G2 INTELLIGENCE

Diagnostic Testing & Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

Issue 12-03/March 2012

CONTENTS

www.G2Intelligence.com

New Technology Behind Rise of Noninvasive Tests

C8 MediSensors (San Jose, Calif.) has broken its eight-year silence with announcements that it closed a $24 million round of financing in December and launched its Web site revealing its noninvasive continuous glucose monitor (nCGM). New investors, including GE's Healthymagination Fund, participated in the raise, which will accelerate the company's planned product launch in 2012.

The device requires no consumables and measures blood glucose levels through an optical technique called Raman spectroscopy. A small portion of incident light causes glucose molecules to vibrate, scattering light with distinct color patterns. This unique spectral "fingerprint" can be used to noninvasively measure how much glucose is present beneath the skin. The 5-ounce device is worn around the abdomen, underneath clothing, and transmits glucose values via Bluetooth to a smartphone or other compatible device.

The HG1-c nCGM is still an investigational device. The company plans to receive CE regulatory approval and launch the product in Europe in the first half of 2012. The list price for the device is $4,000 with an expected four-year minimum life span. By comparison, typical finger stick monitoring runs Type 1 diabetics about $3,650 per year, says Doug Raymond, vice president of marketing. Early adopters in the patient community will be able to purchase the device online. The medical community has expressed interest in the device too, both as a surgical monitoring tool and as a prediabetes diagnostic tool, much like a Holter monitor is worn to make cardiology diagnoses. For more on the rise of noninvasive diagnostic testing technologies, please see *Inside the Diagnostics Industry* on page 5.

Roche Extends Hostile Takeover Bid for Illumina

The battle lines are drawn as Illumina (San Diego) says it will "vigorously resist" Swiss drugmaker Roche's unsolicited $5.7 billion hostile takeover attempt, which Illumina characterized as "grossly inadequate."

Roche offered to pay $44.50 per share when it launched a public bid for Illumina Jan. 25 but on Jan. 3 had quietly made an initial bid of $40 per share. On Feb. 7 Roche reiterated that it believed its offer was "full and fair" and that it was ready to start discussions with Illumina, following a unanimous rejection of the offer by Illumina's board the same day.

"It is the Board's unanimous belief that Roche's offer dramatically undervalues Illumina and fails to reflect the value of the Company's unique leadership position and future growth prospects," said Jay Flatley, Illumina's CEO, in a statement.

Continued on p. 2

▲ **Roche Extends Hostile Takeover Bid for Illumina,** *from page 1*

While scientific hope is high over the prospects of clinical adoption of genome sequencing technologies, tools companies' shares have plummeted over the last year because their customer base relies on researchers dependent on government grants. Sagging share prices are making Illumina and other players in the space vulnerable to buyout bids, analysts say. Illumina, whose shares dropped dramatically from an all-time high of $79.40 in July 2011 to $37.69 Jan. 24, called the timing of the offer "blatantly opportunistic."

In response, Illumina adopted a "poison pill" defense strategy in which shareholders will receive one preferred stock purchase right as a dividend for each common share held as of the close of business on Feb. 6. If Roche or another bidder owns 15 percent or more of Illumina's stock, current shareholders will be able to exercise the rights to buy new common stock at half the market price, diluting the stake of the prospective bidder.

While analysts expect the negotiations to drag out, they take Roche's statement that it is ready to commence discussions as a signal that the company will pay more than what is currently offered. Many believe Roche will have to raise its bid to around $60 per share to win over Illumina. There is also speculation that Roche's bid may spark additional deals in the DNA sequencing space as Roche's offer signals major pharmaceutical companies' acknowledgement that DNA sequencing is pivotal to the future of diagnostics and treatment decisions. Roche is the world's biggest developer of cancer medicines and has extensive experience with gene-targeted therapies.

Sequenom Lawsuits Open New IP Battlefield, May Be Impacted by Rulings in *Prometheus* Case

The battle over diagnostics-related patents shows no signs of letting up as there was a flurry of lawsuits and countersuits filed in January involving Sequenom (San Diego), Aria Diagnostics (San Jose, Calif.), and Natera (Redwood City, Calif.).

"What drives the amount of filings is the value of the patents," says Jonas Anderson, an assistant law professor at American University (Washington, D.C.). "The real driver is money. If money is undergirded by patents, then lawyers and companies will continue to fight."

Sequenom sued both Aria Diagnostics and Natera on Jan. 24, saying that the companies' noninvasive prenatal test and paternity tests infringe on a patent exclusively licensed to Sequenom (U.S. Patent No. 6,258,540). The "540" patent, as the company refers to it, involves researcher Dennis Lo's discovery of fetal DNA in maternal blood. Preemptive complaints were filed by Aria and Natera earlier in January requesting judgment that their respective tests do not infringe Sequenom's patent and alleging that Sequenom has "misrepresented" the scope of its patent.

"The T21 market is the wild, wild West," says Junaid Husain, who follows Sequenom as a senior research analyst at Dougherty & Co. "Sequenom is sitting on a $140 million cash balance and they'll use it offensively to try to squeeze out the other companies

and they will hire very good lawyers." Husain says the estimated $1 million to $2 million in annual legal fees is "immaterial" to the company's well-being.

"With verbs like 'determining' [in the 540 patent], I can't tell how judges will rule. These are the kinds of claims courts are struggling with in methods claims," says Robert Cook-Deegan, M.D., director for genome ethics, law, and policy at Duke University in Durham, N.C. "The methods claims in the *Myriad* case were thrown out because of use of a general verb like 'comparing.' If they had used verbs like 'extract,' 'determine,' and then 'compare,' it might have passed the test."

Legal experts say that while the Sequenom lawsuits represent a "new front" in intellectual property battles, new jurisprudence resulting from existing cases winding their way through the courts may offer improved guidance with which to evaluate diagnostics patent disputes. Other than hoping that impending rulings can provide some legal clarity, legal experts offer no consensus in predicting how the two most prominent diagnostics cases, involving Myriad and Prometheus, will ultimately turn out.

On Dec. 7 the U.S. Supreme Court heard oral arguments in the *Prometheus* case, and the legal and diagnostics communities are awaiting a ruling, possibly in late February, which may clarify the issue of patentability of diagnostics methods.

"Use of ambiguous words in methods patents like 'analyzing,' 'determining,' and 'comparing' can describe abstract thought or mental processes, rather than methodological steps," says William Warren, a lawyer at Sutherland Asbill & Brennan in Atlanta. "Big things are coming down the pipe. We are hopeful the Supreme Court will clarify the line between preempting laws of nature versus sufficiently additional activity applied to nature to qualify for a patent." G2

Noninvasive Prenatal Diagnostic Test Developments

The Sequenom Center for Molecular Medicine announced Feb. 8 that it expanded the recently launched MaterniT21 laboratory-developed test and rebranded the test MaterniT21 PLUS, indicating the added ability to detect trisomies 18 (T18) and 13 (T13). Validation of the expanded test was published online in February in *Genetics in Medicine*. The massively parallel shotgun sequencing test for the three aneuploidies had an overall detection rate of 98.9 percent. The three false negatives (out of 283 cases) included two Down syndrome (T21) and one T13 pregnancy. The corresponding false positive rate was 1.4 percent, but the researchers say that most of these could be avoided by slightly raising the z-score cutoff levels for T18 and T13.

Aria announced on Feb. 6 the name of its noninvasive prenatal test, Harmony Prenatal Test, which couples a biochemistry innovation called DANSR (Digital Analysis of Selected Regions) and a proprietary algorithm called FORTE (Fetal-fraction Optimized Risk of Trisomy Evaluation) to analyze cell-free DNA in maternal blood samples to detect T21 and T18. The FORTE algorithm incorporates the results of the DANSR assay, the percentage of fetal DNA in the patient's sample, and clinical information such as the maternal age to provide a risk score for each patient. Validation results were published in two separate articles in the *American Journal of Obstetrics & Gynecology* online Jan. 24 and Jan. 25, respectively. The first article, an independent study, showed the test had 100 percent sensitivity for detecting T21 and 98 percent sensitivity for T18. The specificity was 100 percent.

Companies Strengthen Positions With New Patents

While patent-related legal challenges continue to unfold in U.S. courts, several new diagnostics-related patents have been issued in the past month.

Seegene (Gaithersburg, Md.) was awarded a patent for its Dual Priming Oligonucleotide (DPO) technology in mid-January, strengthening the company's intellectual property position in multiplex molecular diagnostics (M-MoDx). DPO-based tests allow for the simultaneous detection of multiple targets with consistently high specificity, the company says, using a mechanism involving two functional priming regions separated by the polydeoxyinosine linker. DPO has two functional priming regions – a longer one and a shorter one. The longer segment preferentially binds to the template DNA and acts as a stabilizer. The short segment selectively binds to a target site and acts as a determiner. These two unequally distributed priming regions result in only target-specific products. DPO technology is adaptable to all platforms and is currently used for gel-based detection, capillary electrophoresis based, real-time polymerase chain reaction-based, and chip-based assays. Seegene says its DPO-based M-MoDx assays are used in more than 300 hospitals and laboratories in 50 countries to detect and differentiate infectious diseases, sexually transmitted infections, and tuberculosis. DPO technology previously received a European patent in October 2011.

Microsample collection testing company Advance Dx (Chicago) was issued a patent for its ADx 100 serum separating blood collection card in mid-January. The Advance Dx 100 card collects, stores, and transports microsample blood specimens but uses an alternative collection method, similar to a serum-separating tube, which separates red cells from the serum without the need for centrifuging, reducing the laboratory's preparatory burden and enabling the more rapid turnaround of test results. This technology enables laboratories to perform serum-based tests without red cell contamination while using a dry blood collection format. No special analyzer is required and the ADx100 collection card requires no special handling and has a shelf life of five years. Once dry, the AdvanceDx100 samples are stable and the company says specimens can be processed up to 28 days following collection. Using a sample from either a professional or patient-collected finger stick, the ADx 100 card can run eight diagnostic tests, including a lipid panel with a fasting glucose, vitamin D, testosterone, prostate specific antigen, thyroid stimulating hormone, hemoglobin A1c and high-sensitivity C-reactive protein, the company says.

Myriad Genetics (Salt Lake City) in mid-January secured an exclusive license to the RAD51C gene and its association with an increased risk for hereditary breast and ovarian cancers. RAD51C was identified initially as a susceptibility gene for hereditary breast and ovarian cancer by members of the German Consortium for Hereditary Breast and Ovarian cancers. Papers published in *Nature Genetics* in (April 2010) and *Breast Cancer Research and Treatmen*t (May 2011) found a mutation in the RAD51C gene prevalent in patients with a family history of these cancers. The two studies demonstrate a RAD51C mutation prevalence between 1.3 percent and 2.9 percent in that population. The agreement grants Myriad the exclusive, worldwide license, with coexclusivity in Germany, to provide commercial testing for RAD51C.

G2 INTELLIGENCE
Inside the Diagnostics Industry

Saliva Tests May Be Moving Toward Clinical Adoption, Though Verdict Still Out on Noninvasive Diagnostics

The combination of patient preference for nonpainful, minimally invasive testing options and recognition that the convenience of rapid, point-of-care testing may facilitate earlier diagnosis of many chronic conditions is driving the push toward clinical adoption of saliva-based diagnostics tests.

"Noninvasive could be defined as something that sits on the skin and takes a measurement from the body without a sample, like continuous glucose meters," says James Nichols, Ph.D., director of clinical chemistry at Baystate Medical Center (Springfield, Mass.). "Saliva and urine testing, I might call minimally invasive."

Why the interest in noninvasive testing in general? "It is not a cost issue so much as a convenience and privacy issue," says Nichols, who cautions that the technology will improve in the near term to the point that clinical adoption may be more pervasive. "There is still concern on the lab side about the technical performance. Are they as precise and accurate as a central lab? Are we getting as reliable results? That question is not fully resolved yet, but it will clearly continue to advance in the next five years."

Increasing Scientific Attention

Oral fluids-based diagnostic testing has emerged as a translational and clinical priority with national visibility. Detecting dozens of diseases in a sample of saliva was issued by President Obama as one of the 14 "Grand Challenges" for biomedical research in the 21st century. In order for the scientific community to achieve this, the National Institutes of Health's National Institute of Dental and Craniofacial Research (NIDCR) has invested heavily over the past 10 years in research efforts to substantiate the scientific foundation of salivary diagnostics and to begin to determine which conditions might be correlated with biomarkers found in saliva.

Initial research focused on developing the "diagnostic alphabet" of saliva by first defining and cataloging all the proteins and RNAs present in saliva and at what resolution. To date 1,166 proteins have been identified and represent the foundational toolbox for building clinical diagnostic applications. To disseminate these findings and foster translational efforts, the Salivaomics Knowledge Base, an online database, was developed, and by using bioinformatics applications, saliva proteins can be matched to existing research efforts demonstrating the protein's function elsewhere in the body. In the last few years, researchers from University of California Los Angeles (UCLA) have applied this research tool and discovered they can diagnose early-stage oral cancer and the autoimmune disease Sjögren's Syndrome from saliva.

NIDCR also called for the development of point-of-care biosensor technologies that will permit the use of a drop of saliva for the simultaneous detection of mul-

tiple salivary biomarkers in real time and in a cost-effective manner. While more sensitive technology has aided in identifying salivary biomarkers and detecting them in very small quantities, clinical testing applications for systemic conditions remain relatively few.

Salivary Biomarkers for Detection of Pancreatic Cancer

In a proof-of-concept study published in *Gastroenterology* in 2010 Wong's lab identified salivary biomarkers capable of noninvasively detecting pancreatic cancer. The combination of four messenger RNA biomarkers (KRAS, MBD3L2, ACRV1, and DPM1) could differentiate pancreatic cancer patients from noncancer subjects (both patients with chronic pancreatitis and healthy controls) with 90 percent sensitivity and 95 percent specificity. Validation studies are currently under way.

That distal systemic disease is reflected in the constituents of saliva is enormously significant and potentially highly clinically meaningful for the early detection of disease, monitoring disease progression, and predicting therapeutic outcomes. Salivary biomarkers for disease detection (both oral and systemic), particularly for molecular oncology, are emerging where blood markers are still elusive. Renowned saliva researcher David Wong, D.M.D., Ph.D., the associate dean of research at the UCLA School of Dentistry, says the systemic oncological diseases his lab has studied (including pancreatic cancer, breast cancer, lung cancer, gastric cancer, and ovarian cancer) have all yielded "highly discriminatory" salivary biomarkers. While saliva-based oncological diagnostics may be several years away, routine screening for chronic conditions may be coming to a dentist office soon.

Dentists Take Note

Saliva has attracted widespread interest as a diagnostic medium for rapid, point-of-care testing and dentists have taken active roles in working to integrate the tests into clinical practice.

The role of prevention and the improved integration of health care providers across disciplines frequently emerge during discussion of efforts to enact reform in the U.S. health care system. More patients visit a dentist annually than visit a physician, so utilizing dentists could be an important resource for an integrated health care delivery strategy. In an expanded care role, dentists could screen for underlying conditions in addition to providing oral health care. Utilization of a saliva-based diagnostic platform fits logically into this scenario.

Research suggests that the majority of dentists feel diagnostics screening is important and they are willing to conduct screening for medical conditions. Screening for nonoral conditions could likely include systemic diseases such as cardiovascular and respiratory diseases, diabetes mellitus, HIV/AIDS, and hepatitis.

Patient acceptance of "chairside medical screening" in a dental setting is a critical element for the successful implementation of this strategy. A study of patient attitudes toward chairside medical screening in dental settings was published

online in the *Journal of Public Health Dentistry* in October 2011. The majority of respondents surveyed in both private practice settings (170) and an inner-city dental school clinic (263) were willing to have a dentist conduct screening for heart disease, high blood pressure, diabetes, HIV, and hepatitis infection (55 percent to 90 percent). Sixty percent to 94 percent of respondents were willing to provide oral fluids, finger-stick blood, blood pressure measurements, and height and weight in a dental setting, and half to two-thirds were willing to pay up to $20 for the screening. The fact that the test was not done by a physician was ranked as the least important potential barrier. While all respondents expressed a favorable attitude toward chairside screening, the mean score was significantly lower among clinic patients across most questions.

"The [American Dental Association (ADA)] is embracing it. Nearly 175,000 dentists [can be mobilized to] integrate saliva diagnostic testing in the next two to three years," says Wong. "The ADA sees this as a scientifically driven clinical agenda. Third-party payers are in the picture and on board. The dentist of the future will integrate noninvasive testing and saliva integrates perfectly into it."

The ADA has approved two saliva-diagnostic-related reimbursement codes, Wong says, but they are waiting for a credible test to be ready.

Saliva's Clinical Debut in IVF

In some cases where repeated sampling is necessary, saliva-based diagnostics are designed to replace more invasive blood testing strictly for the sake of being more patient-friendly. At the end of January, Boston IVF, a Northeastern based infertility treatment medical practice, introduced the first needle-free saliva test to monitor infertility treatment.

Following nearly two years of investigation, Boston IVF proved that the hormone estradiol, traditionally measured in the blood, can also be accurately measured in saliva for application in in vitro fertilization (IVF) settings. A typical IVF cycle includes eight to 12 days of hormone therapy to stimulate a woman's egg production. During that time five to seven blood draws are needed to measure estradiol levels and a woman's response to therapy. The Saliva Monitor Test virtually eliminates the need for daily blood testing during a patient's treatment cycle.

"If you superimpose the blood tests with [follicle stimulating hormone] injections, there is a lot of discomfort from punctures. Patients feel like a pincushion," says Michael M. Alper, M.D., medical director at Boston IVF. "Infertility treatment can be very stressful and physically demanding for patients. By replacing daily blood draws with a very simple, patient-friendly saliva test, we can eliminate some of the challenges and painful needle sticks and make treatment more convenient."

Patients can collect their saliva at home in less than five minutes and drop off their sample for analysis each morning. Results from saliva testing are available the same day. Boston IVF is already using the test at one of its 12 centers and plans to launch at all centers "very shortly." Alper says the practice expects to replace most of the 50 blood tests the group performs each day with the saliva test. They plan to release a kit commercially to others in the IVF field by this summer. The group also plans to expand use of the test to other gynecological conditions for which noninvasive estrogen monitoring would be preferred.

Molecular Assay Predicts High-Risk Lung Cancer

Pinpoint Genomics' (Mountain View, Calif.) Pinpoint Dx Lung assay significantly improves prognostic accuracy beyond conventional staging in patients with early-stage nonsquamous non-small-cell lung cancer (NSCLC) by differentiating low-, intermediate-, and high-risk patients within all disease stages. Results validating the assay were published online Jan. 27 in the *Lancet* and coincided with the commercial launch of the test.

The algorithm and quantitative polymerase chain reaction-based assay was jointly developed by the University of California San Francisco Thoracic Oncology Laboratory and Pinpoint Genomics. The 14-gene expression assay runs on formalin-fixed paraffin-embedded tissue samples and was independently validated in two large cohorts following surgical resection—in 433 patients with stage I NSCLC resected at Kaiser Permanente Northern California hospitals and in a cohort of 1,006 patients with stage I to III NSCLC resected in Chinese cancer centers as part of the China Clinical Trials Consortium (CCTC).

The assay successfully identified patients with a higher risk of death than predicted by conventional staging. In the Kaiser cohort five-year overall survival was 71.4 percent in the low-risk group, 58.3 percent in intermediate-risk group, and 49.2 percent in high-risk patients. The CCTC cohort had similar findings with five-year overall survivals of 74.1 percent in low-risk patients, 57.4 percent among those at intermediate risk, and 44.6 percent survival in high-risk patients. The molecular assay was the strongest predictor of five-year mortality compared with standard criteria such as sex, age, smoking status, tumor size, and even disease stage, and outperformed National Comprehensive Cancer Network guidelines used to identify high-risk patients with stage I disease. The researchers say it might be helpful in the identification of the most appropriate application of treatment guidelines to improve clinical outcomes.

While a prospective study is planned that will test the effectiveness of the application of guidelines for adjuvant treatment on the basis of the assay's ability to risk-stratify patients with stage I disease, David Berryman, CEO of Pinpoint Genetics, tells *DTTR* that the test is commercially available as a lab-developed test through Pinpoint's CLIA-certified laboratory for a list price of $3,995.

Blood Test to Predict Effectiveness of Anti-Depressants

A blood test for the protein vascular endothelial growth factor (VEGF) may be able to determine which depression patients will respond well to anti-depressant treatments. According to researchers who presented their findings at the Fourth Annual Illinois Brain, Behavior and Immunity Meeting in December, if the findings are confirmed by additional studies, the test could greatly impact prescription of anti-depressants, which are notoriously difficult to match correctly to the patient on the first attempt.

The researchers examined 35 patients who took escitalopram (Lexapro), an anti-depressant from the selective serotonin reuptake inhibitors family (as are Prozac, Paxil, and Zoloft), to treat major depressive disorder. Among depressed patients who had

higher than normal blood levels of VEGF, more than 85 percent experienced partial or complete relief from depression after taking escitalopram. But of the patients who had low levels of VEGF, only 10 percent of depressed patients responded to the drug.

"Measuring baseline VEGF in depressed patients could be a predictor of response to therapy," wrote study author Angelos Halaris, M.D., Ph.D., medical director of adult psychiatry at Loyola University Chicago Stritch School of Medicine. "Future research in understanding the link between antidepressant therapy and VEGF will help us understand this finding and it could also be a potential target for novel therapeutics."

Chlamydia Testing and Urine Culture Can Be Combined

It may be OK to test for both C. trachomatis and bacterial urinary tract infections on a single midstream urine specimen, simplifying clinical practice. New findings from a pilot study published in the January-February issue of the *Annals of Family Medicine* may prove that C. trachomatis should be added to the usual panel of pathogens that are looked for in urine sample cultures.

Traditionally separate samples have been needed with first-void specimens utilized for chlamydia testing and midstream samples used to test for urinary infections. But this new research shows that midstream specimens are sufficiently sensitive to be considered for routine clinical testing for chlamydia. One hundred women with a first-void urine specimen positive for C. trachomatis also provided midstream specimens for comparison. All specimens had C. trachomatis testing performed using a DNA detection method. Of the 100 eligible participants with a first-void specimen positive for C. trachomatis, 96 percent also had a positive midstream specimen. These results suggest that by using newer, more sensitive nucleic acid amplification techniques, timing of specimen collection is not as important in testing for C. trachomatis as previously thought.

"At present, a choice must be made at the time of the consultation as to which specimen is the most important. The clinical practice implications of these results are important," writes study author Derelie Mangin, M.B.Ch.B., D.P.H., director of the primary care research group, Christchurch School of Medicine and Health Sciences (New Zealand).

While vaginal swabs are the preferred sample for chlamydia testing in the United States, the authors say it is "worthwhile investigating" whether C. trachomatis should be added to the usual panel of pathogens that are looked for in urine sample cultures.

Inexpensive Diagnostics Overlooked in Diagnosing Neuropathy

The evaluation of peripheral neuropathy, which can affect an estimated 15 percent of people over the age of 40, involves substantial use of diagnostic tests, with wide variation in testing patterns. A study published Jan. 23 in the *Archives of Internal Medicine* shows that costly and low-yield tests like magnetic resonance imaging (MRI) are frequently performed during the diagnosis of neuropathy, but inexpensive tests like the glucose tolerance test (GTT) which would identify impaired glucose tolerance or diabetes, one of the most common and treatable causes of distal symmetric polyneuropathy (DSP), are rarely performed. These findings demonstrate an important

opportunity to improve the effectiveness and efficiency of the diagnostic evaluation of this prevalent disease.

The best evidence for diagnostic testing in DSP was summarized in 2009 in a systematic review by the American Academy of Neurology (AAN). Testing for fasting glucose levels, vitamin B12 levels, serum protein electrophoresis (SPEP), and two-hour oral GTTs were supported by the literature based on the yield of these tests and the potential for subsequent interventions.

Using a large, nationally representative health survey, the 1996-2007 Health and Retirement Study Medicare claims-lined database, the researchers identified a cohort with incident peripheral neuropathy and focused on the utilization of 15 relevant tests in the six months before and after the diagnosis.

Of the 1,031 patients diagnosed with neuropathy a median of four of the 15 selected tests were performed on each patient, with more than 400 patterns of testing. MRIs of the brain or spine were ordered in nearly one in four patients, whereas a GTT was obtained in only 1 percent. The other three tests supported by the AAN systematic review (fasting glucose level, B12 level, and SPEP) were ordered less frequently than expected. Only 49.8 percent of patients with neuropathy received one or more of these three tests, and only 17.3 percent received two or more. Mean Medicare expenditures during the diagnostic phase were $14,362.

"These findings suggest substantial opportunity to improve efficiency in the evaluation of peripheral neuropathy," writes study author Brian Callaghan, M.D., of the University of Michigan in Ann Arbor. G2

Call for Glucose Testing for All Hospital Admissions

All patients should have their blood glucose levels tested on admission to a hospital, whether or not they are diagnosed with diabetes, according to an expert panel of the Endocrine Society. New clinical practice guidelines published in the January 2012 issue of the *Journal of Clinical Endocrinology & Metabolism* say that the recommendations are necessary given the poor outcomes associated with inpatient hyperglycemia.

The eight-member panel advised that all patients, whether diabetic or not, have laboratory-based blood glucose testing on admission. For most hospitalized patients with noncritical illness, the premeal glucose target should be less than 140 mg/dL and the random blood glucose target should be less than 180 mg/dL, although the targets may be adjusted according to clinical status. Bedside point-of-care (POC) glucose testing should be used for at least one to two days in all patients with high glucose values on admission and in all patients who are receiving therapies associated with hyperglycemia, such as corticosteroids or octreotide and either parenteral or enteral nutrition. The authors suggest that POC testing should be done before meals and at bedtime for patients who are eating, and every four to six hours for patients who are not eating or who are receiving continuous enteral feeding.

Laboratory experts question whether or not these guidelines with their call for POC glucose testing take into serious consideration questions of accuracy and performance issues in glucose meters. G2

G2 Index Gains 5%; Sector Gets Boost From Bid for Illumina

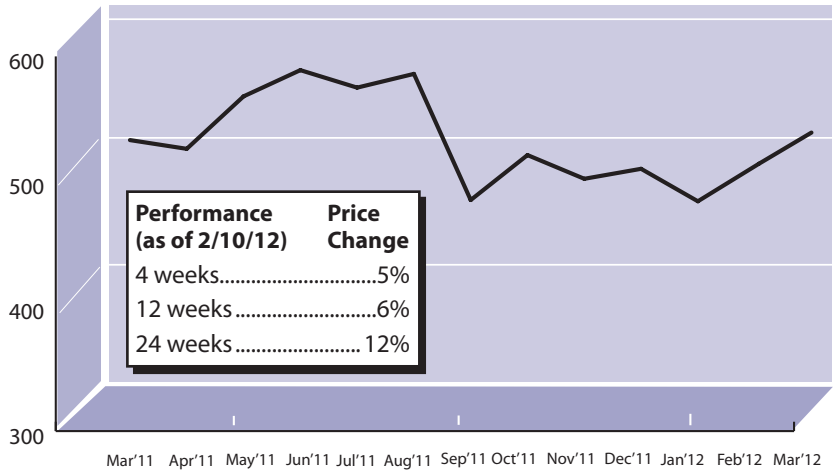
The G2 Diagnostic Stock Index was up 5 percent for the four weeks ending Feb. 10. Ten stocks were up for the period, two stocks were unchanged, and five stocks declined. The Nasdaq and the S&P were also both up over the same period, gaining 7 percent and 4 percent, respectively.

Among the stocks gaining ground was **Illumina** (San Diego), whose stock shot up 51 percent after news broke of the pharmaceutical giant **Roche's** (Basal, Switzerland) takeover offer. Other companies in the space—both tools makers and molecular diagnostics firms—got a related boost as well.

Cepheid (Sunnyvale, Calif.) gained 18 percent over the period in part due to positive financial reports. The company reported its fiscal year 2011 results, which included revenue of $277.6 million, up more than 30 percent over 2010's $212.5 million. Net income for the year was $2.6 million compared to a net loss of $5.9 million in 2010. Record GeneXpert System placements, both commercially and in the company's High Burden Developing Country program, contributed to 39 percent growth in the company's clinical business. In 2012 the company expects total revenue to continue to grow aggressively and reach the range of $333 million to $347 million. Over the next year the company says it also will continue to invest aggressively in Xpert test menu expansion in order to reach broader segments of the market.

Stock prices were up 16 percent for **Alere** (Waltham, Mass.), which recently reported that it received a Clinical Laboratory Improvement Amendments waiver from the U.S. Food and Drug Administration for its Influenza A&B Test. The rapid, nasal-swab test is intended for use in the physician's office and delivers results in 10 minutes. The company also recently announced that its Pima CD4 Test received prequalification from the World Health Organization. By giving health care providers absolute CD4 counts in less than 20 minutes, it reduces both the number of patients lost to follow-up and reduces the time to initiate anti-retroviral therapy.

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
Alere	25.76	16%
Becton Dickinson	76.42	2
Bio-Rad	103.08	5
Cepheid	42.16	18
Gen-Probe	69.22	5
Illumina	53.89	51
IRIS	10.33	5
Luminex	20.97	2
OraSure	10.42	6
Sequenom	4.59	2
Unchanged		
Affymetrix	4.65	0%
Qiagen	15.15	0
Down		
Abbott Labs	55.11	-1%
Abaxis	27.49	-1
Johnson & Johnson	64.60	-1
Meridian	17.99	-6
Quidel	14.72	-7

G2 Insider

The Role of HbA1c Testing—A Rule Out Test? . . . HbA1c is the accepted standard for monitoring long-term glycemic control in patients with diabetes; however, changes in recommendations that call for use of the HbA1c test for the diagnosis and screening of diabetes have caused some clinical disagreement.

In a 2008 consensus statement by the American Diabetes Association (ADA), HbA1c was first proposed as a screening/diagnostic test for diabetes using a threshold HbA1c value of 6 percent. In 2010 the ADA followed the International Expert Panel's 2009 recommendation of using HbA1c as the first-line test for screening and diagnosing diabetes with an HbA1c threshold of 6.5 percent, with the rationale that HbA1c gives a fuller picture of ongoing glucose levels, compared to oral glucose tolerance testing (OGTT), which gives a one-point snapshot of glucose concentrations. But there have been increasing critiques of HbA1c criteria, with some citing the test as too insensitive for screening purposes.

The Canadian clinical laboratory DynaLIFEDx (Edmonton, Alberta), in conjunction with local practitioners, recently published one of the most recent studies to examine the characteristics of HbA1c as a screening test in the December 2011 issue of *Clinical Biochemistry*. A population of patients who physicians had a moderate suspicion of diabetes in were given the oral glucose test along with the HbA1c test. The recommended threshold HbA1c value of 6.5 percent did not give the optimal combination of negative predictive value (NPV; 0.93 to 0.92) and positive predictive value (PPV; 0.40 to 0.61) compared to a 7 percent threshold HbA1c value (NPV, 0.91 to 0.92; and PPV, 0.61 to 0.73).

"HbA1c is not satisfactory for use as a diagnostic test for diabetes using the threshold values recommended by the Consensus Committee and the International Expert panel due to low positive predictive values," the researchers concluded. "About 12 percent of individuals with a normal OGTT test will be diagnosed with diabetes using a threshold HbA1c value of 7.0 percent. . . . However, based on the high negative predictive value, HbA1c may be used as a test to rule out diabetes." G2

Company References

AdvanceDx 312-278-3838
Alere 781-647-3900
American Dental Association 312-440-2500
Aria Diagnostics 408-229-7500
Boston IVF 617-735-9000
C8 MediSensors 408-622-2040
Cepheid 408-541-4191
DynaLIFEDx 780-451-3702
Illumina 800-809-4566
Myriad Genetics 801-584-3600
Natera 650-249-9090
Pinpoint Genomics 888-279-5088
Roche +41-61-688 1111
Seegene (02)2240-4040
Sequenom 858-202-9000

 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.

Kimberly Scott, Editor; Lori Solomon, Writer; Dennis Weissman, Executive Editor; Heather Lancey, Designer; Beth Butler, Marketing Director; Dan Houder, COO and Publisher

Receiving duplicate issues? Have a billing question? Need to have your renewal dates coordinated? We'd be glad to help you. Call customer service at 800-401-5937.