G2 INTELLIGENCE

Diagnostic Testing &Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

Issue 11-08/August 2011

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Medco Expands Pharmacogenomic Portfolio

Pharmacy benefits management company Medco Health Solutions (Franklin Lakes, N.J.) is continuing in its pioneering efforts to advance personalized medicine and lower health care costs through the use of pharmacogenomics testing.

Last month Medco began offering patients diagnosed with chronic myeloid leukemia a companion diagnostic test, the qRT-PCR BCR-ABL assay offered by Molecular MD (Portland, Ore.), to measure a patient's response or potential resistance to tyrosine kinase inhibitor (TKI) therapy. It is the 10th offering in the DNA Direct by Medco's growing personalized medicine portfolio.

In May the Medco Research Institute announced two pilot programs that evaluate pharmacogenomic testing for common conditions. The Novel Interventions in Methotrexate Boosts Levels of Effectiveness, or NIMBLE, program will help physicians better dose methotrexate (MTX) therapy for rheumatoid arthritis patients using Exagen Diagnostics' (Albuquerque, N.M.) Avise PG lab test.

Medco Research Institute has also partnered with AssureRx (Mason, Ohio) to kick off the Pharmacogenetic-Directed Prescribing of Psychotropic Medications, or PREDICT PSYMEDS, pilot. AssureRx's GeneSightRx test will genotype patients to determine if pharmacogenomic-directed prescribing of anti-depressant and anti-psychotic drugs will improve medication adherence and medical care utilization. For more on pharmacogenomic testing and the GeneSightRx test, please see *Inside the Diagnostics Industry* on p. 5.

Venture Capital Investments Flow Into Molecular Diagnostics

Worries about the economy have not deterred venture capital (VC) firms from steadily investing in molecular diagnostics companies. Many in the investment community believe the broader economic challenges help to showcase the value molecular diagnostic testing brings to the health care system and expect investor interest in the industry to remain high in the coming years.

"Health care costs are escalating and we need a way to control costs, and that is where molecular diagnostics comes in," says Lutz B. Giebel, Ph.D., managing partner, SV Life Sciences (Foster City, Calif.), a VC firm. "If you use a diagnostic to match the patient to the best therapy, it saves time, which benefits the patient, and it saves money because you don't have to do trial and error to treat the patient."

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While generally it has become harder for small companies to secure financing in the past several years, the molecular diagnostics industry has fared fairly well.

"We've seen medical care, health care technology, and other areas slow down, but diagnostics has been fairly resistant and cruised through [the economic downturn] relatively unscathed," says Brian Atwood, managing director, Versant Ventures (Melo Park, Calif.), a health care-focused VC firm.

Making the Right Investment

But investors remain selective in which companies they choose to invest in.

"Molecular diagnostics companies appear to be garnering more attention than traditional diagnostics companies," says Scott Weiner, senior principal, Pappas Ventures, a life sciences VC firm based in Durham, N.C. "We are seeing a lot more business plans for molecular diagnostics companies. I have seen more in the last two years than I saw in the previous 10 years."

Venture capitalists say they are particularly interested in molecular diagnostics companies with strong leadership teams who understand the market and generally have "safe" or "low-risk" technologies, given the inherent risks associated with penetrating the health care market.

"When you get a test result, does it change the way the patient is treated?" asks Giebel of companies he might invest in. "It has got to be actionable. Secondly, it has to be a high-value test. We don't want to have to do a bazillion tests in low margins and have a huge company with a big number of sales reps."

High-value areas like cancer and fertility, where there is a willingness to pay for testing, are also attractive investments. In early July Allegro Diagnostics (Maynard, Mass.) closed a $5.4 million Series A financing extension. Proceeds will support the 2012 commercialization of Allegro's BronchoGen test for early detection of lung cancer. In late June Atossa Genetics (Seattle) announced the completion of an oversubscribed round with proceeds of $6.6 million. Financing will be used to commercialize the Mammary Aspirate Specimen Cytology Test (MACST) System.

The Future

"The market is waiting to see how molecular diagnostics settles in and matures as a real business," says Atwood. "Other companies coming along [after Genomic Health] will mature in the next two to three years and they will need to demonstrate they can generate information that is really important and generate savings for payers and the health care system. Venture business is driven by current success; if we see a cluster hit real revenue success . . . in three, four, five years we will see a lot of entrepreneurial interest–we'll see a pop."

Experts say the diagnostics industry will remain "quite active" in the next three to five years with consolidation expected in the industry. Large clinical reference labs, pharmaceutical companies, and traditional diagnostic equipment and reagent manufacturers are all considered potential acquirers.

Potential acquirers are all trying to get their arms around the diagnostics business, says Atwood. "It is more complicated than traditional diagnostics. Fundamentally, biomarkers are a new thing to productize."

Other diagnostics companies have recently closed additional financing rounds:

- HTG Molecular Diagnostics (Tucson, Ariz.) closed $16.2 million in its Series D financing round in June.
- Stratos Genomics (Seattle) announced in early June $2.1 million of funding that was provided by existing shareholders as an "up round" to the company's August 2010 $4 million Series A round.
- CardioDx (Palo Alto, Calif.) closed a $60 million series E round in May.

AMH Hormone Levels Predict IVF Outcome

Serum concentration of antimüllerian (AMH) hormone can predict both oocyte number and the likelihood of pregnancy in in vitro fertilization (IVF) patients, according to results of a study published in the July issue of the *American Journal of Obstetrics and Gynecology*. The findings can aid in counseling IVF patients about the likelihood of a successful outcome and may provide feedback to allow physicians to modify treatments midcycle.

Researchers at Women and Infants Hospital (Providence, R.I.) studied 190 IVF patients at onset of follicle-stimulating hormone treatment. Patients with initial AMH concentrations of 3ng/ml or more produced a mean of 20 oocytes and had a pregnancy rate of 60 percent, as compared to those with AMH values of 1ng/ml or less, who yielded a mean of six oocytes and had a pregnancy rate of 23 percent. AMH was superior to age and follicle-stimulating hormone (FSH) in predicting the probability of pregnancy.

Andrew Blazar, M.D., the study's lead author, says that while the data from the test are clear, the practical application of the data is not yet established. While it makes "good sense" that the data can be used to adjust medication levels to improve IVF outcomes, Blazar cautions this remains unproven. He hopes that that research will be conducted in the future so as to "accelerate the usefulness" of the AMH test.

Conventional testing uses baseline endocrine studies including measurements of FSH and estradiol. AMH is a unique biomarker in that its level is largely unaffected by the menstrual cycle and can be measured anytime. Blazar says this is a convenience for both the physician and the patient.

"If you use the test to exclude patients with low AMH from treatment, that is a misinterpretation of the data," says Blazar, a clinical associate professor of obstetrics and gynecology at the Alpert Medical School at Brown University. "I think the usefulness of the data is that it helps physicians and patients have a realistic expectation of outcomes of the cycle."

The research was partially sponsored by Beckman Coulter (Brea, Calif.), the maker of the AMH assay.

Endocrine Society Issues Vitamin D Guidelines

In newly released clinical practice guidelines the Endocrine Society recommends against populationwide vitamin D screening in favor of testing only those at risk for vitamin D deficiency. The guidelines for the evaluation, treatment, and prevention of vitamin D deficiency are published in the July issue of the society's journal, *Journal of Clinical Endocrinology & Metabolism*.

"At the present time, there is not sufficient evidence to recommend screening individuals who are not at risk for deficiency or to prescribe vitamin D to attain the non-

calcemic benefit for cardiovascular protection," said Michael F. Holick, M.D., Ph.D., of the Boston University School of Medicine and chair of the task force that authored the guidelines, in a statement.

The task force said that measurement of serum circulating 25-hydroxyvitamin D [25(OH) D] level is the best indicator of vitamin D status and should be the initial diagnostic test in at-risk patients. Serum levels of 1, 25 di-hydroxyvitamin D should only be used for monitoring acquired and inherited disorders of vitamin D and phosphate metabolism.

While controversy remains regarding recommended dietary allowances of vitamin D and target serum levels for noncalcemic health benefit, the task force recommends minimum 25(OH)D serum levels of 30 ng/ml, slightly higher than the 20 ng/ml to 30 ng/ml range established for the general population by the Institute of Medicine last year, a level many experts believed was too low.

All methodologies for vitamin D measurement (RIA, HPLC, and liquid chromatrography tandem mass spectroscopy) are adequate using a 40ng/ml cutoff to ensure that the patient's "true" value is greater than 30ng/ml, the study authors say. Implementation of uniform standards established through the National Institute of Standards and Technology will minimize variability in the future.

More Frequent HIV Testing in MSM Might Be Warranted

Adherence to annual HIV testing recommendations for men who have sex with men (MSM) is low, and a substantial proportion of men who reported being tested during the past 12 months were newly infected. According to the Centers for Disease Control and Prevention (CDC) researchers whose study was published in the June 3 issue of *Morbidity and Mortality Weekly Report*, increasing the frequency of recommended HIV testing in all MSM may be warranted.

The data from the 2008 National HIV Behavioral Surveillance System in 21 U.S. cities show that among the 7,271 MSM included in the analysis, 61 percent had been tested for HIV during the past year, but 7 percent were newly HIV-infected. Of those newly infected men, 16 percent had never been tested for HIV, and 29 percent had been tested during the past six months.

Currently the CDC recommends HIV testing at least annually for sexually active MSM, and CDC guidelines recommend that MSM who engage in high-risk behavior, including having multiple or anonymous partners, having sex in conjunction with illicit drug use, using methamphetamines, or whose sex partners participate in these activities be screened for sexually transmitted diseases and HIV more frequently—every three to six months.

Among the 81 percent of MSM reporting high-risk behaviors, less than half (44 percent) had been tested for HIV infection during the past six months. But the findings show that those men who engaged in high-risk behaviors were not more likely to be newly infected.

Given the high prevalence of new HIV infection among MSM who had been tested during the past year, all sexually active MSM might benefit from HIV testing every three to six months, the authors propose. In considering revising guidelines to increase testing frequency among MSM, the authors write that public health officials need to weigh the acceptability and cost-effectiveness of testing MSM more frequently and the sensitivity of tests in the early stages of infection. MSM remains a key population for expanded HIV testing efforts.

G2 INTELLIGENCE
Inside the Diagnostics Industry

Pharmacogenomic Testing Set to Enhance Psychiatric Drug Prescribing

James Burns, CEO

The National Institute of Mental Health reports that nearly one in four adults suffers from a diagnosable mental disorder each year, with 6 percent of Americans living with a serious mental illness. Many are not helped by medication. Of the 27 million Americans taking anti-depressants, more than half fail to achieve remission and more than 10 percent will experience significant adverse drug reactions. Of patients prescribed anti-psychotic medications, more than half will discontinue the medication within the first six months of treatment due to drug side effects.

There is increasing interest in the use of pharmacogenomic testing to improve the treatment of psychiatric patients. GeneSightRx is a laboratory-developed pharmacogenomic test offered by AssureRx (Mason, Ohio). From a cheek swab, the test can provide psychiatrists important information about the patient's ability to tolerate or effectively respond to certain psychotropic medications, thereby aiding the physician in choosing the most appropriate medication for the patient. The test was initially launched in 2010 but has been upgraded this year to assess variations in six genes including the much studied CYP2D6 and CYP2C19 genes.

According to the Mayo Medical Laboratories many anti-depressants and anti-psychotics are metabolized by the CYP450 enzymes, which are encoded by the CYP2D6 gene. CYP2D6 polymorphisms that produce poor metabolizers are found with frequencies of 7 percent to 10 percent in Caucasians, 2 percent in Africans and African Americans, and 1 percent in Asians. It is estimated that more than 15 million American are poor metabolizers of 2D6 substrates. The CYP2C19 enzyme is responsible for metabolizing drugs for anxiety. Poor metabolizers are found in 2 percent to 5 percent of Caucasians, 4 percent of African Americans, and 13 percent to 23 percent of Asians.

The test is gaining recognition in the field, and AssureRx has recently initiated a pilot program with Medco (Franklin Lakes, N.J.) to evaluate the clinical impact of the GeneSightRx test. *DTTR* recently spoke to James Burns, president and CEO of AssureRx, to learn more about the test and the future impact pharmacogenomics testing will have in psychiatric patient populations.

In February AssureRx announced the expansion of the GeneSightRx test. Can you tell us about the expansion and about future plans to expand the test further?

The GeneSightRx test basically reads a number of pharmacokinetic genes—right now four pharmacokinetic genes that relate to how patients metabolize medications primarily through the liver, and then we have two pharmacodynamic genes, the serotonin transporter and serotonin receptor. What we basically do is look for polymorphisms in an individual based on those genes.

We do a multivariate analysis of six genes and 50 polymorphisms of those genes and come down to what we call combination phenotypes. These are the functional implications of those genotypes. We then take those functional phenotypes and array them against 26 Food and Drug Administration-approved anti-depressants and anti-psychotics. The algorithm looks through about 40,000 different drug pos-

sibilities for the particular patient based on their genetic profile. It comes down to a report on an individual patient of which medications are likely to work and which ones are not. At the present time, because we have four pharmacokinetic genes (the newly addedCYP2C9 gene, as well as the CYP2D6, CYP2C19, and CYP1A2 genes), the product is more oriented to safety. We are looking at those medications less likely to cause adverse drug reactions.

We are likely going to add another gene this year, and we will certainly be adding additional polymorphisms into the algorithm. In the next six months, we will be adding several additional drugs based on recent approvals by the FDA, still concentrating on anti-depressants and anti-psychotics.

Medication compliance is notoriously difficult in psychiatric patient populations. How will this test help to improve compliance issues?

As a matter of fact, adverse drug reactions are the principle reason for noncompliance of psychotropic medications. By reducing or cutting down the probability that a drug that will generate an adverse drug reaction, we think compliance will increase. That is one of the principle objectives of our study with Medco. By getting patients on a pharmacogenomic-directed set of medications, the adherence should increase because the adverse drug reactions should decrease.

AssureRx at a glance

- Headquarters: Mason, Ohio
- Total Number Employees: 30
- Total Capital Raised to Date: $18 million
- Year of GeneSightRx Commercialization: 2010
- Number of Drug Combinations Tested for: 40,000

The second principle objective is to look at a reduction in medical utilization. As a result of increased compliance, there should be fewer visits to psychiatrists' offices, fewer visits to emergency departments, and so on. Hopefully, we can track with the members increased productivity or less work absenteeism. Medco is the largest study we are doing. But we are also conducting or sponsoring both retrospective and prospective studies to verify clinical utility for patients and to look at downstream economic benefits.

Getting physicians to adopt pharmacogenomic tests is often a challenge. How has the reception been among psychiatrists?

We were concerned about that when we were working on the commercial release plan. But since we launched the product we have talked to literally hundreds of psychiatrists and the receptivity to having an evidence-based, objective tool to increase the probability of getting patients on to the right medications earlier has been accepted tremendously. There has been a lot of enthusiasm out there for it. Psychiatrists have uniformly told us that they had hoped someday that some technology would be available to increase the probability of better prescribing. They thought it might be five to 10 years away and in many cases are surprised it is already here.

How will pharmacogenomic testing have changed the field of psychiatry in the next five years?

Five years out we think that psychiatric pharmacogenomics will become routine practice. It will be incorporated into clinical guidelines and there will be a number of institutions that will adopt it as the standard of care by then.

Liquid-Based Cytology Overtakes Conventional in Pap Screening

A national survey recently confirmed that liquid-based cytology (LBC) has replaced conventional cytology as the most widespread cervical cancer screening method used by office-based physicians. Data from the National Ambulatory Medical Care Survey, conducted by the Centers for Disease Control and Prevention (CDC), revealed that of the 26.2 million cytology screenings performed from 2006 to 2007, LBC was used in three out of four Papanicolaou (Pap) tests ordered. The findings were published in a newly released National Health Statistics Report.

"The United States, as a country, likes new technology and likes to use it fast," says Mona Saraiya M.D., a medical officer in the Division of Cancer Prevention and Control at the CDC. "Liquid-based testing has so much market penetration. There are still places where the conventional method is being used more in certain populations where cost is a concern. Sometimes market penetration trumps cost and science."

Ob-gyns were significantly more likely to order LBC than other primary care physicians. Given the added expense of LBC tests, it was not surprising that the researchers found that community health centers ordered significantly fewer LBC tests than physician- and group-owned practices.

Saraiya tells *DTTR* that it is unclear what the 2010 data will show. "Colleagues of mine in the clinical world said [the data] was lower than they thought. But others think because of the economic crisis those programs concerned with cost containment might be using the traditional method more, so we just don't know," she explains.

While comparable in their ability to detect cervical cancer, LBC does offer the advantages of facilitating human papillomavirus (HPV) cotesting on the same cervical sample.

"They are feeding into each other. Liquid-based testing is so popular and because of that, HPV testing is more convenient," says Saraiya. "In Europe hardly any country is doing cotesting. There is a big contrast between the United States and Europe where national screening programs are based on randomized clinical trials and cost-effectiveness data." For more on trends in HPV testing, see *G2 Insider* on p. 12.

Inconsistent Newborn Blood Spot Policies Give Rise to Public Mistrust

Recent lawsuits and public concerns over the storage and use of residual dried bloodspots (DBS) from newborn screening programs (NSP) have revealed gaps in state laws and public policy over the storage and use of these specimens.

Of the five spots of blood collected for the screening, typically only two DBS are needed for routine testing, leaving several unused spots. Historically, one spot is saved for the family and other samples have been stored and used for quality assurance and quality improvement purposes. But advances in genome sequencing have greatly piqued researchers' interest in the residual DBS while an increasingly distrustful public has questioned states' right to retain a child's DNA.

In Minnesota families alleged the storage and use of newborn blood spots (NBS) violated the state's Genetic Privacy Act. A lower court and appeals court ruled the act was not applicable to the NBS program, so the case is headed to the Minnesota Supreme Court. In Texas families sued the Texas State Department of Health claiming that storage and use of NBS amounted to unlawful search and seizure. The case was settled but required the state to destroy more than 5 million residual DBS.

"I think the distrust has a more nebulous root more than anything the public health department has done," says Beth Tarini, M.D., an assistant professor of pediatrics at the University of Michigan School of Medicine. "Some individual programs may have made some missteps, but to some degree the newborn screening programs are caught in a greater political battle."

"Some individual programs may have made some missteps, but to some degree the newborn screening programs are caught in a greater political battle."
– Beth Tarini, M.D.

In an attempt to beef up policies, the U.S. Department of Health and Human Services' (HHS) Advisory Committee on Heritable Disorders in Newborns and Children issued a briefing paper to provide national guidance to states for storage and use of DBS. In the paper the group urges that in addition to traditional NBS uses, policies should focus on "protecting privacy and confidentiality and ensuring the public's trust while recognizing the value of residual newborn screening specimens and their potential for advancing science and clinical care."

Newborn screening is considered a highly successful public health program that identifies rare genetic, congenital, and functional disorders. While mandatory, program design is left up to each state to implement, which has created a lack of uniform policies surrounding the handling of DBS.

In the April issue of *Pediatrics* researchers published results of an evaluation of state DBS policies. The authors found that 18 states fail to address the retention or use of NBS. Only eight states require that parents be provided information about the retention of DBS, and in five states parents may request the destruction of their child's sample. One state prohibits DBS from being used for research purposes.

The HHS group recommends states establish policies, educate both families and health professionals about the NBS program and about potential uses for DBS, and says that HHS should explore the utility and feasibility of establishing a voluntary national repository for DBS.

In a commentary piece published online ahead of print in the journal *Genetics in Medicine*, Tarini says that states need to allow parents a choice in whether their child's blood spot is used for research that is not directly related to quality improvements of the existing tests with NBS programs.

"I don't endorse in-depth informed consent. It is not a workable solution to parent permission. But not engaging the parents is not workable from a public policy perspective," Tarini tells *DTTR*. "In the middle ground parents are made aware of the process in general and at the end of the day parents elect whether the spot is used. It is not perfect, but it brings awareness, transparency, and dialogue but not a laborious permission process."

Saliva PCR Assay Effective for CMV Screening in Newborns

Researchers found real-time polymerase-chain reaction (PCR) assays of both liquid- and dried-saliva specimens showed high sensitivity and specificity for detecting cytomegalovirus (CMV) infection in newborns and say they should be considered as potential tools for widespread screening of CMV in newborns. The research appeared in the June 2 issue of the *New England Journal of Medicine*.

The investigators compared real-time PCR assays of liquid-saliva and dried-saliva specimens to rapid culture testing of saliva specimens. Widespread CMV testing is not in place because rapid culture testing cannot be automated and PCR of dried blood spots has proven unreliable in trials.

A total of 177 of nearly 35,000 infants (0.5 percent) tested positive for CMV. While the dried samples had a slightly lower sensitivity than liquid samples (97.4 percent vs. 100 percent), the authors contend that dry samples may be the best option for wide-scale screening because of added collection, storage, and transport efficiencies.

"We now know that we have a test with saliva that works," said lead author Suresh Boppana, M.D., a professor of pediatrics at the University of Alabama. "The challenge is, unlike the dried blood spot, which is already used for newborn screening in hospitals across the country, we don't have a system in place for the collection of saliva. But we've shown that if you wanted to test a lot of babies for congenital CMV infection, it can be done."

CMV is the most common infection passed from a mother to her unborn child. Of the 20,000-30,000 infants who are born infected with CMV each year, roughly 10 percent to 15 percent are at risk for developing hearing loss, but most infected babies don't show symptoms at birth.

Sixteen additional samples tested positive using the PCR assay but not for the rapid culture. Follow-up testing revealed that three of these samples were indeed positive, leading the researchers to conclude that PCR may be superior to rapid culture. CMV is occasionally shed in the genital tract of seropositive women at delivery and in breast milk. The false positive results could be due to CMV-contaminated maternal secretions present in the infants' saliva samples. The overall frequency of false positive results for saliva-based assays was less than 0.03 percent.

Patent Reform Passes the House; Patentability to Be Debated at the Supreme Court

Lingering uncertainty surrounding patent regulation continues to plague the diagnostics industry even as patent reform cleared the U.S. House of Representatives and a prominent patent case officially heads to the U.S. Supreme Court.

The America Invents Act passed the House (H.R. 1249) with bipartisan support in late June. Patent reform previously passed the Senate (S. 23) in the spring. If signed into law, the bills' key provisions would change the U.S. patent system from "first to

invent" to "first to file" and would create a post-grant review and opposition system. The bills differ in distribution of the revenues from patent fees. With debate over the debt ceiling dominating legislative efforts this summer, it is unlikely that patent reform will be re-examined before Labor Day.

"I don't see patent reform as having much effect in the diagnostics industry because it does not change what is patentable," explains John Conley, Ph.D., William Rand Kenan Jr. Professor of Law at University of North Carolina at Chapel Hill. "In general, though, the change to first to file favors bigger companies that have the resources to file right away."

Patentability Heads to the Supreme Court

But, in a surprise move that could have important ramifications for defining patentability for the diagnostics industry, the Supreme Court agreed to hear the case *Prometheus vs. Mayo* this fall.

> ***"Whatever disadvantage there is to incrementally narrowing what is patentable will be offset by the benefits of certainty. There is a cost to uncertainty now. I bet in the diagnostics industry they are willing to trade some scope of patentability for some certainty."***
>
> ***– John Conley, Ph.D., William Rand Kenan Jr. Professor of Law UNC – Chapel Hill***

At issue in the *Prometheus* case is whether or not a method for administering a drug (thiopurine drugs used to treat gastrointestinal and other autoimmune diseases), measuring that drug's level in a patient's body, and appropriately adjusting the dosage of the drug, is in fact patentable. In its petition to the Supreme Court the Mayo Clinic argued that "the case concerns whether a patentee can monopolize basic, natural biological relationships."

In 2009 the Federal Circuit ruled that the claimed methods sufficiently transformed the body, satisfying the machine-or-transformation (MoT) test and were patentable. The Federal Circuit was asked to re-examine the *Prometheus* case in light of the Supreme Court's 2010 *Bilski* ruling on methods patents which said that MoT was not the exclusive test for evaluating methods patents.

"The Federal Circuit gave the legal equivalent of five minutes to do this and came to the same result that the machine-transformation test was still useful," Conley tells *DTTR*. "At least four justices were put out that the Federal Circuit was very quick and superficial and didn't give the case the serious reconsideration that the Supreme Court had in mind."

Conley, who is also of counsel at the law firm Robinson Bradshaw (Charlotte, N.C.), says he hopes the Supreme Court will use the case to clarify medical methods patentability.

"Whatever disadvantage there is to incrementally narrowing what is patentable will be offset by the benefits of certainty," says Conley. "There is a cost to uncertainty now. I bet in the diagnostics industry they are willing to trade some scope of patentability for some certainty."

The outcome of the *Prometheus* case, which is not expected until next summer, is likely to ultimately affect the methods patents portion of Myriad Genetics' (Salt Lake City) much-watched pending litigation.

IVD Stocks Up Slightly, Driven by Acquisitions

The G2 Diagnostic Stock Index was up slightly, just 1 percent for the four weeks ending July 15, with 14 stocks up in price, three down, and one unchanged. Both the Nasdaq and the S&P 500 outperformed the G2 Index, with the Nasdaq increasing by 7 percent, and the S&P 500 increasing by 4 percent.

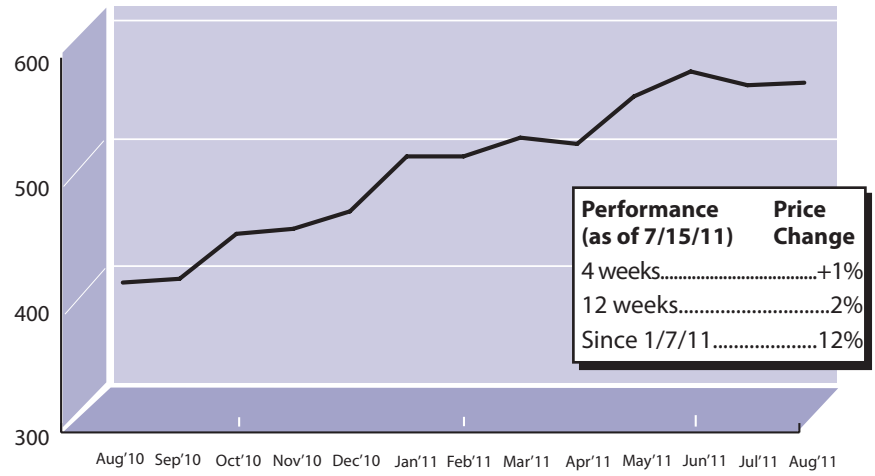
Danaher Corp. (Washington, D.C.) completed its acquisition of **Beckman Coulter** (Brea, Calif.) on June 30. As a result, Beckman Coulter is no longer traded on the New York Stock Exchange and has been removed from the G2 Stock Index.

Two of the largest stock gains for this period resulted from acquisition news. **Immucor** (Norcross, Ga.) stock soared 37 percent to a closing price of $26.87 per share on the news that the company entered into a definitive agreement to be acquired by TPG Capital (Fort Worth, Texas), one of the world's largest private equity investment firms. The transaction, which is expected to close in the second half of the year, has a fully diluted value of $1.97 billion. Immucor shareholders will receive $27 in cash for each share of common stock, a premium of approximately 30 percent over the closing share price on July 1, 2011, the last full trading day before the announcement.

Luminex (Austin, Texas) announced the completion of its acquisition of **EraGen Biosciences**, (Madison, Wis.) for $34 million in cash. Luminex expects the EraGen acquisition will add between $5 million and $7 million to 2011 consolidated revenue but expects the acquisition to be dilutive in 2011 and accretive to earnings in 2012. EraGen develops, manufactures, and markets molecular reagent products.

While final results won't be announced until the end of July, **Affymetrix** (Santa Clara, Calif.) declined 9 percent based on reports of what the company called "disappointing" preliminary second-quarter financial data. The company expects total revenue for the second quarter of 2011 to be in the range of $64 million to $65 million, with consumable sales of approximately $55 million, which are down about 10 percent from the previous year. G2

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 18 IVD companies.

Up	Price	% Chg
Abbott Labs	$53.04	3%
Abaxis	28.86	5
Alere	36.95	4
BectonDickinson	87.09	2
Bio-Rad	118.37	1
Illumina	72.82	2
Immucor	26.87	37
IRIS	10.28	8
Johnson & Johnson	67.45	2
Luminex	20.68	10
Meridian	26.57	11
OraSure	9.82	20
Quidel	15.67	3
Sequenom	7.55	3
Unchanged		
Cepheid	32.09	0%
Down		
Affymetrix	6.45	-9%
Gen-Probe	63.83	-6
Qiagen	18.28	-4

G2 Insider

HPV Testing Soars as Does Questionable Usage . . . The rate of human papillomavirus (HPV) testing has soared in recent years, but not everyone is convinced that's a good thing.

According to Dan Leonard of investment firm Leerink Swann, sales of HPV tests nearly tripled from $120 million in 2005 to $350 million in 2009. HPV testing growth is expected to remain in the double-digits for the next few years, Leonard predicts, with existing manufacturers (Qiagen, Hologic, and Roche) trying to expand market penetration and others (Gen-Probe) hoping to enter the market.

But some policy experts say the growth of HPV testing is coming at great expense to the greater health care system and believe that a critical examination of HPV testing is warranted given the inconsistencies between recommended guidelines and actual practice.

High-risk HPV (HPV DNA) testing has been used since the early 2000s as a reflex test following an abnormal Papanicolaou (Pap) test and can provide greater sensitivity in detecting precancerous lesions. But an analysis of self-reported testing practices by Pap providers published in July in *Obstetrics & Gynecology* highlights the widespread inappropriate use of HPV testing:

- 47 percent of providers used HPV test with Pap test for routine cervical cancer screening (cotesting);
- 60 percent used cotesting in women younger than 30 years old, a doubling of 2004 levels; and
- Despite no clinical indications for low-risk HPV testing, nearly one-third report using low-risk testing.

The researchers suggest removing low-risk HPV testing from the U.S. market, educating providers about extending screening intervals, and implementing reimbursement interventions as necessary to encourage guideline-consistent test use.

"Cotesting in the U.S. could be transitory," says Mona Saraiya, M.D., a medical officer at the Centers for Disease Control and Prevention. "As more data emerges, HPV could become a primary screen, but the FDA has not approved HPV as a primary test yet. [However] the evidence and guidance is moving in that direction." G2

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 Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by G2 Intelligence, 1 Phoenix Mill Lane, Fl. 3, Peterborough, NH 03458-1467. Tel: 800-401-5937. Fax: 603-924-4034. Web site: www.G2Intelligence.com.

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