Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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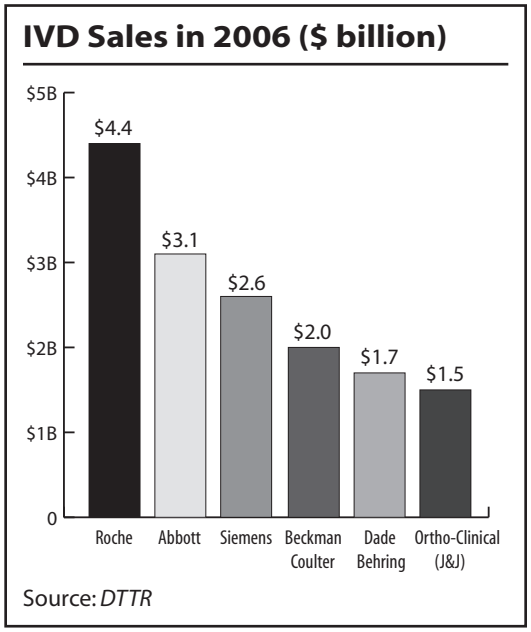
WASHINGTON G-2 REPORTS

Established 1979

Siemens To Buy Dade, Position Itself IVD Market Leader

While rival conglomerate General Electric has pulled the plug on its diagnostics deal with Abbott, Siemens is barreling head first into the sector. On July 25, the Berlin- and Munich-based company announced that it has signed a merger agreement to acquire Dade Behring (Deerfield, IL) in a deal valued at approximately $7 billion. Siemens will submit a cash offer of $77 per common share to Dade shareholders, which represents a 38% premium to the stock's Tuesday closing price of $55.91 per share. The transaction is expected to close in the second quarter of the 2008 fiscal year.



Source: *DTTR*

"The takeover will create the first and only fully integrated diagnostics company," said Peter Löscher, the newly appointed CEO of Siemens, in a conference call with analysts. "We will surpass Roche as the market leader."

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FDA Releases Revised IVDMIA Draft Guidance

On July 26, the United States Food & Drug Administration (FDA) released for public comment a revised version of its draft guidance on in vitro diagnostic multivariate index assays (IVDMIAs). The novel test category, initially defined by the FDA last fall, consists of molecular tests, some of them laboratory developed, that combine assays and algorithms to produce patient-specific results. Comments on the revised IVDMIA guidance are due August 27.

The revised draft clarifies several points in response to comments the FDA received. First, the agency clarified its definition of an IVDMIA by providing examples that are representative of the category's fairly narrow scope. The examples echo those presented at the FDA's February public meeting on the draft guidance, where Courtney Harper, Ph.D.,

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▲ **Revised IVDMIA Draft Guidance,** *from page 1*

a representative of the FDA's Office of In Vitro Diagnostic Device Evaluation and Safety, gave the following as examples of IVDMIAs: a microarray that predicts colon cancer recurrence based on an RNA expression pattern, an assay that integrates quantitative results from seven immunoassays to obtain a qualitative "score" that predicts a person's risk of developing Alzheimer's disease, and a test that integrates a patient's age, gender, and genotype of five genes to diagnose cardiovascular disease.

The revised draft also addresses worries that further regulation would discourage innovation. According to the document, the FDA would exercise enforcement discretion for laboratory-developed IVDMIAs intended to diagnose rare diseases. The exception is based on the agency's humanitarian use classification, which was created for devices that are intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

An IVDMIA:

1) Combines the values of multiple variables using an interpretation function to yield a single, patient-specific result (e.g., a "classification,""score,""index"), that is intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, and
2) Provides a result whose derivation is nontransparent and cannot be independently derived or verified by the end user.

Source: FDA

Additionally, the new document points out that CLIA quality system requirements will be recognized as partially fulfilling FDA's post-market QS requirements until final guidance is issued.

The FDA also states that it believes that most IVDMIAs would be either class II or class III devices, although it is possible that an IVDMIA for a low-risk indication could be class I. Class I medical devices are usually exempt from premarket review and rely on general controls such as registration, listing, and good manufacturing practices to assure their safety and effectiveness. Class II medical devices typically require FDA clearance of a premarket notification submission, and class III devices require the submission of an application for premarket approval.

Quest Extends Agreement With Digene For HPV Testing

Digene (Gaithersburg, MD) will continue supplying Quest Diagnostics (Lyndurst, NJ) with instrumentation and reagents for human papillomavirus (HPV) testing. The new agreement extends the companies' previous three-year contract for an additional four years. Digene manufactures the only FDA-approved test for high-risk types of the virus and an automated, high-throughput instrument on which the HPV test and other assays can be performed. Quest Diagnostics, the nation's largest commercial laboratory, is Digene's largest HPV testing customer.

The Digene HPV Test is FDA-approved for use with a Pap test in women age 30 and older as a primary screening method for cervical cancer. The test identifies the presence of the genetic code (DNA) of 13 high-risk types of HPV.

Inverness Medical Innovations To Acquire HemoSense

Over 7 million people worldwide take oral anticoagulants such as Coumadin (warfarin) to help reduce the formation of blood clots.

Inverness Medical Innovations (Waltham, MA) is buying into two powerful trends in diagnostics—point-of-care testing and personalized medicine—for the price of one. The company has signed an agreement to acquire HemoSense (San Jose, CA), which specializes in point-of-care testing for warfarin dosing, in an all-stock deal worth approximately $165 million. For each HemoSense common share, stockholders will receive 0.274192 shares of Inverness common stock. This represents a 38% premium to the average trading prices of both companies over the five trading days preceding the August 6 agreement. The deal is expected to close in the fourth quarter.

Founded in 1997 as CardioSense, HemoSense manufactures and sells the INRatio system, a rapid, point-of-care testing system that provides prothrombin time (PT) and international normalized ratio (INR) results using a small (15-microliter) sample of fresh capillary whole blood from a fingerstick. This measure of blood clotting time, or PT/INR values, is used to manage a patient's warfarin dosing. The company has 79 employees and is forecasting 2007 revenue of $32 million to $34 million.

HemoSense's INRatio Monitor.

The INRatio system consists of a small, portable monitor and disposable test strips. After being applied to the test strip, a drop of fresh whole blood is drawn into the test area by capillary action where it mixes with reagents that initiate coagulation. The monitor then simultaneously performs the PT test and two quality control tests (normal and therapeutic) and determines whether the controls are within preset limits. If they are, strip integrity is verified and the monitor reports the PT test result. If they are not, the monitor displays an error message. Test results are displayed in less than two minutes as an INR only, PT seconds and INR, or INR, PT, and QC, whichever the user prefers. The monitor can electronically transmit the results or send them to a printer.

"HemoSense is a particularly good fit with Biosite and [Quality Assured Services], which we have recently acquired," says Ron Zwanziger, chairman and CEO of Inverness. The global diagnostics company, which has 2,561 employees, earned 2006 revenues of $569.5 million.

Misys To Sell Off Diagnostic Systems Business

Healthcare information technology company Misys Healthcare Systems (Raleigh, NC) has signed an agreement to sell its diagnostic systems business to private equity firm Vista Equity Partners (San Francisco, CA), which invests in software and technology firms. The agreement includes the Misys laboratory, commercial laboratory, and clinical financial products, as well as stand-alone systems for radiology and pharmacy departments. Financial terms of the deal, which is expected to close by October, were not disclosed.

The sell-off is indicative of a new focus for Misys, which is reorganizing around "the ambulatory space and the role that segment plays in building connected healthcare communities," according to Vern Davenport, the company's executive vice president and general manager.

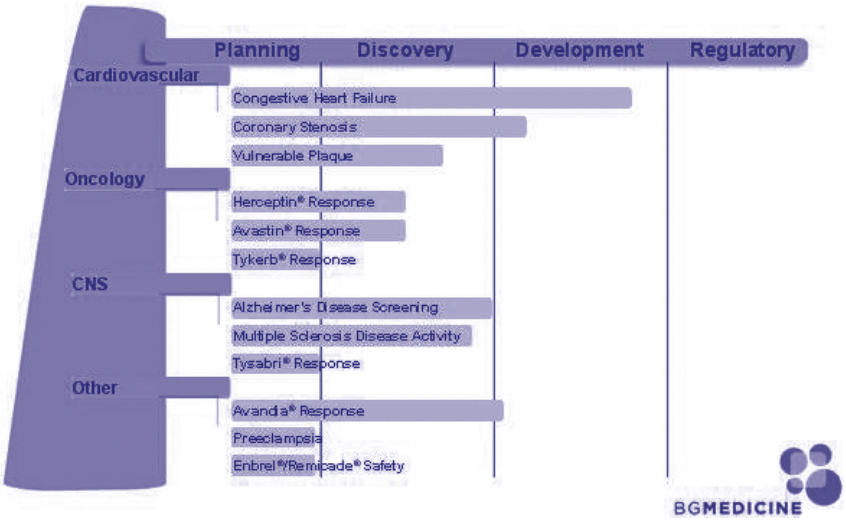
Vista plans to continue operating Misys's diagnostic systems division as a cohesive business. The deal agreement establishes both a detailed transition plan providing for the continuity of clinical customer operations and a multi-year strategic agreement to resell Misys Connect and market Misys EMR as its preferred electronic medical record solution for ambulatory physicians.

Vista Equity Partners has experience in the healthcare market, having acquired Surgical Information Systems (SIS; Alpharetta, GA) in February of 2006. SIS provides integrated surgery management software for more than 250 hospitals.

Biomarker-Based Diagnostics Company BG Medicine Files For IPO

Molecular diagnostics company BG Medicine (BG; Waltham, MA) filed for an $80 million IPO on August 6. The company plans to trade on the Euronext Amsterdam under the ticker symbol BGMDX.

BG was founded in 2000 as Beyond Genomics. It is focused on the discovery, development, and commercialization of novel molecular diagnostics based on biomarkers. The company uses a proprietary technology platform to rapidly and cost-effectively discover new high-value biomarkers over a broad range of therapeutic categories. Its product pipeline includes molecular diagnostic tests related to cardiovascular disease, cancer, and central nervous system disorders.



BG Medicine's Pipeline

Earlier this year, BG licensed from ACS Biomarker (Maastricht, Netherlands) exclusive worldwide rights to develop and commercialize a biomarker-based molecular diagnostic test as a prognostic indicator of congestive heart failure (CHF). The company also recently received approval from the United States Food and Drug Administration (FDA) to initiate the first phase of a liver toxicity biomarker discovery project to be conducted with the FDA's National Center for Toxicological Research as part of FDA's Critical Path Initiative.

Since 2000, BG Medicine has raised around $37 million in venture capital funding from firms such as Flagship Ventures, Gilde Investment Management, and Koniklijke Philips Electronics.

A Closer Look At Developing, Validating, And Marketing Molecular Diagnostics

What are the key factors to consider when developing, validating, and marketing a molecular diagnostic technology? *DTTR* looked to Dawn Maghakian, supervisor for the biochemical genetics and molecular pathology clinical laboratories at Stanford University Medical Center (Palo Alto, CA) and a speaker at Washington G-2 Reports's recent oncomolecular diagnostics conference in San Francisco, for insights into every step of this complex process.

Black Box Versus In-House Development

It is often necessary to use a "black box" technology, one where you put the sample in and get the result out. Among the factors that may limit a laboratory's ability to develop a diagnostic technology in-house include the need for rapid turnaround time/stat testing, lack of technical expertise or molecular diagnostics manpower, and the space requirements necessary to prevent contamination. Finally, black box technologies can be used to more rapidly build an esoteric test menu in the clinical lab to meet local needs.

On the other hand, there are reasons to continue the in-house development of analyte specific reagent (ASR)-component testing. "I believe that in-house testing with proper validation design is the key to moving novel technologies in the most rapid manner to the forefront of clinical medicine," says Maghakian.

The reasons to develop in-house assays include:

1. A one- to five-day turnaround time is sufficient to meet clinical needs.
2. Desire to offer novel technology that is not available commercially.
3. Flexibility in future expansion or utility (open platforms save money).
4. Often a more cost-effective alternative if expertise is in-house for development and interpretation.
5. Open platforms allow more options for monitoring quality control.

The Validation Model

For the purpose of illustration, Maghakian uses a laboratory-developed test system designed for a fusion transcript analysis. "In this instance, if we imagine that this is quantitative polymerase chain reaction (QPCR) design to detect the common fusion transcripts associated with BCR-ABL, you would want a design to detect not only the fusion gene transcript (FG) but also a 'housekeeping' control gene (CG) that is constitutively expressed at a similar level to your fusion transcript."

According to Maghakian, several choices are critical to the validation model.

❑ **Detection method.** "You want to be able to have numerical values that you can objectively measure run to run and week to week," she says. "By choosing an appropriate detection source you can do that," she says. "For instance, if you choose SYBR Green Technology, you have the option of having a numerical value for a very precise melting temperature (Tm). You can tell each week and each day whether your assay is in control. The downside here is that your primer design must be highly specific to prevent detection and quantification of primer-dimer or mis-primed artifact," Maghakian explains.

❑ **Target RNA extraction.** Are you going to employ a manual extraction, or will your volumes be so high that you also need to validate an automated system? Will your method provide you with enough high-quality target? "If you do choose an automated system, you must also have a backup manual system validated because automation does break down," she says. "These are things you have to consider in the whole process—a lot of time for a laboratory to spend to develop their own in-house assays."

❑ **Housekeeping gene.** "Current literature has pointed this out over and over, and yet there is a tendency to rush to market with products that may not be complying with the current recommendations. It's not a small point to make sure that you are relating your fusion transcript expression level to a housekeeping gene expression level that is in a similar range," she says. "However, you also must consider how your results will relate to results that are obtained at other laboratories."

❑ **Nucleic acid extraction.** There are a number of questions to consider when selecting a method, including: Does the isolation method affect the Tm or the final qualitative or quantitative result? Are there RNase issues and how can you prevent them? Is there variation in copy number between automated and manual methods? Is a backup required? Are you interested in mRNA only, or total RNA? What is your primer choice for the RT-PCR step (random, polyT, sequence specific)? Are there quality-control steps in place in your design from the RNA extraction onward, or only from the RT (cDNA synthesis) step?

She also notes that you need to keep three factors in mind—pre-analytical, analytical, and post-analytical—in your validation study.

Next, Maghakian outlines seven quality control measures for a validation model:

1. Efficiency. "Efficiency is not a small matter in QPCR test systems," Maghakian stresses. "A small change in efficiency can markedly change the number of target copies you have after 30 cycles. Measuring your efficiency on an open platform that's going to allow you to do that will give you another variable that you can monitor run to run. The efficiency is measured according to the equation [E = 10 (-1/slope) – 1], where the slope of the line is calculated on a graph of the cycle threshold (CT) value (y-axis) versus a 10-fold change in target concentration (x-axis). Perfect efficiency would demonstrate a slope of -3.32. While you may not be able to achieve 100% efficiency, you should make sure that all targets in your assay amplify with a similar efficiency, which is generally greater then 90%."

2. Diagnostic sensitivity. For diagnostic sensitivity, a false-negative rate assesses the degree that the assay is positive in patients with disease (True positives). The equation is:

TP/TP + FN x 100 using a "Gold Standard" reference method

3. Diagnostic specificity. For diagnostic specificity, the false-positive rate assesses the degree that the assay is negative in patients without disease (True negatives). The equation is:

TN/TN + FP x 100 using a "Gold Standard" reference method

"While we typically do this against a gold standard or reference method, we know these standards are not always readily available for esoteric testing—at least not in the numbers that are required for a valid total number of tests," Maghakian points out. "We should be aiming for at least testing 100 positives and 100 negatives. If it's an FDA-approved or cleared test, 50 positives may be a good goal, but keep

in mind that 10 positives are not. Also, you should replicate your experiments in your validation design to assess intra-run and inter-run variation."

4. Analytical sensitivity. This is defined as the ability of an assay to detect a given analyte. There are two terms to remember—limit of quantification (LoQ) versus limit of detection (LoD)—when dealing with minimal residual disease (MRD). "With LoQ, we're talking about the lowest limit in the dynamic reportable linear range. During your validation you need to establish that you have a certain range that is indeed linear in your established parameters, and your lowest value of that range is your LoQ as opposed to your LoD in MRD, which is the lowest value you can reproducibly detect with an acceptable coefficient of variation."

5. Analytic specificity. This is defined as the degree to which interfering substances are not detected by an assay. In other words, how certain are you that you are detecting your analyte or 'specific sequence'? "Clinical laboratories should not be doing laboratory-developed in-house testing unless they have capability to sequence their amplicon or send the amplicon out for sequencing," says Maghakian. "The sequence is the analyte, and you need to validate by sequence that it is what you are detecting."

6 & 7. Accuracy (agreement or correctness) and Precision (reproducibility). For accuracy, you need to measure against the reference method or same method if available, and a sequence is necessary. For precision, you need to have many replicates on inter-run, intra-run, and even between users. "For instance, when you're ready to move this to the clinical side from R&D, you should have several of your technologists run the assay to see if they are still performing in your validated quality-control range," she explains. "One method to keep control over your assays once they are being performed clinically is to do a simple Levy Jennings Plot Format. Again, any numerical value will suffice for your assay that's going to indicate when it is falling out of control."

Finally, you also need to demonstrate analytical measurement range on the clinical bench. "When you receive new lots of your reagents, you should be demonstrating and documenting that that the new lot performs in the same manner and in the same established parameters of your initial validation study," she stresses.

Key Factors To Consider When Going To Market

Maghakian offers the following key factors to consider when trying to move an in vitro diagnostic to market.

- ❑ Limit multiplex capabilities in that rush to market. "We do need to meet a critical need, but we also need to narrow the focus and make sure that we design comprehensively and that the design may allow for further adaptation as science changes," she says. Also, you need to maintain a working knowledge of CLIA regulations to enable lab compliance and proficiency.
- ❑ Keep consumables to a minimum. "This is very helpful for a clinical lab because then we can use various consumables for different assays and it decreases our expense. In addition, the leftover resources can then be used to purchase more in vitro diagnostic products."
- ❑ Design for the small- to medium-throughput users. "The market is huge if you design for the small- to medium-throughput users; you have flexibility because the larger laboratories can also use your product."
- ❑ Design black-box technology where turnaround time is critical or there is an unmet need. "You need to provide enabling technology for critical solutions so that clinicians can use it for their patients."
- ❑ Open platforms are good. "They allow a lot of creativity in design and ability to monitor assays in a laboratory," Maghakian says.
- ❑ Communicate with the FDA early and often. "What we really need is a lot of FDA-cleared and -approved assays on the market," she notes. "The only way we're going to move forward to that is through full disclosure to the FDA on what you're intending to do."
- ❑ Design the test system and instrumentation for ease of use. Key criteria include:
  - —Automation and low-to-moderate repetition
  - —Small footprint, plan data output for ease of review
  - —Easy maintenance
  - —Good visual access and ergonomics
  - —Readily available standards and control materials
- ❑ Good customer support is very, very important. You need to include online tutorials, user groups, timely updates, preventive maintenance, and rapid response for downtime. "Often, the scientists on the bench required to run your assays may not have a clear background in molecular biology; they're forced to learn this on the job. Having a ready resource where they can pick up the phone or get on the Web and get an immediate answer is critical," Maghakian concludes.

Genetic Risk Factor For Multiple Sclerosis Discovered

In a discovery that could ultimately translate to promising diagnostics and therapeutics, researchers have uncovered a gene linked to the neurodegenerative disease multiple sclerosis (MS), according to studies published in the July 28 issue of *Nature Genetics* and the July 29 issue of the *New England Journal of Medicine*. The studies report only the second MS genetic risk factor confirmed through research.

MS is an unpredictable, chronic inflammatory disease of the central nervous system that affects about 350,000 individuals in the United States. While thought to result from a complex interplay of genetics and environmental triggers, the disease has a clinically significant heritable component.

In the 1970's, researchers found that a variant of the human leukocyte antigen (HLA-DRB1) increases the likelihood of getting the disease up to fourfold. When combined with IL7R, these two genes increase the risk of getting MS by fivefold.

"We have identified the first gene to be genetically and functionally implicated in the development of MS in the last 30 years," said Simon Gregory, Ph.D., assistant professor at Duke University's Center for Human Genetics and first author of the *Nature Genetics* paper. The researchers found that a variation in the interleukin 7 receptor (IL7R) alpha chain gene can increase an individual's risk of getting MS by about 20%. Gregory and others are now further probing the role of IL7R in the development of MS.

In the *NEJM* paper, the International Multiple Sclerosis Genetics Consortium (IMSGC) confirmed these findings through whole genome association, which scans the entire human genome for variants that are associated with MS. This effort also identified a statistical association with the IL7R gene, along with another previously suspected gene, IL2R.

High-Risk Types Of HPV Are Consistent Across Continents

Merck's Gardasil vaccine, which was approved last year by the Food and Drug Administration, protects against HPV 16 and 18. A similar vaccine developed by GlaxoSmithKline also protects against these types of HPV.

The types of human papilloma virus (HPV) that cause invasive cervical cancer (ICC) are largely consistent across continents, according to a meta-analysis-based study published in the August issue of the International Journal of Cancer.

"Our data confirm that HPV types 16 and 18 are the most common in invasive cancer," said lead study author Jennifer Smith, Ph.D., a research assistant professor of epidemiology at the University of North Carolina School of Public Health. "As a result of this analysis, we now have additional information about other high-risk HPV types that cause invasive cancer to target for future HPV vaccine development."

HPV, a sexually transmitted virus, can cause high-grade cervical lesions, increasing a woman's risk of developing ICC. There are approximately 14 high-risk types of HPV that cause invasive cervical cancer. The two most common types are 16 and 18, named for their genetic patterns. These virus types are responsible for about 70% of ICC and 50% of high-grade lesions worldwide, the study shows.

In a meta-analysis of the distribution of HPV infection in more than 14,000 invasive and 7,000 high-grade cases worldwide, the researchers found that ICC HPV16 was the most common, and HPV18 the second most-common type in all continents. Combined HPV 16/18 prevalence among ICC cases was slightly higher in Europe, North America, and Australia, from 74% to 77%, than in Africa, Asia, and South/Central America, where the rates were between 65% and 70%. Data on HPV-typed ICC and high-grade lesions were particularly scarce from large regions of Africa and Central Asia.

OraSure Readies Rapid HCV Test

Hepatitis C, the most common blood-borne infection in America, affects approximately 4 million people or about one in every 50 adults, according to the Centers for Disease Control and Prevention.

Oral fluid diagnostics company OraSure Technologies (Bethlehem, PA) is moving ahead in the development of a saliva-based immunoassay for hepatitis C (HCV). At the 2007 annual meeting of the American Association of Clinical Chemistry, OraSure announced preclinical study results for a prototype rapid HCV antibody test that uses the company's OraQuick test platform, using oral fluid, finger-stick whole blood, venous whole blood, serum, and plasma samples.

In preclinical studies conducted by OraSure, performance of the prototype HCV test for all specimen types was shown to be equivalent to or better than results obtained from currently available laboratory-based enzyme immunoassay tests using serum and plasma specimens.

According to Douglas A. Michels, president and CEO of OraSure, the company plans to begin the final clinical studies required to obtain FDA approval during the next several months. "Our plan is to complete these studies as soon as possible and file an application for FDA approval in early 2008," says Michels. "Assuming we are successful, we expect that our test will be the first rapid HCV antibody test approved by the FDA for use in the United States."

Prospective preclinical testing of 419 low-risk human subjects using oral fluid, finger stick, and venous whole blood, serum, and plasma, generated concordant results across all specimen types for each individual. Specificity, which is the percentage of tests that correctly show a negative result when an individual is not infected, was 99.8% in all specimen types. Three individuals in this group were newly identified as having been infected with HCV. In testing of 92 individuals known to be infected with HCV, preclinical results indicated sensitivity in venous whole blood and oral fluid of 100%. In addition, 639 archived HCV-positive plasma samples were tested and similarly resulted in 100% sensitivity. Sensitivity is a measure of the percentage of tests that correctly show a positive result when an individual is infected with HCV.

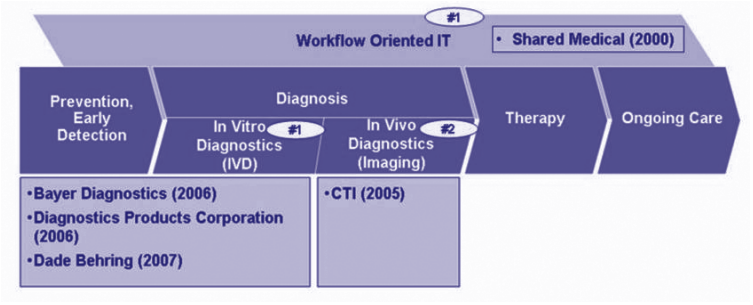
The preclinical studies also evaluated the test's sensitivity during seroconversion, the period of time immediately after infection during which detectable antibodies to HCV are generated. Out of 22 seroconversion panels tested, the prototype HCV test detected HCV antibody on average three days earlier than a laboratory-based assay and in no case did the prototype test detect HCV antibody later than the laboratory assay.

▲ **Siemens To Buy Dade,** *from page 1*

Dade, which has operations in 35 countries and approximately 25,000 customers worldwide, provides clinical laboratory equipment and integrated solutions for routine chemistry testing, immunodiagnostics, hemostasis testing, and microbiology. The company has approximately 6,400 employees. Dade earned 2006 revenues of $1.7 billion and an EBIT of $201 million, which included a $21 million restructuring expense.

In a statement issued on July 25, Löscher pointed to "demographic changes and increasing demand for higher quality healthcare systems" as a driver of growth in the market for diagnostic testing. Last year, the company acquired Diagnostic Products Corporation and Bayer Diagnostics, which has combined and integrated into its Siemens Medical Solutions division. The division reported sales of €8.23 billion, orders of €9.33 billion, and a group profit of €1.06 billion for fiscal 2006 (Sept. 30).

Buying into diagnostics. How Siemens has built its market position.



Source: Siemens

Siemens employs about 475,000 people worldwide. In fiscal 2006 (ended September 30), the company had sales of €87.3 billion. The company aspires "to become the global leader in full-service diagnostics, offering imaging diagnostics, clinical laboratory diagnostics, and healthcare IT solutions - from a single source and along the entire value chain."

According to Löscher, the company's strategy is now "to concentrate and focus on three application fields and core areas: energy, industry, and healthcare."

Advion BioSciences Buys NanoTek

Microfluidics company Advion BioSciences (Advion; Ithaca, NY) has completed its purchase of NanoTek (Knoxville, TN), a manufacturer of microfluidic chemistry systems. Advion was previously Nanotek's global distribution and support partner. Financial terms of the deal were not disclosed.

The addition of NanoTek will help Advion fulfill its plan to provide a complete chemistry and analytics approach for imaging diagnostics, drug discovery, and biomarker research. Advion CEO David B. Patteson said that the company plans to rapidly accelerate NanoTek's global commercialization and extend its product lines into areas where there is existing demand.

Founded in 1993, Advion was the first to develop and to market a novel, automated chip-based technology for mass spectrometry users. The company also provides a range of services, including a full range of ligand binding assays for the development and validation of traditional and custom designed ELISAs, immunoassays, immunogenicity tests, multiplexed biomarker assays, cell-based assays, and flow cytometry.

IVD Stocks Up 1%; Dade Climbs 37% On Acquisition News

The 21 stocks in the G-2 Diagnostic Stock Index rose by 1% in the four weeks ended August 3, with 11 stocks down in price and 10 up. So far this year, the Nasdaq is up 4% and the S&P 500 is up 1%.

Dade Behring (Deerfield, IL) spiked 37% to $74.45 per share for a market capitalization of $6 billion on the news that engineering giant Siemens has agreed to acquire the company for $77 per share (see p. 1). According to Dade CEO Jim Reid-Anderson, the deal with Siemens would create the world's largest clinical diagnostics company. Regulatory approval of the deal is likely within three to six months.

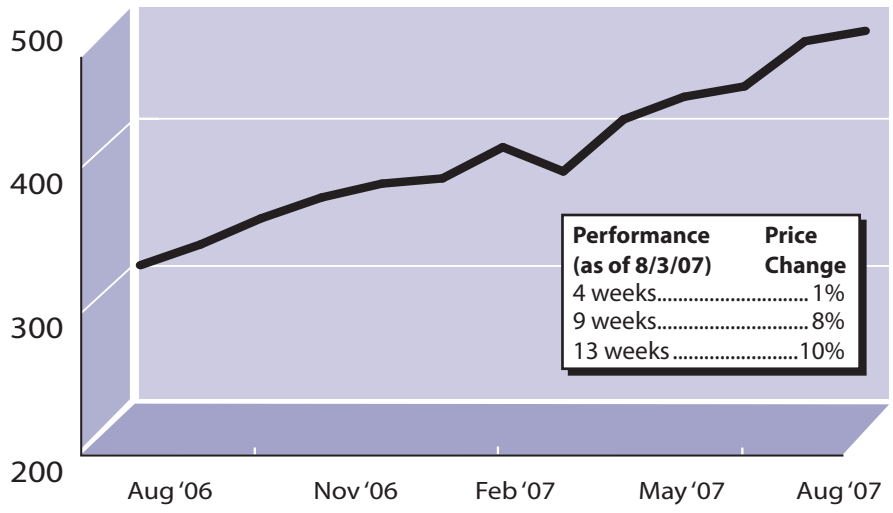
Dade also recently announced that it earned $50.3 million in the second quarter, up 34% from the same period last year. Sales were up 8% to $480.8 million.

Known for its proprietary Invader chemistry-based molecular diagnostics, **Third Wave Technologies** (Madison, WI) jumped 23% to $7.33 per share for a market capitalization of $2.08 billion in the wake of its update on its patent litigation with Digene. In that litigation, Digene alleges that Third Wave infringes its patent covering probes and methods for detecting human papillomavirus (HPV) type 52, a high-risk type of HPV.

On July 24, the United States District Court for the Western District of Wisconsin issued a patent claim construction order and opinion (known as a Markman order) in which the court agreed with all of Third Wave's definitions for the disputed patent claim terms. Pre-trial discovery and other proceedings in the case are scheduled to continue for the remainder of 2007, and a jury trial is currently scheduled for the first quarter of 2008. However, this month, Third Wave plans to file a motion for summary judgment of non-infringement and invalidity.

This month, **Digene** (Gaithersburg, MD) leaves the G-2 Diagnostic Stock Index. Shares in the molecular diagnostic company were de-listed on August 1 upon the closing of its acquisition by Qiagen (Venlo, Netherlands).

G-2 Diagnostic Stock Index



Source: The G-2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 21 IVD companies.

Up	Price	% Chg
Becton Dickinson	$76.20	1%
Beckman Coulter	71.00	7
Clinical Data	22.43	2
Dade	74.45	37
Gen-Probe	65.95	9
Immucor	31.71	15
Meridian	22.10	1
OraSure	8.82	5
Third Wave	7.33	23
Ventana	82.37	5
Down		
Abaxis	18.14	-13
Abbott Labs	51.09	-5
Affymetrix	25.31	-1
Bio-Rad	74.20	-4
Cholestech	19.98	-11
Cytyc	42.37	-4
Inverness Medical	46.15	-11
Johnson & Johnson	60.55	-3
Luminex	12.05	-1
Nanogen	1.33	-3
Quidel	14.55	-21

G-2 Insider

Don't miss the silver anniversary edition of Lab Institute! Registration is now open for the 25th Annual Lab Institute: *What's Next Now!* Oct. 10-13, 2007, at the Crystal Gateway Marriott in Arlington, Virginia. Sponsored by Washington G-2 Reports and the American Pathology Foundation, this year's Institute features some of the diagnostic and laboratory industry's most influential leaders tackling a range of key issues, including these blockbuster sessions:

- Genzyme Genetics President **Mara Aspinall** will address the exploding market for molecular testing, including the "brave new world" of personalized medicine and the marriage of diagnostics and therapeutics.
- **Bruce A. Friedman, M.D.**, active emeritus professor of pathology at the University of Michigan Medical School, will consider the implications of a "diagnostic-centric" healthcare model.
- A panel of international experts, including **Arvind Lal**, chairman and managing director of Dr. Lal PathLabs in India, and **Sachin Shetty**, president of Ssurepath, will discuss the globalization of lab testing.
- **James H. Nichols, Ph.D.**, director of clinical chemistry at Baystate Health will provide insights into point-of-care testing strategies.

Other must-see sessions will focus on issues such the intersection of pathology and imaging, outsourcing U.S. lab testing, and the outlook from Capitol Hill on lab reimbursement and oversight. For a complete Lab Institute program go to ***www.g2reports.com*** or call 1-800-401-5937, ext. 2.

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