johnson & Johnson	70.67	-1
Luminex	21.27	-5
Meridian	23.03	-4
Nanogen	0.18	-33
Nanosphere	4.12	-16
Quidel	13.51	-14

G-2 Insider

Harness the power of molecular diagnostics for your laboratory . . . Learn how to best apply the emerging science, novel business models, and consumer demand of molecular diagnostics to grow your lab at *Business & Financial Strategies for Molecular Diagnostics 2009*. This Washington G-2 Reports conference will take place Feb. 2 to 4, 2009, at the Hyatt Regency Pier Sixty-Six in Ft. Lauderdale, Florida. A roster of experts will provide insight and advice on how laboratories can and are successfully integrating molecular diagnostics into their business strategies, given the current regulatory and business environment. Scheduled sessions include:

- ❑ *Molecular Diagnostics: From Revolution to Mainstream to Genomic Medicine,* a keynote address by Daniel H. Farkas, Ph.D., vice president, clinical diagnostics, Sequenom Center for Molecular Medicine;
- ❑ *Selecting the Best Molecular Platform for Your Laboratory,* presented by John Greg Howe, Ph.D., assistant professor of laboratory medicine and director of the molecular diagnostics laboratory at Yale University;
- ❑ *Building a Better Molecular Test Menu,* a joint session featuring Lynnette C. Savaloja, cytology technical supervisor at Regions Hospital Pathology Department, and E. Blair Holladay, Ph.D., vice president for scientific activities and executive director, board of registry, American Society for Clinical Pathology; and
- ❑ *PGx in the Laboratory: Choosing and Using Pharmacogenomic Tests,* presented by Domnita Crisan, M.D., medical director of molecular diagnostics at William Beaumont Hospital.

For full program details or to register, visit www.g2reports.com/molecular09 or call 800-401-5937 ext. 4710.

References

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Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by Washington G-2 Reports, 1 Washington Park, Suite 1300, Newark, NJ 07102-3130. Tel: 973-718-4700. Fax: 973-622-0595. Web site: www.g2reports.com.

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