Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Vol. VII, No. 6/February 2007

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WASHINGTON G-2 REPORTS

Established 1979

Siemens, GE Build Diagnostic Powerhouses

The medical division of the industrial conglomerate Siemens (Berlin and Munich, Germany) has completed its purchase of Bayer Healthcare's diagnostic division and merged it with Diagnostic Products Corporation (DPC), which Siemens Medical Solutions acquired last July, to create Siemens Medical Solutions Diagnostics. The new entity is headquartered in Tarrytown, New York, and Los Angeles, California, and has approximately 8,000 employees. The business will be led by CEO Anthony Bihl, who previously served as president of Bayer's diagnostics division.

The integrative approach of Siemens has been echoed by GE Healthcare, which is also pursuing research and development in both in vitro and in vivo medicine. At press time, GE was reportedly nearing a deal to buy the medical diagnostics division of Abbott Laboratories (Abbott Park, IL) for as much as $5 billion. In 2004, the company established a molecular diagnostics division, appointing a former Abbott executive to head it up.

Siemens Medical Solutions Diagnostics will specialize in clinical chemistry, patient tests, laboratory automation, and hematology. It is also developing product lines in molecular diagnostics, including pharmacogenomic testing. The company's diagnostic portfolio targets adrenal/pituitary dysfunction, allergy, anemia, diabetes, reproductive and thyroid *Continued on p. 10*

FDA To Hold Meeting On IVDMIA Draft Guidance

The Food and Drug Administration (FDA) Office of In Vitro Diagnostic Evaluation and Safety (OIVD) will hold a public meeting on In Vitro Diagnostic Multivariate Index Assays (IVDMIAs) on February 8 at 8:00 a.m. at the Hilton Washington, DC/Gaithersburg Hotel. The meeting is intended to provide a public forum during which OIVD will hear presentations and comments from interested stakeholders, regarding the draft guidance issued late last year, which is intended to provide clarification on FDA's approach to regulation of in vitro diagnostic multivariate index assays.

Issued in September of last year, along with Q&A guidance on FDA's rule governing analyte-specific reagents (ASRs), the draft guidance on IVDMIAs defines a subgroup of molecular tests as a new class of in vitro diagnostic devices. These assays use complex mathematical formulas to interpret large amounts of gene and protein data to produce results that govern medical decision making. *Continued on p. 2*

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

The FDA believes that IVDMIAs should require clearance, and most of them will likely be subject to class II and III special controls. The draft guidance gives the example of a device intended as an indicator of a patient's risk of cancer recurrence, which may be a class II device, while the same device intended to predict which patients should receive chemotherapy might require premarket approval.

The February 8 meeting will begin with a brief presentation by FDA on the draft guidance document, and presentations by the public will make up the remainder of the agenda. FDA is accepting requests to make a presentation through February 1 and registrations until February 5. On-site registration will be permitted if space remains. For more information see the *Federal Register* notice: www.fda.gov/OHRMS/DOCKETS/98fr/07-93.htm.

Pfizer Buys Diagnostic Rights For Genizon's Disease Markers

Pfizer will pay Genizon upfront license fees and funding for research on genetic variations associated with Alzheimer's disease, attention deficit hyperactivity disorder, and endometriosis.

Change is afoot at the world's largest drug company. After safety concerns led Pfizer (New York, NY) to halt development of Torcetrapib, the blockbuster cholesterol drug in which it invested $800 million, the company has been scrambling to refocus itself. As Pfizer seeks to fill the gaps in its pipeline, it is hungry for acquisitions in the areas of "diabetes, neurology, infectious disease, and oncology that combined have a worldwide market potential significantly in excess of $200 billion," according to management.

One of its first acquisitions is a telling one: Pfizer has purchased the diagnostic rights to three gene discovery programs of Genizon BioSciences (St. Laurent, Quebec, Canada), which has a proprietary gene discovery platform using whole-genome association studies of Quebec's founder population and also provides genotyping and genetic analysis services. Genizon retains the therapeutic rights.

Under the terms of the license and collaboration agreement, Pfizer will pay Genizon upfront license fees and funding for research on genetic variations associated with Alzheimer's disease, attention deficit hyperactivity disorder, and endometriosis. Pfizer will also purchase an equity stake in Genizon. Financial terms of the deal were not disclosed.

The deal will give Pfizer access to genetic markers of disease susceptibility, which could translate into predictive diagnostics for these conditions and valuable companion diagnostics for drugs in Pfizer's pipeline.

New ACOG Guidelines Urge Earlier Screening For Down Syndrome

The American College of Obstetricians and Gynecologists (ACOG) now recommends universal screening for Down syndrome and other fetal chromosomal abnormalities in the first trimester of pregnancy, according to revised clinical management guidelines published in this month's issue of *Obstetrics & Gynecology*. Down syndrome, the most common major chromosomal abnormality in the United States, occurs in about 5,000 infants each year.

ACOG's recommendations, which are already followed by most academic medical centers but not in many private practices, are based on new markers and strategies

for Down syndrome screening, including nuchal translucency (ultrasound) testing. The guidelines call for a combination of a blood test to screen for biochemical markers of Down syndrome and a nuchal translucency test to be offered to all pregnant women during the first trimester.

Historically, maternal age (of 35 or older at the time of delivery) has been used to identify women at highest risk of having a child with Down syndrome, and these women have been offered genetic counseling and amniocentesis or chorionic villus sampling (CVS). In the mid-1980's, biochemical serum screening for women under 35 was introduced based upon how levels of maternal serum alpha-fetoprotein (AFP) and / or human chorionic gonadotropin (hCG) are affected by Down syndrome pregnancies. This testing was previously performed during the second trimester.

FDA Approves Ortho-Clinical's Chagas Disease Screening Test

The U.S. Food and Drug Administration (FDA) has approved the first test to screen blood donors for Chagas disease, also known as American trypanosomiasis, a potentially fatal parasitic infection. The ORTHO T. cruzi ELISA test system, manufactured by Johnson & Johnson subsidiary Ortho-Clinical Diagnostics (Raritan, NJ), qualitatively detects antibodies to the *Trypanosoma cruzi* parasite in serum and plasma. The test is not yet approved to diagnose the disease.

Caused by a parasite, Chagas disease is endemic to Mexico and most countries in Central and South America. It is transmitted through insect bites, blood transfusions, organ transplants, and in utero via infected pregnant women. The Centers for Disease Control and Prevention (CDC) estimates that 16 to 18 million people worldwide are infected with Chagas disease; of those, 50,000 will die each year. Chagas disease can be treated successfully if detected soon after the infection occurs, but there is no cure once the disease has entered the chronic stage.

The ORTHO T.cruzi ELISA test system is fully automated on the Ortho Summit System. It will be used to screen blood donations for the presence of antibodies that develop in response to exposure to the parasite that can cause Chagas disease. Ortho-Clinical Diagnostics will immediately launch the ORTHO T. cruzi ELISA test system to blood banks nationwide. In addition to screening blood donors, this test is intended for use in screening plasma and serum samples from organ, cell, and tissue donors.

Initiative Seeks Routine SCID Screening For Newborns

A new initiative is laying the groundwork to add severe combined immune deficiency disease (SCID) to the 47 existing screening parameters in Wisconsin's newborn screening program. Several other states are expected to follow Wisconsin's lead. SCID, often called "the bubble boy disease," is one of the most lethal primary immune deficiency diseases. The defining characteristic is usually a severe defect in both the T- and B-lymphocyte systems. Because physicians do not routinely perform a test in newborns to count white blood cells, early diagnosis of SCID is rare.

The pilot program, a collaboration between the State Laboratory of Hygiene at the University of Wisconsin in Madison and Children's Hospital of Wisconsin in Milwaukee, will use residual blood specimens from the state's newborn screening program to develop laboratory testing protocols to demonstrate the feasibility of

routine SCID screening. The goal is to extend this screening to every newborn in Wisconsin, about 70,000 each year.

"SCID can now be cured with a relatively simple bone marrow transplant, if diagnosed in the first weeks or months of life," says Jack Routes, M.D., medical director of Allergy and Clinical Immunology at Children's Hospital of Wisconsin. "We believe routine screening of all newborns will find more SCID babies, whose disease in the past may have been masqueraded as unexplained deaths in early infancy."

The SCID screening initiative is being driven by the Jeffrey Modell Foundation (JMF), a nonprofit research foundation devoted to primary immune deficiency, with funding for the Wisconsin program coming from JMF and Children's Hospital. Other states now considering pilot programs similar to Wisconsin's include California, Maryland, Massachusetts, Missouri, New York, North Carolina, and Ohio.

Wisconsin's State Laboratory of Hygiene has a reputation as an innovator in newborn screening. It was the first laboratory to develop and fully implement routine screening for cystic fibrosis coupled with a treatment program.

Genomic Health Gets United, Aetna Reimbursement For Oncotype DX

Genomic Health (Redwood City, CA) has signed national contracts with both United Healthcare (Minnetonka, MN) and Aetna (Hartford, CT) for Oncotype DX, the company's flagship test that quantifies the likelihood of breast cancer recurrence and predicts the likelihood of chemotherapy benefit for many early-stage breast cancer patients.

The new arrangements establish coverage across all United Healthcare and Aetna plans, for women with early-stage breast cancer. United coverage is scheduled to become effective for claims for services performed after January 2 of this year. Coverage under Aetna began late last year.

Genomic Health launched Oncotype DX in 2004. The test measures the expression of 16 cancer-related genes plus five reference genes of an individual tumor to generate a "recurrence score" to quantify risk of recurrence and likelihood of response to chemotherapy. Oncotype DX is the first commercially available multigene expression assay that has clinical evidence validating its ability to predict the likelihood of breast cancer recurrence, the likelihood of patient survival within 10 years of diagnosis, and the likelihood of chemotherapy benefit.

The company has also recently announced the results of several studies that examined the roles and relationships of genes measured by Oncotype DX, including an analysis of more than 10,000 node-negative tumors indicating that all 21 genes impact the assessment of an individual woman's tumor.

Aetna's Policy on Oncotype DX

Aetna will cover Oncotype DX to assess necessity of adjuvant chemotherapy in women with recently diagnosed breast tumors, where all of the following criteria are met:

- ❑ Breast cancer is nonmetastatic (node negative);
- ❑ Breast tumor is estrogen receptor positive;
- ❑ Breast tumor is HER2 receptor negative or breast tumor is HER2 receptor positive and less than one cm in diameter;
- ❑ Adjuvant chemotherapy is not precluded due to any other factor (e.g., advanced age and/or significant comorbidities); and
- ❑ Member and physician (prior to testing) have discussed the potential results of the test and agree to use the results to guide therapy (i.e., member will forgo adjuvant chemotherapy if Oncotype DX score is low).

Source: Aetna Clinical Policy Bulletin, Tumor Markers (December 2006)

Pharmacogenomics: Are Labs Believing The Hype?

Slowly, test by test, the clinical laboratory industry is entering the field of pharmacogenomics, or what is often called "personalized medicine" or "predictive medicine," the use of advanced molecular diagnostic tools to tailor therapeutics.

Although in some cases the tests have been approved by the Food and Drug Administration (FDA) and marketed, laboratories have been rather slow to adopt the tests. "The whole emphasis on personalized medicine has been way over-hyped," says Jeffrey A. Kant, M.D., Ph.D., professor of pathology and human genetics and director of molecular diagnostics at the University of Pittsburgh Medical Center. "Eventually we'll get there, but in regard to the promise of pharmacogenetics, the clinicians don't know what to do with it. Clinicians are not, by and large, asking for this."

Anticipated Benefits of Pharmacogenomic Testing

- ❑ More powerful medicines
- ❑ Avoid trial-and-error-style drug prescription
- ❑ Improvements in drug discovery and approval process
- ❑ Increased drug safety
- ❑ More accurate dose determination
- ❑ Advanced disease screening
- ❑ Improved vaccines
- ❑ Decrease overall healthcare costs

Although market penetration seems relatively sluggish, it seems that new pharmacogenomic tests are hitting the market every week. Two tests that pioneered this niche of esoteric testing are the Affymetrix AmpliChip Cytochrome P450 Genotyping Test and Third Wave Technologies' Invader UGT1A1 Test.

Affymetrix AmpliChip Cytochrome P450 Genotyping Test

Manufactured and commercialized jointly by Roche Molecular Systems (Pleasanton, CA) and Affymetrix (Santa Clara, CA), the Roche AmpliChip Cytochrome P450 Genotyping test, which runs on the Affymetrix GeneChip Microarray Instrumentation System, was approved by FDA on Dec. 23, 2004. At its simplest, the CYP450 test helps to determine a patient's susceptibility and tolerance for a wide range of drugs.

"The whole emphasis on personalized medicine has been way over-hyped. Eventually we'll get there, but in regard to the promise of pharmacogenetics, the clinicians don't know what to do with it."

The test screens a patient's genome for two specific genes, Cytochrome P450 2D6 and 2C19, which are implicated in the body's ability to metabolize many commonly prescribed drugs. Approximately 25% of all drugs are primarily metabolized by CYP2D6 and CYP2C19. Drugs in this category include antidepressants, antipsychotics, beta-blockers, proton Pump Inhibitors, and anti-epileptics.

There are 29 known polymorphisms (variations in the gene) in the 2D6 gene and two significant polymorphisms of the C19 gene. The CYP450 test distinguishes these polymorphisms in both genes and provides the associated predictive phenotype (poor, intermediate, extensive, or ultra-rapid metabolizer). Detection of CYP2D6 polymorphisms results in the identification of 33 unique alleles, including seven CYP2D6 gene duplication alleles.

The test is performed on a standard blood sample. The laboratory first performs PCR amplification on selected segments of DNA extracted from the blood sample. Amplified and labeled DNA segments, or "PCR products," are then

applied to the AmpliChip CYP450 microarray. The microarray is placed into the Affymetrix hybridization chamber. Once completed there, the PCR products that have bound to the microarray are stained with a fluorescent dye. The entire microarray is moved to the Affymetrix scanner, in which a laser scans the hybridization pattern and software analyzes it to determine which specific genetic information is present.

Third Wave Technologies' Invader UGT1A1 Test

Third Wave Technologies (Madison, WI) has a collaborative agreement with Genzyme Corporation (Cambridge, MA) to manufacture and provide testing using the Invader UGT1A1 Molecular Assay. The Invader UGT1A1 test is used for colorectal cancer patients who are being considered for the chemotherapy agent irinotecan, manufactured by Pfizer under the trade name Camptosar. The Invader UGT1A1 identifies patients who may be at increased risk for adverse reactions to Camptosar. The FDA approved the Invader UGT1A1 Molecular Assay on Aug. 22, 2005.

While irinotecan is an effective treatment for metastatic colorectal cancer, irinotecan-associated toxicity can result in both neutropenia (reduced white blood cell count) and severe diarrhea. The UGT1A1*28 allele that the Invader UGT1A1 Molecular Assay detects, homozygous in approximately 10% of the North American population, has been shown to be an effective genetic marker for predicting irinotecan-induced toxicity. On July 7, 2005, the FDA revised the safety labeling for irinotecan, recommending that treatment be altered for individuals who are homozygous for the UGT1A1*28 allele.

The UGT1A1 gene produces the enzyme UDP-glucuronosyltransferase, which is active in the metabolism of certain drugs. Variations in the gene can affect a patient's ability to break down irinotecan. One study showed that people with one type of genetic variation have a five times greater risk of experiencing irinotecan toxicity. Similar to the Affymetrix AmpliChip Cytochrome P450 Genotyping Test, the Invader UGT1A1 test works with a combination of PCR and Invader chemistry.

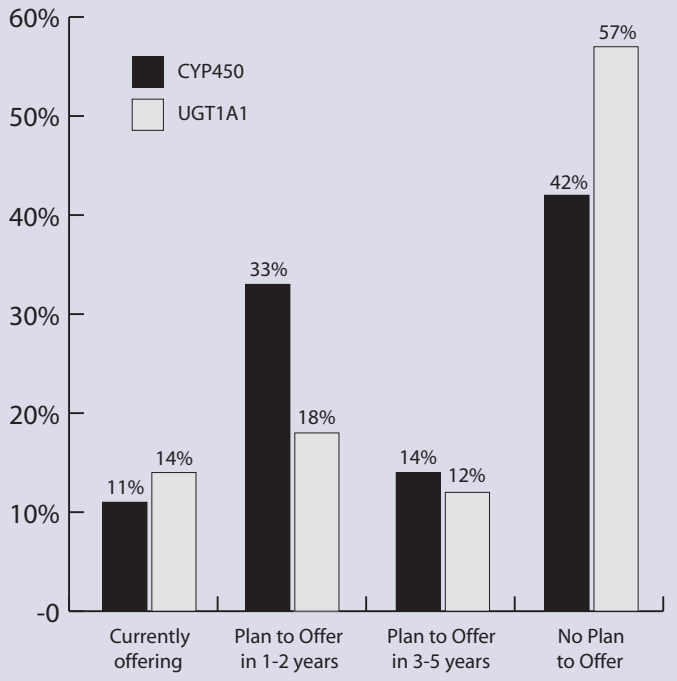
Laboratory Integration

Despite intense media attention to pharmacogenomic tests, this young, highly specialized, and expensive area of molecular-based testing has been relatively slow in its market penetration. The molecular laboratory at Dartmouth-Hitchcock Medical Center was the first to begin offering the Invader UGT1A1 test. According to Greg Tsongalis, Ph.D., director of molecular pathology at Dartmouth-Hitchcock, the lab began marketing the test in the fall of 2005, but demand for the assay has been rather low. Dartmouth-Hitchcock is selling the test at a list price of $300.

Participants in Washington G-2 Reports's 2006 Molecular Diagnostic Test Survey were given a list of 16 molecular tests and asked which ones they currently offer, which ones they plan to offer within one to two years, which ones they plan to offer within three to five years, and which ones they have no plans to offer.

More than a third of respondents indicated they do not have plans to offer HLA-typing (67%); prenatal testing for chromosomes 13, 18, 21, X, Y (61%); UGT1A1 (57%); CYP450 (42%); or HER-2/neu (36%). Although HLA-typing is typically the domain of a flow cytometry laboratory, and HER-2/neu and prenatal testing are typically handled by cytogenetics laboratories, the relatively low interest in CYP450 and UGT1A1 is something of a puzzle, given the amount of media attention personalized medicine receives.

Do You Offer/Plan To Offer CYP450 or UGT1A1 Testing?



Source: Washington G-2 Reports' 2006 Molecular Diagnostic Test Survey

Of the laboratories surveyed, 11% indicated that they were currently offering CYP450, and 14% were offering the UGT1A1. A full third (33%) of laboratories surveyed indicated they had plans to offer CYP450 in the next one to two years, and 18% planned to offer UGT1A1 in the next one to two years. In terms of long-range planning, 14% planned to offer CYP450 in three to five years, and 12% planned to offer UGT1A1 in the same time period.

This test or series of tests may be too new for laboratories to be actively considering adoption, or there may as yet be difficulties in interpretation, as well as in demand. If physicians feel the CYP450 results will limit treatment options rather than fine-tune treatment options, they may be slow to require them.

New Report Questions Clinical Value Of CYP450 Testing For SSRI Patients

Does testing for CYP450 polymorphisms in adults entering selective serotonin reuptake inhibitor (SSRI) treatment for depression lead to improvement in outcomes, or are testing results useful in medical, personal, or public health decision making? This was the overarching question posed by a team of investigators at the Duke Evidence-based Practice Center. The short answer, according to the team's recently issued report, is that it's too soon to tell.

According to the report, supported by a collaboration of the Agency for Healthcare Research and Quality (AHRQ) and the Centers for Disease Control and Prevention's National Office of Public Health Genomics, there is insufficient evidence to determine if CYP450 testing intended to personalize dosing of SSRIs, the most commonly prescribed class of drugs for treatment of depression, improves patient outcomes or aids in treatment decisions in the clinical setting.

This report is the first step in the two-step process of CDC's Evaluation of Genomic Applications in Practice and Prevention (EGAPP) pilot project to evaluate and make recommendations regarding the use of gene-based tests.

Although the report found that CYP450 testing was largely accurate in evaluating differences in genes that affect the rate at which a person metabolizes SSRIs, the researchers did not find any evidence that such tests led to improved patient outcomes or affected treatment decisions for patients with depression. The report also noted that other genetic and non-genetic factors, such as diet and other medical conditions, may affect therapeutic response.

CYP450 Testing: Key Questions

- ❑ What is the analytic (sensitivity, specificity, reproducibility, reliability) and clinical validity of tests that identify key CYP450 polymorphisms?
- ❑ How well does CYP450 testing predict drug efficacy?
- ❑ How well does CYP450 testing predict adverse drug reactions?
- ❑ Do other factors, such as race/ethnicity, diet, other medications, affect test accuracy?
- ❑ What are the harms associated with testing for CYP450 polymorphisms?
- ❑ What are the management options for patients based on CYP450 test results?
- ❑ Does the identification of the CYP450 genotypes lead to improved patient outcomes in terms of decreased symptoms/improved function, mortality/morbidity (avoiding adverse drug responses), or management decisions by patients and providers?
- ❑ What are the harms associated with subsequent management options?

The researchers' literature review turned up no well-designed studies that evaluated clinical outcomes of tests to detect differences in genes belonging to the CYP450 family. They found that the majority of studies included a small number of people, did not test for all variations of the enzymes, and were poorly designed. Most studies also reported the rate of metabolism after just one SSRI dose or were conducted in patients without depression.

SSRI dosing has been considered a particularly good candidate for pharmacogenomic testing, because patient response to this class of drugs is known to vary widely. By sorting out the ultra-rapid metabolizers from the poor metabolizers of SSRIs, CYP450 testing could theoretically prevent side effects and help clinicians to optimize dosing without having to resort to trial and error. The likelihood that a person will experience relief from all symptoms of depression after one year of SSRI treatment is about 40%, and side effects cause 12% to 15% of those who start treatment to stop taking the drug.

"This report emphasizes that well-designed observational studies and clinical trials are needed to clearly establish the clinical validity and utility of the many emerging genomic tests for treatment and prevention of common diseases of public health significance," said Muin Khoury, M.D., Ph.D., director of CDC's National Office of Public Health Genomics. "Early availability of the evidence base is key to the effective use of genomics for the benefit of population health."

"The availability of [Roche's AmpliChip CYP450 Test] has brought the field of pharmacogenentics to the threshold of influencing clinical practice," wrote the study's authors.

Within the next couple of months, the EGAPP working group will issue recommendations on the use of CYP450 tests in the treatment of depression based on the evidence report and other considerations. Future reports that are part of the AHRQ/CDC collaboration will evaluate the use of genomic tests for specific diseases or conditions, such as a rare type of inherited colorectal cancer.

The report, *Testing for CYP450 Polymorphisms in Adults With Non-Psychotic Depression Treated With SSRIs*, can be downloaded from the following Web site: *www.ahrq.gov/downloads/pub/evidence/pdf/cyp450/cyp450.pdf.*

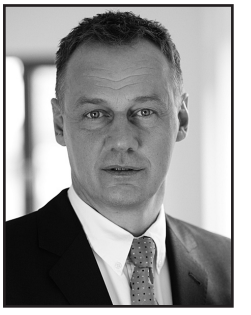
JAMA Study Links Expanded Medicare Reimbursement With Increased Colon Cancer Screening, Earlier Diagnosis

Since Medicare's 1998 reimbursement expansion for colon cancer screening, more Medicare beneficiaries are getting colonoscopies and patients are being diagnosed with colon cancer at an early stage, according to a study published in the December 20 issue of the *Journal of the American Medical Association (JAMA)*. Before 1998, Medicare did not routinely reimburse for colon cancer screening, and many have pointed to this as a barrier to widespread screening and early detection.

In the study, Cary P. Gross, M.D., and colleagues from Yale analyzed data from a Medicare-linked database of individuals who were 67 years of age and older and had a primary diagnosis of colon cancer during 1992 to 2002, as well as a group of Medicare beneficiaries who were not diagnosed with cancer. They found that among the Medicare beneficiaries who did not have cancer, there was an increase in colonoscopy use during the study period, and that patients diagnosed after the reimbursement change were significantly more likely to have early-stage illness than patients diagnosed before the Medicare reimbursement change.

Epigenomics Chooses New CEO, Contracts With Centocor For Cancer Biomarkers

Molecular diagnostics company Epigenomics (Berlin, Germany), which specializes in cancer testing using DNA methylation markers, will appoint Geert Walther Nygaard as its new CEO on February 1. Nygaard, 46, joins Epigenomics from Abbott, where he served as managing director and a member of the management board and was responsible for the diagnostic division. A native of Denmark, Nygaard previously held positions with Beckman Instruments and Dako. Alexander Olek, the founder of Epigenomics, stepped down from his position as CEO in August of last year.


Geert Walther Nygaard

Epigenomics has also recently landed a contract with pharmaceutical company Centocor (Horsham, PA) to identify and analyze potential pharmacodiagnostic biomarkers for use in Centocor's oncology program. Under the agreement, Epigenomics will use its proprietary differential methylation hybridization (DMH) microarray platform to perform genome-wide DNA methylation profiling on samples provided by Centocor. The goal is to identify candidate DNA methylation biomarkers that may support drug development and could ultimately be used to identify those patients that have a higher chance of benefiting from a drug candidate in development at Centocor. Financial details were not disclosed.

In the spring of 2006, Epigenomics began offering its DNA methylation profiling services to pharma and biotech companies looking to identify biomarkers for oncology drugs. Centocor is the fourth client to contract for these services, according to Christina Dahlstroem, Epigenomics's senior vice president of clinical solutions.

▲ **Siemens, GE,** *from page 1*
disorders, infectious diseases, kidney ailments, cardiology, oncology, and virology applications.

In 2005, DPC and Bayer Diagnostics generated combined sales of $2.3 billion, and Siemens spent about $7.4 billion on the acquisitions. Siemens is now touting itself as "the world's only full-service diagnostics company," bringing together, under one roof, medical imaging, laboratory diagnostics, and clinical IT.

As healthcare giants, such as Siemens and GE, bring together specialties that previously had little contact with one another, many see molecular diagnostics as a catalyst. "Siemens talks about the diagnostic value chain, and I think they are right on target," says Bruce Friedman, M.D., active emeritus professor at the University of Michigan Medical School's Department of Pathology. "It's like the three legs of a stool—imaging, in vitro diagnostics, and clinical informatics, and none of them can stand on their own. Together, they are the future of diagnostic medicine."

Luminex To Buy Tm Bioscience For $37.9M

Molecular diagnostics company Tm Bioscience (Toronto, Canada) has been acquired by Luminex (Austin, TX), best known for its xMAP testing platform. Under the terms of the agreement, valued at $37.9 million, each Tm Bioscience share will be exchanged for 0.06 shares of Luminex common stock. This represents a 41.5% premium for Tm shares based on the stock's closing price on the day of the acquisition. The transaction is expected to close in the first quarter of this year.

The purchase will give Luminex an impressive genetic testing portfolio and another powerful platform technology, namely Tm Biosciences's Tag-It assays and platform, and a range of analyte specific reagents (ASRs). Tm Bioscience's products include tests for infectious diseases, as well as tests for genetic mutations related to cystic fibrosis (CF), sepsis, and pharmacogenomic applications. The company's CF test is the first multiplexed human disease genotyping test to be cleared by the FDA for diagnostic use in the United States. For the first nine months of last year, Tm Biosciences reported revenue of C$8.6 million (USD$7.4 million), a 62% increase over the same period of 2005.

BD Closes On $350m TriPath Acquisition

Global medical technology company Becton, Dickinson, and Company (BD; Franklin Lakes, NJ) has closed on its $350 million purchase of the approximately 93.5% of outstanding shares in TriPath Imaging (Burlington, NC), a leading player in the increasingly crowded market for cervical cancer screening. BD has held a 6.5% equity interest in TriPath since 2001, when the two companies began their ongoing collaboration to discover cancer biomarkers.

TriPath is best known for SurePath, its liquid-based Pap test. Every year, 110 million Pap tests are performed worldwide, about half of them in the United States. Washington G-2 Reports estimates that about 20% of U.S. Pap tests use SurePath. In addition to expanding its cervical cancer screening portfolio, TriPath is developing molecular diagnostics for breast, ovarian, and prostate cancers.

IVD Stocks Rose 20% In 2006 Led By Immucor, Cholestech, Digene

The 21 IVD stocks in the G-2 index climbed an unweighted average of 20% last year versus respective gains of 14% and 10% for the S&P 500 Index and the Nasdaq.

Blood-testing company **Immucor** (Norcross, GA) was the best-performing stock in 2006 with a gain of 87% to $29.23 per share. The company has made progress in improving margins on both reagent and instrument sales, and it recently signed a new sales agreement with Quest Diagnostics, which may order as many as 27 of its Galileo instruments in 2007.

Also performing strongly in 2006 was **Cholestech** (Hayward, CA), which climbed 86% to $18.43 per share. The company, which specializes in cholesterol testing, has seen steady revenue gains and recently pushed into the consumer-directed health-care market by teaming up with Life Line Screening to offer cholesterol, glucose, and C-reactive protein testing directly to consumers.

The worst performing IVD stock in 2006 was **Affymetrix** (Santa Clara, CA), which declined 52% to $23.06 per share, reaching its low for the year when it announced a price cut in one of its screening arrays. CFO Greg Schiffman left the company in December to obtain the same position at cancer biotechnology company Dendreon, and Affy is still searching for his replacement. So far this year, the company has rebounded on rosy fourth-quarter earnings projections of about $100 million.

At year-end 2006, the least expensive IVD stock based on its price-to-earnings ratio was **Orasure**, with a P/E of 17, followed by **Johnson & Johnson**, with a P/E of 18.

IVD Stock Review for 2006

Company (ticker)	*Price 12/31/05*	*Price 12/31/06*	*52-Week % Chg*	*P/E Ratio*	*Market Capitalization*
Immucor (BLUD)	$15.57	$29.23	87%	47%	2.29B
Cholestech (CTEC)	9.92	18.43	86	46	285M
Digene (DIGE)	29.17	47.92	64	93	1.18B
Inverness Medical (IMA)	23.71	38.70	63	N/A	1.54B
Third Wave (TWTI)	2.98	4.81	61	N/A	208M
Abbott Labs (ABT)	38.17	48.43	27	25	78.23B
Quidel (QDEL)	10.76	13.62	27	36	457M
Bio-rad (BIO)	65.44	82.52	26	23	2.22B
Meridian (VIVO)	19.76	24.53	24	39	696M
Becton Dickinson (BDX)	59.28	70.15	18	25	17.77B
Abaxis (ABAX)	16.48	19.25	17	48	393M
Johnson & Johnson (JNJ)	58.72	66.02	1	18	193.33B
Gen-Probe (GPRO)	48.79	52.37	7	46	2.72B
Beckman Coulter (BEC)	56.45	59.80	6	27	3.77B
Ventana (VMSI)	42.35	43.03	2	48	1.50B
Cytc (CYTC)	28.23	28.30	0	26	3.23B
Dade (DADE)	40.67	39.81	-3	27	3.47B
Orasure (OSUR)	8.82	8.26	-6	17	394M
Biosite (BSTE)	56.29	48.85	-13	24	906
Bayer (BAY)	40.67	53.36	-31	22	43.19B
Affymetrix (AFFX)	47.75	23.06	-52	200	1.71B
Unweighted Average			**20**		

G-2 Insider

Make 2007 the year that your lab puts molecular diagnostics to work! Learn key strategies for success at **Washington G-2 Reports's 2nd Annual Molecular Diagnostic Conference: Integrating MDx Into Your Lab**, Feb. 7-9, 2007, at the Renaissance Tampa Hotel International Plaza in Tampa, Florida. This year's conference will focus on how to leverage molecular diagnostic manpower, intellectual property, and novel technology.

Conference co-chairperson **Daniel H. Farkas, Ph.D.,** executive director of the Center for Molecular Medicine, will discuss the 10 reasons not to add molecular diagnostics to your test menu—and then consider 10 rebuttals.

Ronald McGlennen, M.D., president and medical director of Access Genetics, will moderate a discussion on the topic of how to select test menus that are right for your lab and business model. Expert panelists **Cindy Johnson,** director of laboratory operations at CentraCare Laboratory Services, and **Mark Tulecke, M.D.,** medical director at Seacoast Pathology, will share their experiences from a variety of practice settings.

Company References

ACOG 202-638-5577

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Siemens Medical Solutions 888-826-9702.

Third Wave 888-898-2357

TriPath Imaging 336-222-9707

United Healthcare 800-328-5979

Biomarkers: Ready for Primetime? **Jorge Leon, Ph.D.,** acting chief science officer for Orion Genomics, will address the question in a discussion of new biomarkers for disease management and therapy selection, including which ones are ready for implementation and how to evaluate and predict market acceptance.

For a complete conference program, go to *www.g2reports.com/molecular07* or call 1-800-401-5937, ext. 2.

Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by Washington G-2 Reports, 3 Park Avenue, 30th Floor, New York, NY 10016-5902. Tel: 212-244-0360. Fax: 212-564-0465. Order line: 212-629-3679. Web site: www.g2reports.com.

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