G2 INTELLIGENCE

Diagnostic Testing &Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Breath Test Found to Be Effective Way to Diagnose B12 Deficiency

Researchers have developed a simple, noninvasive, and low-cost diagnostic breath test (BT) to detect functional deficiency of vitamin B12. Initial results, published online in the *Journal of Breath Research*, show that the BT is more accurate than serum B12 and homocysteine in assessing vitamin B12 status. Identification of an increasing number of volatile organic compounds associated with disease states, combined with technological advances making testing cheaper and less time-consuming, are creating mounting hope among researchers that breath testing may soon gain widespread clinical acceptance.

The B12 BT quantitates the metabolism of 13C-labeled propionate to 13CO2. The pathway from propionate to CO2 requires B12 as a cofactor. B12 insufficiency limits the formation of labeled CO2 exhaled in the breath, as compared to individuals with normal vitamin B12 status.

The researchers from University of Florida at Gainesville and Metabolic Solutions (Nashua, N.H.), found that breath collection times could be reduced to just at baseline and 10 to 20 minutes following administration of propionate. The BT may provide clinicians with a noninvasive, accurate, reliable, and reproducible diagnostic test to detect vitamin B12 deficiency in at-risk populations. For more on developments in breath testing and its clinical applications, please see *Inside the Diagnostic Industry* on page 5.

Are New Screening Tests Needed for U.S. Blood Supply? Yes and No

As the number of blood transfusions continues to rise and the Department of Health and Human Services calls for better patient blood management and professional standards on appropriate blood use, there have been questions raised about whether the nation's blood supply is adequately screened.

New Centers for Disease Control and Prevention (CDC) case study analysis shows a sharp rise in the number of post-transfusion Babesia infections from 2000 to 2009. Babesia is a tickborne parasite of red blood cells. The study, published online in the *Annals of Internal Medicine*, calls for development of a screening test to reduce the vulnerability of the nation's blood supply to tickborne infections.

Looking at data since 1979, the first known year of a case of transfusion-associated babesiosis, the researchers found 159 transfusion-related babe-

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siosis cases with 77 percent of cases occurring from 2000 to 2009. Total transfusion-related infections are likely underestimated, the authors say, due to unreported cases. Most cases were associated with red blood cell (RBC) components. Cases occurred in all four seasons and occurred in 19 states, but 87 percent (138 cases) were in the seven main B. microti–endemic states in the Northeast and the upper Midwest.

"The observed rise in cases begs the question of whether the parasite's endemic range is expanding, if prospective donors are becoming infected more frequently, or if physicians and hospitals are more attuned to potential Babesia infections in blood recipients," writes David Leiby, Ph.D., head, Transmissible Diseases Department, American Red Cross's Jerome H. Holland Laboratory (Rockville, Md.) in an accompanying editorial. "As with many questions regarding emerging infectious agents, this is difficult to answer, but the explanation is probably multifactorial."

"In the absence of a feasible and approved method for screening the blood supply, B. microti has become the infectious agent most frequently transmitted by blood transfusion in the United States."

—David Leiby, Ph.D.

Infected persons can feel fine and meet blood donor eligibility criteria but have low-level parasitemia that remains infective for a year. The findings underscore the fact that, the authors write, Babesia parasites can survive blood bank procedures and storage conditions for RBC components. They say the nation's blood supply is vulnerable year-round especially, but not only, in and near babesiosis-endemic areas. In January 2011 babesiosis became a nationally notifiable disease.

No Food and Drug Administration (FDA)-approved Babesia test is available for screening prospective blood donors, but in July 2010 the FDA's Blood Products Advisory Committee supported the concept of regional donor testing for Babesia.

"In the absence of a feasible and approved method for screening the blood supply, B. microti has become the infectious agent most frequently transmitted by blood transfusion in the United States," writes Leiby. "In part, manufacturers have shown a reluctance to develop a test for a regionalized agent that may require only a limited number of tests compared with other agents (for example, HIV) that are screened universally."

Screening for CFS Virus Not Needed

In a study published online in *Science Express*, researchers from the National Institutes of Health with academic and industry collaborators could not validate previous research findings that suggested the presence of several viruses in blood samples from chronic fatigue syndrome (CFS) patients. The study was conducted in response to concern these viruses could affect the safety of the nation's blood supply.

Murine leukemia viruses (MLV), including xenotropic MLV-related virus (XMRV), have been controversially linked to CFS. The scientists compiled coded replicate samples of blood from 15 subjects previously reported to be XMRV/MLV-positive (14 with CFS) and from 15 healthy donors. The samples were distributed blindly to nine laboratories. The labs performed assays designed to detect XMRV/MLV nucleic acid, virus replication, and antibodies. No assay at any of the labs could reproducibly detect XMRV/MLV in the previously reported infected subjects.

Experts say these findings are reassuring and indicate that routine blood donor screening for XMRV/MLV is not warranted. The researchers conclude that previous results indicating a XMRV/MLV-association with CFS may have resulted from laboratory error, contamination, or false-positive results.

State Public Health Labs Not Ready for Major Radiological Event

Survey data show serious gaps in the United States' preparedness to handle radiological emergencies, including deficiencies in laboratory assets to handle exposure testing in the wake of a potential widespread radiation exposure. In the study published online in *Disaster Medicine and Public Health Preparedness*, researchers from the Association of Public Health Laboratories (APHL) found it could take years to analyze the thousands of specimens that an event similar to the nuclear crisis following the 2011 Japanese earthquake would likely generate.

Researchers analyzed data from the APHL's 2009 All-Hazards Laboratory Preparedness Survey to examine baseline radiological response capabilities and capacity from the 50 states and territories. Only 14 respondents (27 percent) from the All-Hazards Laboratory Preparedness Survey reported the ability to measure radionuclides in clinical specimens. The authors say it is likely that many of these laboratories are not certified to perform diagnostic testing for radiation exposure.

In the event of a large-scale incident at least 70 percent of states would send their clinical specimens to the Centers for Disease Control and Prevention (CDC). Even with improved CDC throughput since 2007, when federal experts estimated using then-existing assets it would take more than four years to screen 100,000 individuals for radiation exposure and six years to test environmental samples from a large-scale radiological emergency, capabilities and capacities remain insufficient to respond to a major event.

Federal investment and initiatives in environmental testing yielded greater public health laboratory capabilities for food and environmental samples. Of respondents from a separate Radiation Capabilities Survey, 60 percent reported the ability to test environmental samples.

Adding to the lack of readiness is the researchers' finding that laboratories reported on average fewer than one employee working on clinical radiochemistry, which likely reflects both budget constraints and broader laboratory personnel shortages. The authors conclude that improved preparation requires new investments including adding radiological preparedness to the Laboratory Response Network.

CAP Expanding Content for Clinical Next-Gen Sequencing

The College of American Pathologists (CAP) is updating its laboratory accreditation program's molecular pathology checklist to include accreditation content for clinical applications of next-generation sequencing. The checklist, which is used in the accreditation inspection process to meet CLIA requirements, will cover technical, bioinformatics, and interpretative methods to report findings of genomic analysis.

The CAP's efforts to further clinical adoption of next-generation sequencing go beyond accreditation and will include expansion of proficiency testing products in molecu-

lar genetics and developing standards for reporting genetic variants, both for their interpretation for clinical use and for interoperability of results in health information systems. Preparing for the transition of next-generation sequencing technology from research to patient care requires the establishment of standards that CAP will work with other professional organizations on, including the American College of Medical Genetics, the Association for Molecular Pathology, and Health Level 7.

"The CAP's work in accreditation, proficiency testing, and standards ensures that laboratories implement and maintain quality processes covering preanalytic, analytic, and post-analytic methods to deliver reliable results for use in patient care," said Karl V. Voelkerding, M.D., medical director for genomics and bioinformatics, ARUP Laboratories, Salt Lake City, in a statement. Voelkerding chairs the workgroup developing the accreditation checklist. "As the CAP did with its PT and accreditation programs, the college is proactively moving forward in producing quality metrics for forthcoming clinical use in the burgeoning field of genomics."

The updated molecular pathology checklist is estimated to be released in 2012.

Physicians Not Properly Referring for BRCA Testing

Results of a new vignette-based survey show that adherence to recommendations for BRCA testing is low, with physicians reporting they refer too many average-risk women and fail to refer many high-risk women. The study, published online in *Cancer*, shows that interventions are necessary to improve primary care physicians' ability to assess a female's risk of breast or ovarian cancer, thereby improving efficient use of resources and the resulting clinical benefit of genetic testing referrals.

Genetic counseling and testing is recommended for women at high-risk, but not average risk, of breast or ovarian cancer. The researchers from the Centers for Disease Control and Prevention (CDC) analyzed survey results from more than 1,500 family physicians, general internists, and obstetrician/gynecologists. Only 41 percent of responding physicians indicated they would refer high-risk women for testing, which is "concerning," the authors say, given the availability of evidence-based interventions to decrease breast and ovarian cancer risk in high-risk women. Among average-risk women, 29 percent of physicians self-reported unnecessarily referring these women to genetic counseling and testing services. Since most women are average-risk, the authors write, "even a modest degree of testing among this group could translate into substantial numbers of women receiving unnecessary care."

Younger patient age, physician sex (female vs. male), and practicing obstetrician/gynecologists all improved guideline adherence among high-risk patients. But the physicians' ability to estimate ovarian cancer risk was the most powerful predictor of guideline adherence in both average-risk and high-risk groups of women.

"Primary care physicians are carrying more and more of medicine's burden," says Katrina Trivers, Ph.D., an epidemiologist, Division of Cancer Prevention and Control at the CDC, and lead author of the study. Family history and genetic risk are difficult to assess and keep abreast of, but "When physicians were able to accurately assess risk, they did tend to do the right thing in terms of recommendations."

G2 INTELLIGENCE
Inside the Diagnostics Industry

Long-Awaited Breath Testing Improves, But Hurdles to Use in Clinical Practice Remain

Breath smell can offer physicians diagnostic clues. The breath of patients with uncontrolled diabetes may smell fruity, and ammonialike breath may indicate kidney failure. Clinicians have been able to use the smell of compounds generated from within the body to diagnose disease since the days of Hippocrates. In recent years scientists have been able to identify more than 3,000 volatile organic compounds (VOCs) in exhaled breath. Yet in the last 30 years, diagnostic breath testing has made few inroads into routine clinical practice. As technologies evolve and the ability to definitively link thousands of VOCs to disease states advances, many in the field are hopeful that in the next five years there will be progress translating noninvasive breath testing research into clinical practice.

"The problem is that the breath has so many other things—byproducts of the diet and things you are exposed to in the environment that also show up. . . . The EPA looks to breath to see about environmental exposures, but in the medical application you want to avoid them. Somebody's trash is somebody [else's] treasure."

—Raed Dweik, M.D., Cleveland Clinic

Breath testing can be used for noninvasive disease diagnosis and detection of enzyme deficiencies and drug efficacy monitoring for personalized medicine. Breath biomarkers can be either endogenously produced by the body because of a physiological problem, like acetone in the breath of a diabetic patient, or exogenously produced such as 13CO2, a labeled isotope produced as a test byproduct. Clear signatures exist in the breath for many diseases, including gastrointestinal problems, heart disease, and cancer. There are so many compounds in the breath at such low concentrations (parts per billion or trillion), it has made analyzing breath challenging.

"We talk about the promise of breath testing to diagnose disease. But the problem is that the breath has so many other things—byproducts of the diet and things you are exposed to in the environment that also show up. How do you control for those variables?" asks Raed Dweik, M.D., director of the Breath Analysis Program, Cleveland Clinic. "The EPA looks to breath to see about environmental exposures, but in the medical application you want to avoid them. Somebody's trash is somebody [else's] treasure."

Anything in the blood that is potentially volatile or has a volatile metabolite can be measured in exhaled breath. Materials such as lipids, amino acids, or drugs labeled with 13C are being used in research. The labeled substrate is given orally and the specific metabolic function is analyzed by measuring the increase of 13CO2 in the subject's breath over a period of time. 13C-labeled compounds have been used as diagnostic probes for over 30 years. The instrumentation used to measure the isotopes has advanced from mass spectrometry to infrared spectrometry in the mid-1990s. While instrumentation costs have dropped, it is still hard for small labs to justify the equipment prices, given the dearth of tests available.

"Breath testing has been a big disappointment from the time the first breath test was approved by the FDA," says David Wagner, Ph.D., president, Metabolic Solutions

Inc., an independently owned Clinical Laboratory Improvement Amendments-certified lab that process over 25,000 breath samples annually.

Regulation Not the Only Hindrance

A few breath tests have been approved for clinical use by the U.S. Food and Drug Administration (FDA), including the urea breath test (Meretek) to identify infections by H. pylori bacteria, Heartsbreath test (Menssana Research) to identify methylated alkanes, signs of organ rejection in heart transplant patients, and the nitric oxide test (Solna) for asthma testing. Experts point to the asthma testing as the only success story, aside from the widespread use of breath tests for alcohol detection and CO2.

"Most lab tests are cleared as medical devices, but breath tests are considered combination products—a drug and a device," explains Wagner. "What you are giving the person to drink is considered a drug. Combination products are very expensive to get through the approval process."

Selected Breath Analysis Devices Approved by the FDA

DETECTED MOLECULE	DISEASE/ CONDITION	DEVICE NAME	MANUFACTURER	FDA APPROVAL
NO	Asthma	NIOX MINO	Aerocrine AB; Solna	3/2008
13CO2	H pylori	POCone Infrared Spectrophotometer	Otsuka Pharmaceutical Co. Ltd.	7/2004
H2	Lactose Malabsorption	Micro H2 Breath Monitoring Device With Hydra Software Utility	Micro Direct Inc.	5/2004
Alkanes	Grade 3 heart allograft rejection	Heartsbreath	Menssana Research Inc.	2/2004
NO	Asthma	NIOX	Aerocrine AB; Solna	4/2003
13CO2	H pylori	BreathTek UBiT UBT	Meretek Diagnostics Inc.	1/2002

Source: G2 Intelligence and Raed Dweik, M.D.

A lot of small companies, like Metabolic Solutions, don't have the resources to get their tests approved and are trapped in a vicious cycle in which revenue from reimbursement is contingent on approval. Additionally, each application of a test requires separate premarket approval submission, adding to the regulatory burden.

The field has self-inflicted other hindrances to breath test acceptance, namely the lack of standardization. Standardized protocols on the dosage of the 13C substrates, test period, times, methods for sample collection, and methods of 13CO2/12CO2 measurements are lacking, making comparisons of results between different research laboratories difficult.

"[Not having] standardization delayed the process," says Dweik. "With the nitric oxide test in the mid-1990s you couldn't compare results between labs or clinics. Once you have clear guidance you know how to build the device and progress follows quickly."

One of the benefits of breath testing, its lower test cost, may actually hamper adoption. Some in the field say it is in the physicians' financial interest to continue using more invasive tests.

"Urea test reimbursement is $100 and that is the problem," says Anil Modak, Ph.D., associate director of medical products research and development at Cambridge Isotope Laboratories Inc. (Andover, Mass.). "A physician would get $700 for an endoscopy. Most physicians do endoscopies. The patients don't know about the noninvasive option. The physicians could easily do 20 breath tests instead of two endoscopies [in a day], but the test was not sold well to the patients or the insurers. It is a question of selling these tests."

> ***"It will catch on if [there is] no other alternative or [if] the alternative is so expensive. There will be no major advances unless a major player gets into it."***
>
> ***—David Wagner, Ph.D., Metabolic Solutions***

"Two things will determine success [of a breath test]—can it detect and is there a clinical need? Can the test tell us something?" explains Dweik.

Researchers in the breath testing field have paid increasing attention to the physicians' needs in creating breath tests: namely, the tests must be quick, simple, and accurate.

"Physicians don't want multiple sampling. Physicians and nurses just don't have the time," says Modak. "The only way to get breath testing into clinical practice is one breath sample within one hour after administering the substrate."

Coming to a Clinic Soon?

Despite the seeming benefits of breath testing as a noninvasive, low-cost alternative to invasive diagnostic methods, why hasn't breath testing gained better traction in the clinical community?

"It will catch on if [there is] no other alternative or [if] the alternative is so expensive," says Wagner. But he cautiously adds, "There will be no major advances unless a major player gets into it."

Given the high cost of getting tests approved and advances in molecular genetics there is a movement toward using breath tests as a companion diagnostic to shift some of the cost toward deeper-pocketed pharmaceutical companies. Breath biomarkers can identify responders or nonresponders to prevent unnecessary adverse drug reactions and improve clinical outcomes.

"Breath testing is the best way to personalize medication," says Modak. "People are treated like guinea pigs and it doesn't work. Give people the right drug for the right disease at the right time. They can't wait . . . and it doesn't work to give the same drug, same dose to everybody who walks in."

Modak says phenotype breath tests with cutoffs produce more actionable information than genotype tests. Genetic polymorphisms contribute to considerable variation in the metabolism of the majority of FDA-approved drugs. The use of 13CO2 breath testing can evaluate enzyme activity (CYP2D6, CYP2C19, and CYP1A2) necessary for drug metabolism, identifying patients for whom the drug would be most effective or the most toxic.

"I hope in the next four to five years at least two new tests are approved. Once a couple are, there will be a cascade," predicts Modak.

Lab Tests Included in Top 5 Overordered, Costly Clinical Activities

Routine lab tests are among the most frequently ordered unnecessary medical care provided by primary care physicians, according to a report published in the October issue of *Archives of Internal Medicine*. Researchers found that unnecessary tests and medications account for more than $6.7 billion in avoidable annual medical costs.

The researchers examined the frequency and associated cost of the top five overused clinical activities across the three primary care specialties (pediatrics, internal medicine, and family medicine) using a national sample of ambulatory care visits. The overused clinical activities were designated earlier this year by the Good Stewardship Working Group of the National Physicians Alliance. The top-five lists, which were developed through physician surveys and field testing and funded by a grant from the American Board of Internal Medicine Foundation, represent evidence-based, quality-improving, resource-sparing activities that could be easily incorporated into the practices of primary care providers.

While the dollar amount unnecessarily spent on laboratory testing is small in comparison to the $5.8 billion it costs the health care system to prescribe brand-name statins to treat cholesterol, laboratory testing was the most frequently overused clinical activity. The ordering of a complete blood cell count for a general medical examination was the most prevalent, nonrecommended activity (56 percent of visits), costing $32.7 million. Urinalysis or basic metabolic panel was ordered or performed unnecessarily in 18 percent and 16 percent of patient visits, respectively, and Pap tests were misordered and performed in girls under 21 years of age in an estimated 22 million physician visits or 3 percent of all cases. In all, laboratory tests accounted for $93.9 million, or 1.4 percent of the total unnecessary costs.

"We know that the overuse of care is part of the medical landscape," says Minal Kale, M.D., a fellow in the Division of Internal Medicine at Mount Sinai School of Medicine (New York), and study author. She is hopeful with the implementation of accountable care organizations and other efforts that encourage greater coordination of care, improvements can be made in reining in unnecessary care, while acknowledging such developments could mean a loss of some testing volumes for labs.

Labs Assess Costs of Proposed Rule Allowing Direct Patient Access to Lab Reports

The 60-day comment period will expire this month on a rule proposed by Department of Health and Human Services (HHS) to give patients and their authorized representatives direct access to laboratory test results. The measure parallels other HHS efforts aimed at coordination of care across providers and patient-centered care.

The proposal would amend Clinical Laboratory Improvement Amendments (CLIA) laboratory regulations and Health Insurance Portability and Accountability Act (HIPAA) privacy regulations whose provisions are creating barriers to health information exchange. It would also strengthen patients' rights to access their own laboratory

test result reports and enable them to take on a larger role in health care decisions. The proposed rule, originally published in mid-September, was jointly issued by the Centers for Medicare and Medicaid Services and the Centers for Disease Control and Prevention, which are responsible for laboratory regulation under CLIA, and the Office for Civil Rights, which is responsible for administering HIPAA.

If implemented, the measure would override some state laws requiring test reports to go directly to health care providers. Currently in 39 states—accounting for 22,671 laboratories—patients do not have direct access to laboratory test results without the consent of the health care provider. Labs in these impacted states perform approximately 6.1 billion lab tests annually, generating an estimated 305 million to 611 million lab reports annually, according to HHS. The extent to which patients will request reports is unclear, but based on HHS assumptions could vary from 152,000 to 3 million requests per year.

While acknowledging there is a cost in implementing this new rule, HHS estimates the costs would not be "economically significant." The recurring annual costs of handling patient report requests could reach an estimated $764,000 to $46 million, with one-time compliance costs ranging between $2 million and $10 million. G2

OraSure's Rapid HCV Oral Swab Test Accurate, Could Expand Testing in High-Risk Populations

The first field test of OraSure Technologies' (Bethlehem, Pa.) OraQuick rapid oral swab hepatitis C virus (HCV) test validated the test's accuracy compared to the current standard enzyme immunoassay (EIA) test and highlighted the impact that rapid oral swab testing may have on HCV screening programs, particularly in high-risk populations.

The study, funded by OraSure and published in the September issue of the *American Journal of Public Health*, examined the performance of the oral swab test for HCV antibodies in a community setting serving high-risk populations. The oral swab test performed comparably to a blood-based EIA HCV antibody test with the rapid test matching EIA results in 97.5 percent of samples. In six of the seven discordant pairs, the rapid test result agreed with the confirmatory polymerase chain reaction result.

The study, conducted by the Office of Viral Hepatitis Coordination, Division of Disease Control, New York City Department of Health and Mental Hygiene, included 486 samples, and the test was able to produce results on-site in 20 minutes. Of the participants, roughly half returned for EIA test results.

"Test results that never reach patients represent scarce public health dollars wasted, and at-risk individuals remain unaware of a health issue that may greatly affect their lives," write the authors. "Rapid HCV testing can shift valuable resources into client education, counseling, and linkage of care."

According to the New York Department of Health findings, research staff preferred using the rapid swab test as it overcomes some of the challenges with traditional

phelebotomy-based testing in urban outreach testing programs, including reduced risk of needle stick injury, improved patient tracking with immediate results, and potentially expanded testing capabilities even in nontraditional settings.

The test is based on OraSure's OraQuick HCV Rapid Antibody Test for finger stick blood. In February 2011 the OraQuick HCV Rapid Antibody Test received Food and Drug Administration (FDA) approval for use with a finger stick whole blood sample and had previously received approval for venous whole blood specimens in 2010.

The company told analysts on a conference call in August that it has submitted a Clinical Laboratory Improvement Amendments waiver submission for the OraQuick HCV test to the FDA and is working with the FDA to provide additional requested information—a small reproducibility study that is expected to be delivered by early fourth quarter. The company declined to comment on when or if the oral swab test will be submitted to the FDA or be commercially available. The OraQuick HCV test was CE marked in Europe in December 2009 for use with oral fluid, fingerstick whole blood, venous whole blood, serum, and plasma.

OvaGene Set to Launch Series of Predictive, Molecular Gynecologic Cancer Assays

OvaGene Oncology Inc. (Irvine, Calif.), a privately held company specializing in diagnostics for gynecologic cancers, announced earlier this fall that the company has received Clinical Laboratory Improvement Amendments certification for its newly constructed molecular diagnostics laboratory.

With the certification in hand the company in October launched its first proprietary test, EndoGene, for the prediction of recurrence and assessment of drug response in early-stage endometrial cancers. One in five women fails initial therapy, and the company says its prospective study of 1,000 endometrial cancer patients validated that high expression of the proprietary STMN-1 (Stathmin) biomarker is significantly correlated to aggressive carcinoma and a higher recurrence risk and poor disease-specific survival. The assay combines the STMN-1 biomarker with DNA mismatch repair gene status to provide "substantial guidance" for early-stage endometrial cancer treatment. The proprietary technology was initially licensed in July 2010 from researchers at the University of Bergen (Norway).

According to Denise Chua, the company's vice president of clinical operations and marketing, the test will be reimbursed through "standard CPT coding" and the company expects to complete 1,000 tests in its first year.

The company's pipeline is robust with plans to expand its proprietary test offerings with the addition of gene-based profile assays for ovarian and cervical cancers in 2012, Chua says. The OvariGene drug response panel is a molecular assay that identifies chemotherapy resistance in ovarian cancer patients, while the company's third proprietary assay, CerviGene, identifies genes associated with chemo-radiation resistance to platinum agents in women with cervical cancer. This technology was also licensed in July 2010 from Norwegian researchers at Oslo University Hospital.

G2 Index Down 4%, Driven by Illumina's Dramatic Losses

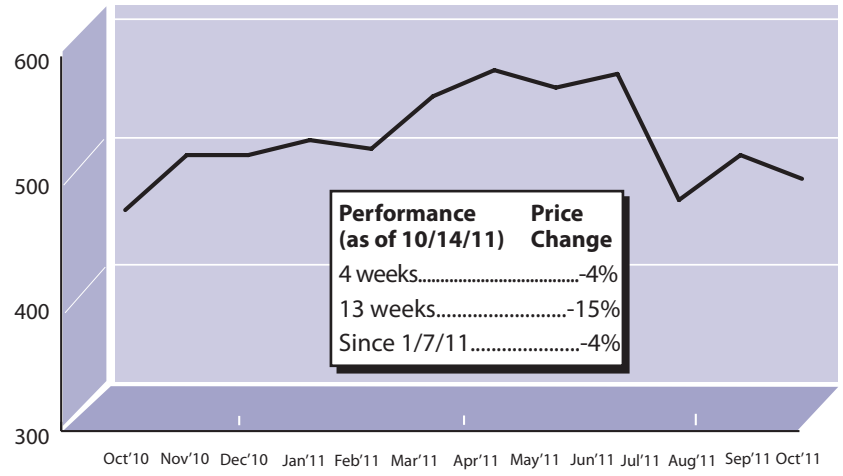
The G2 Diagnostic Stock Index was mixed for the four weeks ending Oct. 14. Despite six stocks that rose in value and two that remained unchanged, the index was driven down 4 percent by nine stocks losing value. The Nasdaq and the S&P remained fairly flat over the same period, gaining 2 percent and 1 percent respectively.

The G2 Index was driven down by **Illumina** (San Diego), which lost 44 percent of its value and ended the period at 26.91, hovering near its 52-week low. Illumina announced a significant shortfall in its estimated third-quarter revenue and suspended its full-year forecast. The company attributed its underperformance to delays in both instrument and consumables purchases resulting from uncertainty surrounding future research funding from the National Institutes of Health.

Alere's (Waltham, Mass.) stock decreased during this period following developments in the company's hostile takeover of **Axis-Shield** (Dundee, Scotland). By mid-October, though, Alere's stock had partially rebounded following news that Axis-Shield accepted Alere's recommended takeover offer following an increase in cash offered. Alere had previously made a hostile bid of 460 pence a share but raised the offer to 470 pence a share or approximately $364 million, ending a four-month takeover battle. According to a Bloomberg report, Alere maneuvered to acquire Axis-Shield for less than analysts estimated the company was worth by buying shares in the open market, discouraging other suitors. Another potential bidder reportedly backed away after Alere said it owned or had agreed to buy as much as 29.9 percent of Axis-Shield's stock, Axis-Shield said Sept. 30.

Cepheid (Sunnyvale, Calif.) is up again this period and is catching the notice of market watchers as a "high momentum" stock. Cepheid's stock is up nearly 105 percent for the past 52 weeks, outperforming the general market for the same period. The company is set to report its third-quarter results later in the month, but it increased its 2011 guidance forecasting $265 million to $270 million in revenue, more than a 25 percent increase over 2010 revenue.

G2 Diagnostic Stock Index



Source: The G2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 17 IVD companies.

Up	Price	% Chg
Abbott Labs	$52.73	1%
Cepheid	40.16	9
IRIS	9.14	5
Luminex	22.48	1
OraSure	9.17	17
Quidel	16.21	5
Unchanged		
Affymetrix	5.43	0
Johnson & Johnson	64.72	0
Down		
Abaxis	24.07	-6
Alere	21.49	-10
Becton Dickinson	74.29	-4
Bio-Rad	94.88	-3
Gen-Probe	57.86	-7
Illumina	26.91	-44
Meridian	16.77	-6
Qiagen	13.41	-7
Sequenom	5.32	-11

G2 Insider

AFIP Closure Puts Access to World's Largest Tissue Repository at Risk . . . The Armed Forces Institute of Pathology (AFIP; Washington, D.C.) shut its doors in September as a result of cost-cutting measures by the U.S. Department of Defense. With a reputation for expert second opinions for difficult cases and the world's largest tissue repository, the closing will affect pathologists around the globe who face potential loss of access to millions of pathology samples acquired over the institute's 150-year history.

The AFIP was established in 1949 as the central pathology laboratory for all branches of the armed forces. The 2005 cost-saving decision to disestablish the AFIP was in part due to the lack of military value of its significant nonmilitary workload. The institute was a resource for civilian clinicians through its publications of the *Atlas of Tumor Pathology* and through consultations, with more than 50,000 requests for second opinions annually, including from clinicians in developing countries lacking pathology expertise. Over the years, the institute accumulated the world's largest tissue repository, with 90 million samples including 55 million glass slides, 31 million paraffin blocks, and more than 500,000 wet tissue samples.

The military will retain its pathology capabilities but under a more targeted mission. The Joint Pathology Center (JPC; Silver Spring, Md.) opened as a pathology reference center that will consult strictly on military cases. But the fate of the institute's famed tissue repository is uncertain. Officials have asked the Institute of Medicine (IOM) to recommend how best to use the repository, including deciding who should have access to it, if clinical samples can be used for research, and if existing or emerging technologies should be considered in developing a plan for utilization of the tissue repository and how this would this affect the mission of JPC.

Given the rare and complex cases that have accumulated in the repository over time, experts say it would be an "incalculable loss" if nongovernment scientists were denied access to the repository and if emerging molecular technologies could not be applied to both the rare and complex cases stored there. The IOM's recommendations are due in June 2012.

Company References

Alere 781-647-3900
American Red Cross 301-738-0600
Association of Public Health Laboratories 240-485-2745
Breath Analysis Program, Cleveland Clinic 216-444-2200
Cambridge Isotope Laboratories 978-749-8000
Centers for Disease Control and Prevention 800-232-4636
Cepheid 408-541-4191
College of American Pathologists 847-832-7000
Department of Health and Human Services 877-696-6775
Illumina 800-809-4566
Joint Pathology Center 301-295-4819
Metabolic Solutions 603-598-6960
National Physicians Alliance 202-420-7896
New York City Department of Health and Mental Hygiene 212-788-4423
OraSure Technologies 610-882-1820
OvaGene Oncology 949-748-6415

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