Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

Vol. V, No. 6/February 2005

CONTENTS

WASHINGTON G-2 REPORTS

Established 1979

Roche Still Waiting For Full Clearance Of AmpliChip

On December 23, the FDA cleared Roche's AmpliChip Cytochrome P450 Genotyping Test for use with the Affymetrix's GeneChip Microarray. In a press release, the FDA said the test was "the first DNA microarray test to be cleared by the FDA, and its clearance paves the way for similar microarray-based diagnostic tests to be developed in the future."

Furthermore, Lester Crawford, D.V.M., Ph.D., acting FDA Commissioner, declared, "Physicians can use the genetic information from this test to prevent harmful drug interactions and to assure drugs are used optimally, which in some cases will enable patients to avoid less effective or potentially harmful treatment choices."

However, the FDA has cleared only one of the two genes that are analyzed on the microarray—the CYP2D6 gene has been cleared, but the CYP2C19 has not. This means that Roche still cannot market the complete test, which is designed to analyze variations in both genes to determine how an individual patient will metabolize certain drugs. A Roche spokesman would only confirm that the company was still awaiting approval for the second gene, CYP2C19.

DTTR speculates that the FDA may have rushed a press release for AmpliChip in an effort to soften criticism it has received for approving the prescription drugs Vioxx, Celebrex, Bextra, and Aleve, which have now been shown to be harmful to certain patients. *DTTR* believes the current prescription drug controversy is likely to accelerate the "pharmacogenomic revolution" and be a boon for all diagnostic companies and laboratories involved in genetic testing. *More details on page 12.*

XDx Raises $20M; Launches Molecular Transplant Test

XDx Inc. (South San Francisco, CA) has raised $20 million from a fourth round of venture capital funding to help with the commercial launch of its AlloMap molecular expression testing. AlloMap is a real-time PCR-based blood test, which monitors immune-system rejection for heart transplant patients.

The venture firm Sprout Group (New York City and Menlo Park, CA) led the latest round of financing with a $7 million investment. Other investors included JP Morgan's Bay Area Equity Fund, Integral Capital Partners, and Burrill & Company. Since its inception in 2000, XDx has raised a total of $44 million. The company's largest shareholders are the venture capital firms Kleiner Perkins and Texas Pacific Group. *Continued on p. 2*

Pierre Cassigneul

▲ XDx Launches Molecular Transplant Test, *from page 1*

Pierre Cassigneul, chief executive of XDx, says the company received a CLIA certificate for its 4,000-square-foot laboratory in South San Francisco in November and has just begun selling AlloMap as a homebrew test. XDx is charging $2,950 per test.

Cassigneul says the initial targeted market is the eight transplant centers that participated in the validation trial, including Cleveland Clinic, Columbia University, Ochsner Clinic, Stanford University, Temple University, University of California at Los Angeles, University of Florida, and the University of Pittsburgh. These eight centers account for roughly 20% of the 2,200 heart transplants that are performed each year in the United States, according to Cassigneul. He says the company is in the process of hiring a direct sales force to begin marketing the test to all 252 transplant centers in the United States.

Cardiac biopsy is the current standard method of monitoring for rejection in heart transplant recipients. In this procedure, biopsy shears are inserted into a vein in the patient's neck and threaded through blood vessels into the heart. Small pieces of the heart muscle are clipped off and sent to pathologists to evaluate whether inflammatory patterns in the specimen indicate rejection.

XDx at a Glance

Founders:	Jay Wohlgemuth, M.D., Peter Aultman, Ph.D., Tom Quertermous, M.D.
CEO:	Pierre Cassigneul
Headquarters/lab:	South San Francisco
Test name/price:	AlloMap/$2,950
Employees:	54
Est'd revenue, 2005:	$10 million
Total venture capital:	$44M raised in four series of financings

Source: XDx

Most heart transplant recipients have at least 10 cardiac biopsies in the first-year post-transplant, and periodic biopsies often continue thereafter, according to Cassigneul. He notes that these invasive procedures are necessary despite the fact that over 75% of the time, they provide a negative result—the patient's immune system is not rejecting the transplanted heart. He estimates that each cardiac biopsy has a total average cost of roughly $5,000, including the cost of the heart cath lab and cardiologist and pathologist fees; average turnaround time for results is two days.

XDx is offering AlloMap molecular expression testing as a non-invasive and less-costly alternative for monitoring rejection for stable outpatients (not for emergency patients). Results are expected to be provided within three days.

AlloMap was developed from a study (*The Cardiac Allograft Rejection Gene Expression Observational Study—CARGO*) initiated in 2001 that involved the eight leading U.S. transplant centers mentioned above. The study monitored 650 cardiac transplant recipients and their post-transplant course, consisting of 5,000 clinical encounters.

The test involves real-time PCR expression measurement of a panel of genes derived from peripheral blood cells and applies an algorithm to the results. The algorithm outcome is a single score that correlates strongly to immune status and predicts the likelihood of rejection, according to Cassigneul.

He anticipates that XDx will generate about $10 million (equal to 3,390 tests priced at $2,950 each) of revenue from AlloMap in 2005 and reach profitability in mid-2006. He says the company is developing a similar test for lung transplants as well as tests for various autoimmune diseases, such as multiple sclerosis, rheumatoid arthritis, Lupus, and Crohn's Disease. At least one of these tests will be in late-stage validation by the end of 2005, with a potential launch in mid-2006, according to Cassigneul.

XDx was founded in 2000 by three scientists/physicians: Peter Aultman, Ph.D., chief executive of the biotechnology firm BioCardia (South San Francisco); Tom Quertermous, M.D., chief of cardiology at Stanford University; and Jay Wohlgemuth, M.D., vice president of clinical and new product development at XDx. Cassigneul joined the company as chief executive in mid-2003. He has 20 years experience in the diagnostics industry, including, most recently, as vice president of diabetes management at Becton Dickinson.

NEJM Study Shows Mixed Results For Exact's PreGen-Plus Test

The *New England Journal of Medicine* (*NEJM*) has published the results of Exact Sciences' major study of its stool-based DNA test, PreGen-Plus, which showed that the test was four times more sensitive in detecting colorectal cancer than the widely used fecal occult blood test (FOBT), Hemoccult II. However, when compared with colonoscopy, PreGen-Plus was only one-half as sensitive.

The study, published in the December 23 issue of *NEJM*, looked at 4,404 people who were at least 50 years old, had no symptoms of cancer, and were at average risk of the disease. Eligible patients submitted one stool specimen for DNA testing, underwent standard Hemoccult II testing, and then underwent colonoscopy.

The DNA test panel detected 16 of 31 invasive cancers, whereas Hemoccult II identified four of 31 (51.6% vs. 12.9%). The DNA test detected 29 of 71 invasive cancers plus adenomas with high-grade dysplasia, whereas Hemoccult II identified 10 of 71 (40.8% vs. 14.1%). Among 418 subjects with advanced neoplasia (defined as a tubular adenoma at least 1 cm in diameter, a polyp with a villous histologic appearance, a polyp with high-grade dysplasia, or cancer), the DNA test was positive in 76 (18.2%), whereas Hemoccult II was positive in 45 (10.8%). Specificity in subjects with negative findings on colonoscopy was 94.4% for the DNA test and 95.2% for Hemoccult II.

Sensitivity of PreGen-Plus and Hemoccult II

	Invasive cancers	*Adenomas with high-grade dyplasia*	*Advanced neoplasia*
PreGen-Plus	(16/31) 51.6%	(29/71) 40.8%	(76/418) 18.2%
Hemoccult II	(4/31) 12.9%	(10/71) 14.1%	(45/418) 10.8%

Source: *New England Journal of Medicine* (Vol. 351, No. 26: 2704-2714)

"The findings show that the genetic test cannot yet be recommended," Steven Woolf, M.D., of Virginia Commonwealth University, wrote in an editorial in the same issue of the journal. Woolf cited the high cost of the DNA test (list price: $795) versus the FOBT ($3 to $40). He also questioned whether people would be any more willing to collect an entire stool sample for DNA testing than they are to take smears for an FOBT.

Xenomics Developing Urine-Based Test For Down's Syndrome

Randy White, Ph.D.

Xenomics (New York City) is developing a urine DNA test for detecting Down's Syndrome that could provide pregnant women with a safer and quicker alternative to amniocentesis tests. A homebrew version of the Xenomics test could be on the market within 18 months with FDA clearance possible by year-end 2006, according to Randy White, Ph.D., chief executive.

The test involves the analysis of transrenal nucleic acids (Tr-NA's), which are fragments of DNA that have moved from the blood stream through the kidneys, where they accumulate in urine. Tr-NA's, like circulating DNA, contain genetic information from all cell types of the body. "These pieces are unique, and we can tell where they came from—from a fetus, from a tumor, from a transplanted organ," says White. In addition, he notes that urine is a relatively simple aqueous solution and, unlike plasma, contains fewer components that can attack and break down these DNA fragments.

Using the Xenomics method, a woman could provide a urine sample during an OB/GYN visit as early as six weeks after pregnancy. The sample would be sent to a lab where the Tr-NA's could be isolated and analyzed for abnormalities associated with Down's Syndrome, using the company's reagents and conventional methods like PCR amplification, says White. He estimates reference labs could perform the test for about $400 with a turnaround time of less than 24 hours.

Because of the risks associated with amniocentesis, the procedure is usually only recommended for women older than 35 years. However, White believes that the safety offered by the Xenomics test might open it to the entire six million pregnancies (4.1 million births) that occur each year in the United States.

Today's methods for detecting or evaluating the risk of having a baby with Down's Syndrome include the triple screen and amniocentesis. The triple screen is a blood test used to identify pregnancies at higher-than-average risk of certain serious birth defects, including Down's Syndrome. The test is usually performed after 15 weeks of pregnancy at a lab price of roughly $100. Women with abnormal test results are usually offered further testing with ultrasound and/or amniocentesis.

Approximately 150,000 to 200,000 amniocentesis tests are performed each year in the United States. White says that approximately 1.6 million women annually are recommended to have the procedure, but the compliance rate is only 1 in 8. Because amniocentesis involves a risk of miscarriage (1-2 miscarriages per 400 procedures, according to the CDC), many women chose not to have it performed. Amniocentesis is also more expensive, with an average total cost of about $1,200, including physician, ultrasound, and lab charges, according to White.

He believes the Xenomics test could be used as a replacement to the triple test. It would give pregnant women and their doctors a definitive answer about Down's Syndrome, rather than level of risk, thereby reducing the number of amniocenteses that would need to be performed for final confirmation.

White says that Xenomics is developing additional prenatal tests using its Tr-NA technology; the next nearest to reaching the market is a test for Rh incompatibility.

Xenomics was founded in April 2002 by its chairman, David Tomel, Ph.D., and its chief scientific officer, Samuil Umansky, M.D., Ph.D., in April 2002. White joined the company in September 2004 and was formerly chief executive at Nanogen (San Diego, CA) from June 2001 to December 2002. White also served as executive vice president of technical operations and research and development at American Medical Laboratories (Chantilly, VA) from 1999 to 2001.

How Big Will The BNP Testing Market Grow?

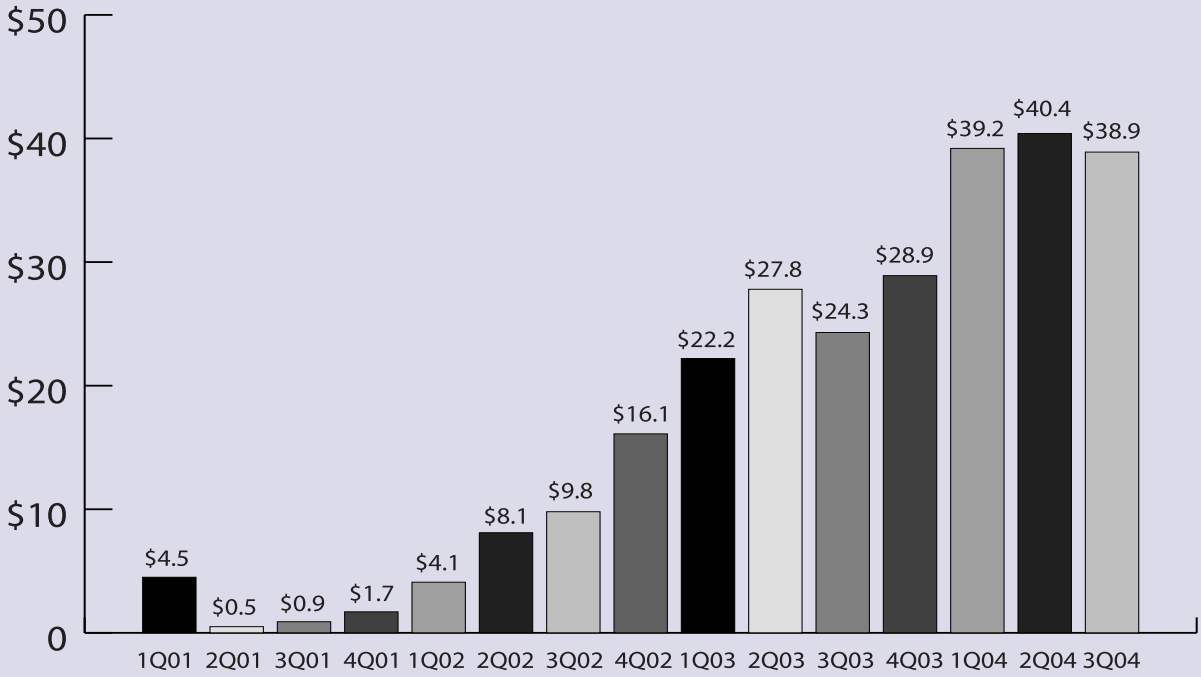
BNP tests measure levels of B-type natriuretic peptide, or BNP, a hormone that is elevated in patients suffering from congestive heart failure. CHF is the single most common cause of hospitalization in the United States for patients older than 65, with more than one million hospitalizations per year.

The U.S. market for B-type natriuretic peptide (BNP) testing has surged to an estimated $200 million per year in kit sales in the four years since Biosite (San Diego, CA) introduced the first FDA-cleared BNP test. The test has already become one of the largest and most profitable ever for the IVD industry. And even though approximately 70% of all hospital labs in the United States now perform BNP testing, the size of the market is still expanding rapidly due to increasing utilization.

The market for BNP got a boost in 2003 when CMS established a specific CPT code for BNP testing (CPT 83880) at a reimbursement rate of $47.43 under the Medicare Part B fee schedule. Previously, BNP testing had been reimbursed under CPT code 83520 (immunoassay, not otherwise specified) at $17.89. Biosite and other reagent manufacturers sell their BNP tests at an average price of between $15 to $21 per test, leaving plenty of room for profit for laboratories performing outreach/outpatient BNP testing, observes *DTTR*.

Although five major IVD companies have now received FDA clearance and three more are expected to this year, Biosite has remained the market leader in BNP test sales. The company's current annual run rate for its Triage BNP point-of-care test is nearly $160 million, representing an estimated 80% of all BNP test sales in the United States. Kim Blickenstaff, chairman and chief executive of Biosite, believes the total U.S. market could reach $350 million to $400 million in a few years.

Biosite's Quarterly Revenue from Triage BNP *($ millions)*



Source: Biosite

In the nine months ended Sept. 30, 2004, Biosite added 614 new BNP customers to reach a total of 3,093, including 2,736 hospitals and 357 physician office labs. Blickenstaff says that roughly half of Biosite's new customers are now coming from the sale automated BNP test kits through the company's arrangement with Beckman Coulter (*see page 6*).

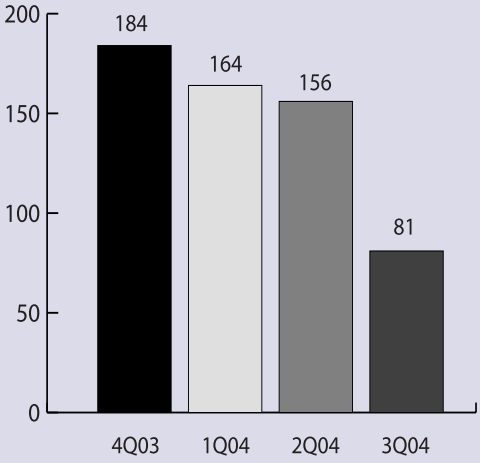
But new competition from automated tests sold by Roche, Bayer, Abbott, and Dade has started slowing Biosite's ability to add new hospital customers. In third-quarter 2004, Biosite added only 81 hospital customers, down from 156 added in the second quarter, 164 added in the first quarter, and 184 added in fourth-quarter 2003 (*see graph on page 6*).

Blickenstaff says that the pricing competition from Roche, Bayer, Abbott, and Dade has been fairly rational. "They are trying to sell the benefits of automation, rather than lower pricing," he adds. The lowest prices he has seen from competitors has been $15 per test, but after factoring in the costs of calibration and controls, the complete costs gets nearer to Biosite's average selling price of $20 to $25 per test (after distributor markups), according to Blickenstaff. He says Bayer has been Biosite's toughest BNP competitor to date.

Nonetheless, Blickenstaff says that many of Biosite's hospital customers have gotten used to the Triage BNP test. "There's less of a hassle factor and a quicker turnaround time [20 minutes]," he notes.

To help offset the growing competition in the hospital market, Blickenstaff says Biosite is focusing more attention on BNP test sales to physician office labs and the international markets. But, he says the physician office market has been hard to crack because "they don't know how to integrate BNP testing into their practice." In addition, *DTTR* notes that Triage BNP has not yet received CLIA-waived status, even though the company filed an application with the FDA more than two years ago.

Net New Hospital Customer Additions for Biosite



Source: Biosite

Blickenstaff says the international markets currently represent just 10% of Biosite's overall sales, but the company hopes to raise that figure to 33% over the next five to eight years. "The heterogeneity of payer systems throughout the world is a challenge," he notes. He says France is currently Biosite's fastest-growing international market. "France has the highest recognition of the impact point-of-care testing has on global costs," he observes.

Finally, he says Biosite is working to bring new products to market to diversify its revenue base. Currently, Triage BNP sales ($160 million per year) account for nearly two-thirds of the company's total annualized revenue of $245 million. Among the most promising new products is the Triage Stroke Panel, a rapid immunoassay for diagnosing stroke. Biosite submitted a premarket approval application for the test in early January and market launch is expected in about one year, according to Blickenstaff.

Biosite's Triage BNP test currently holds an estimated 80% market share in the United States, but competing tests are gaining ground. Here's a quick update:

Bayer Diagnostics (Tarrytown, NY) received FDA clearance for its automated BNP test in June 2003. Bayer has developed its BNP test for use on its automated Advia Centaur Immunoassay System based on a licensing agreement with the Japanese pharmaceutical company Shionogi & Co., Ltd. (Osaka, Japan). BNP has been Bayer's fastest growing test since its market introduction in late 2003, according to Tony Bihl, senior vice president of business planning and administration and acting head of the diagnostics division at Bayer.

Roche Diagnostics received FDA clearance for its Elecsys proBNP test in December 2002. Initial marketing efforts have been focused on the hundreds of labs in the United States where Elecsys instruments are installed. The test has been sold in Europe since late 2001. Heino von Prondzynski, head of the diagnostic division at Roche, believes the U.S. market for BNP testing, which he estimates is currently $200 million to $220 million, will continue to expand. "This is not the end. There's still room for more players. That's why we've licensed proBNP to Dade and OCD," he tells *DTTR*.

IVD Manufacturers with BNP Tests Cleared by the FDA

Company	FDA Clearance
Biosite	November 2000
Roche Diagnostics	December 2002
Bayer Diagnostics	June 2003
Beckman Coulter	December 2003
Axis/Shield/Abbott Diagnostics	January 2004
Dade Behring	July 2004
Diagnostic Products Corp.	expected sometime in 2005
Ortho-Clinical Diagnostics	expected sometime in 2005
Nanogen	expected sometime in 2005
i-Stat/Abbott Diagnostics	expected sometime in 2005

Source: *DTTR* from companies

Biosite developed an automated version of its Triage BNP Test in partnership with **Beckman Coulter** and received FDA clearance in December 2003. Under the agreement, Beckman Coulter manufactures the automated test for its immunoassay systems, and Biosite sells and markets the product. A Biosite spokeswoman says that since market launch in January 2004, it has gained "several hundred" hospital lab customers for the automated test.

Axis-Shield (Oslo, Norway) received FDA clearance for a BNP test for use on **Abbott Diagnostics'** AxSym system in January 2004. The test is exclusively marketed and distributed by Abbott worldwide, except in Japan. In addition, Abbott acquired **i-Stat Corp.** in late 2003 and a rapid BNP test for i-Stat's handheld analyzer is in development.

Dade Behring received FDA clearance for its proBNP test (licensed from Roche) in July 2004. In addition, **Diagnostic Products Corp.** and **Ortho-Clinical Diagnostics** are developing proBNP tests for their immunoassay systems as well, and each expects FDA clearance by year's end.

Finally, **Nanogen** (San Diego, CA) gained access to a non-exclusive license to Roche's proBNP marker when it acquired **SynX Pharma Inc.** in April 2004. Nanogen hopes to introduce a point-of-care proBNP test to the U.S. market by year's end.

NEJM Study Says OncotypeDx May Reduce Unneeded Chemotherapy

A study published in the December 30 issue of the *New England Journal of Medicine* (*NEJM*) shows that the OncotypeDx test can accurately quantify the likelihood of recurrence for women with breast cancer that has not yet spread elsewhere in the body. The test could potentially spare tens of thousands of women from unnecessarily undergoing expensive and often debilitating chemotherapy.

Approximately 50,000 to 100,000 women are diagnosed with localized breast cancer in the United States each year. Many of these women undergo unneeded chemotherapy after getting surgery and radiation.

OncotypeDx uses real-time PCR to analyze 21 genes associated with breast cancer from fixed-paraffin biopsy tissue. The test provides a quantitative score that physicians can use to help decide whether chemotherapy will benefit a breast cancer patient.

The NEJM article was based on an independent multi-center study of stored tissue from 668 patients who had undergone treatment in the Breast and Bowel Project from 1982 to 1988. All were tamoxifen-treated patients with node-negative, estrogen-receptor-positive breast cancer.

The test accurately predicted which patients were most likely to have gone on to suffer a recurrence in the next decade. Of the 51% of patients that scored in the low-risk group, only 6.8% had a recurrence. Of the 22% in the intermediate-risk category, 14.3% had a recurrence. And of the 27% at high risk, 30.5% suffered a recurrence.

Genomic Health (Redwood City, CA) helped develop and owns the rights to OncotypeDx (see *DTTR*, September 2004, pp. 5-6). The company is performing the test at its CLIA-certified lab near San Francisco at a list price of $3,460.

Icelandic Study Shows Many Cancers Are Hereditary

Inheritance plays a part in 16 out of 27 cancers, according to a recent study published in the open-access journal *Public Library of Science Medicine* (*PLoS Medicine*).

The study, conducted by Decode Genetics (Reykjavik, Iceland), examined the rates at which cancer occurred among all first- to fifth-degree relatives of 32,000 patients who had cancer diagnosed between 1955 and 2002. A first-degree relative is a parent or child or sibling who shares 50% of an individual's DNA. Fifth-degree relatives, such as great-great-great grandparents, share 3.125% of DNA with an individual.

Decode utilized patient information from the Icelandic Cancer Registry and linked it to an extensive genealogical database, containing all living Icelanders and most of their ancestors since the settlement of Iceland by the Vikings in the 9th and 10th centuries.

The study found that 16 of the 27 cancers types looked at showed significant "familiality," in which the risk extended to distant (third- to fifth-degree) relatives. The seven diseases with the highest increased familial occurrence both in close and distant relatives were breast, prostate, stomach, lung, colon, kidney, and bladder cancers.

The Role of Heredity and Lifestyle/Environment for Various Cancers

Cancer Site	Number of Cancer Cases Studied	Heredity a Factor? (1°-5° Relatives)	Mates at Higher Risk?
Breast	3,812	Yes	No
Prostate	3,380	Yes	No
Lung	2,904	Yes	Yes
Stomach	2,890	Yes	Yes
Colon	2,224	Yes	Yes
Bladder	1,384	Yes	No
Kidney	1,227	Yes	No
Thyroid	957	Yes	No
Pancreas	930	Yes	No
Ovary	906	Yes	na
Non-melanoma skin	781	No	No
Rectum	767	Yes	No
Endometrium	753	Yes	na
Cervix uteri	724	Yes	na
Brain	663	No	No
Melanoma skin	618	No	No
Esophagus	535	Yes	No
Diffuse non-Hodgkin's lymphoma	422	No	No
Multiple myeloma	391	No	No
Lymphoid leukemia	368	Yes	No
Myeloid leukemia	342	No	No
Meninges	291	Yes	No
Liver	257	No	No
Lip	244	No	No
Hodgkin's disease	239	No	No
Testis	222	No	na
Larynx	208	No	No

na=not applicable (sex-specific disease)

Source: *Cancer as a Complex Phenotype: Pattern of Cancer Distribution* within and beyond the Nuclear Family (*http://medicine.plosjournals.org/archive/1549-1676/1/3/pdf/10.1371_journal.pmed.0010065-S.pdf*)

Another significant finding was that cancers in certain sites also showed a familial association with other cancers—for example, relatives of individuals with colon cancer are at an increased risk not only for cancer of the colon, but also for cancers of the rectum, prostate, and stomach.

Three cancers—stomach, lung, and colon cancer—were also seen more frequently in the spouses of patients, confirming that shared lifestyle or environmental factors also contribute substantially to the increased risk.

"The next step is to isolate the key genes contributing to the common forms of the disease and to use this to develop better medicine," said Kari Stefansson, M.D., chief executive of Decode.

Decode was founded in 1996 with the goal of developing drugs and DNA-based diagnostics. In June 2001, Decode signed a five-year alliance with Roche's diagnostics division to develop DNA-based tests that can identify individuals who are highly predisposed to disease or are likely to respond to particular drugs.

The alliance has made progress for tests that determine predisposition to osteoporosis, heart attack, stroke, and drug response to asthma and hypertension, but no products have reached the market yet. Since its inception, Decode has accumulated losses totaling $368 million.

What's Next For Diagnostic Products Corp.?

In late December, *DTTR* got the opportunity to speak with Michael Ziering, chief executive of Diagnostic Products Corp. (DPC-Los Angeles), about his outlook for the company in the new year. Here's a summary of our interview:

DTTR: *Please update your progress in resolving DPC's issues with the FDA.*
Ziering: We still believe that by the end of first-quarter 2005, we could be off the FDA's AIP. The independent auditor has completed their audit of our corrective

Michael Ziering

action plan and we can comply with their recommendations. It now depends on how long before the FDA can come in and look at our corrective actions and sign off on our plan.

[Note: In February 2004, DPC was informed by the FDA that, based on data integrity and procedural issues related to the company's application for the Immulite Chagas test, the company was subject to the FDA's Application Integrity Policy ("AIP"). The FDA suspended its review of all pending and future applications submitted by DPC until these issues are resolved (see *DTTR*, April 2004, page 8). The suspension does not affect DPC's ability to bring new tests to markets outside the United States.]

DTTR: *What tests does DPC plan to add to its U.S. menu this year?*
Ziering: The biggest new test for us in the United States, assuming we resolve our issues with the FDA, and internationally will be proBNP, which we have licensed from Roche. We also hope to bring an ANA screen and Epstein Barr test to worldwide markets.

In the U.S., for our Immulite 2500, we're also planning a new faster test for B12/folate and a hepatitis B test [already on the market internationally].

Internationally, we just rolled out an Internet-based service for monitoring and servicing our systems. In the U.S., we have 200 customers hooked up so far.

Longer term, we're planning to bring our Immulite 3000 system to market in late 2006/early 2007. This system is designed for larger labs and will perform 300 to 400 immunoassays per hour, with 15-minute stat testing for cardiac tests.

DTTR: *What are your fastest-growing markets outside the United States?*
Ziering: We have been doing well in Brazil and we just started in Vietnam last year. The United Kingdom was fast, then slowed down. Our toughest market is Japan, the second-largest IVD market in the world, where we face competition from Fujirebio and regulatory issues.

[Note: In the first nine months of 2004, DPC grew its worldwide revenue by 18% to reach $325.5 million. Sales to U.S. customers grew by 18% and accounted for 29% of total revenue. Sales in the Brazil region increased by 24% and accounted for 9% of total revenue.]

DPC in Brief *($ millions)*

	9 mos. ended 9/30/04	9 mos. ended 9/30/03	Chg
Total sales	$325.5	$276.6	18%
Immulite products	296.8	243.7	22
Radioimmunoassay	18.3	20.3	-10
Other products	10.5	12.6	-17
Net income	50.6	46.3	9

DTTR: *What is DPC doing to better position itself as the industry moves toward the consolidation of chemistry and immunoassay?*
Ziering: More and more customers are looking for dual systems and that's why we have an alliance with Dade Behring. In the United States, Dade distributes our Immulite systems in combination with its Dimension chemistry systems to three group purchasing organizations: Novation, Consorta, and HealthTrust. And we recently formed a marketing alliance with Thermo Electron, which makes chemistry analyzers and automation systems, that covers international markets.

IVD Stocks Rose 30% In 2004 Led By Immucor And Biosite

BioMerieux completed its IPO in July at 30 euros per share and ended the year at 31.75 euros for a gain of 6%.

Twenty-five IVD stocks jumped an unweighted average of 30% last year versus a 9% gain for both the S&P 500 Index and the Nasdaq.

Immucor (Norcross, GA), which specializes in automated instrument-reagent systems for blood banks, led all IVD companies last year with a stock price gain of 159% to $23.51 per share for a market value of $1.1 billion. The company has benefited from the introduction of its automated blood-bank analyzer, the Galileo, which was cleared by the FDA in April 2004. As of Sept. 30, 2004, Immucor had placed 158 Galileo instruments worldwide: 147 in Europe, six in the United States and five in Japan.

Biosite (San Diego) was up 113% to $61.54 per share for a market value of $997 million. The company rebounded after investors realized that sales of its key Triage BNP test were not slowing down, despite competition from the major IVD vendors (*see page 5-7*).

Other IVD stocks that booked gains of more than 80% in 2004 included **Cytyc** (Boxborough, MA), up 99% to $27.57 per share; **Third Wave Technologies** (Madison, WI), up 93% to $8.60 per share; and **Gen-Probe** (San Diego, CA), up 84% to $45.21 per share.

IVD Stock Review for 2004

Company (ticker)	12/31/03 Price	12/31/04 Price	52-Week % Chg	P/E Ratio	Dividend Yield
Immucor (BLUD)	$9.06	$23.51	159%	78	NA
Biosite (BSTE)	28.95	61.54	113%	30	NA
Cytyc (CYTC)	13.84	27.57	99%	46	NA
Third Wave (TWTI)	4.45	8.60	93%	NA	NA
Gen-Probe (GPRO)	24.57	45.21	84%	44	NA
Meridian (VIVO)	10.44	17.55	68%	29	2.3%
Ventana (VMSI)	39.40	63.99	62%	NA	NA
Dade Behring (DADE)	35.74	56.00	57%	36	NA
Affymetrix (AFFX)	24.61	36.55	49%	61	NA
Becton Dickinson (BDX)	41.14	56.80	38%	26	1.2%
Beckman Coulter (BEC)	50.83	66.99	32%	20	0.7%
Johnson & Johnson (JNJ)	51.66	63.42	23%	21	1.7%
Diagnostic Products (DP)	45.91	55.05	20%	25	0.5%
Bayer (BAY)	29.41	33.98	16%	NA	1.8%
Inverness Medical (IMA)	21.78	25.10	15%	35	NA
TriPath Imaging (TPTH)	7.80	8.97	15%	NA	NA
Cholestech (CTEC)	7.64	8.20	7%	16	NA
Abbott Labs (ABT)	46.60	46.65	0%	23	2.2%
Bio-Rad Labs (BIO)	57.67	57.37	-1%	22	N/A
Luminex (LMNX)	9.38	8.88	-5%	NA	NA
OraSure (OSUR)	7.96	6.72	-16%	NA	NA
Abaxis (ABAX)	18.09	14.49	-20%	12	NA
Digene (DIGE)	40.10	26.15	-35%	38	NA
Quidel (QDEL)	10.77	5.08	-53%	12	NA
Exact Sciences (EXAS)	10.12	3.83	-62%	NA	NA
Unweighted Avg.			30%		

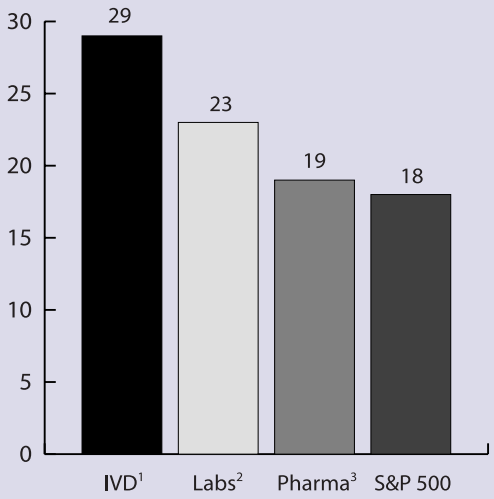
NA=The company has reported a loss in the most recent four quarters or the P/E is 100 or more.

Source: *DTTR*

G-2 Insider

Recent news that Vioxx, Celebrex (and other COX-2 type inhibitors) may have played a role in the deaths of thousands of patients will speed the drive toward pharmacogenomics, *DTTR* believes. But, in addition to the lifesaving clinical benefits personalized medicine can offer, there are also serious economic advantages to be gained.

Comparative P/E Ratios*



*P/E calculated using trailing 12-month earnings
1) Beckman Coulter, Becton Dickinson, Diagnostic Products Corp., Gen-Probe; 2) Bio-Reference, LabCorp, LabOne, Quest Diagnostics; 3) Abbott Labs, Bristol Myers, J&J, Merck, Pfizer Source: *DTTR* as of Jan. 5, 2005

In an article published in the December issue of *Nature Medicine* ("Creating Incentives for Genomic Research to Improve Targeting of Therapies"), researchers from Indiana University noted that only an estimated 60% of prescriptions written produce the desired therapeutic benefits in patients. The remaining 40% either fail to produce a positive response or occasionally harm the patient.

"In 2002, overall prescription drug spending in the U.S. was approximately $162 billion. A back-of-the-envelope calculation suggests that up to $65 billion (or 40% of this total) may have been spent on drugs that, for one reason or another, did not help the patient get well. Pharmacogenomics only addresses some of these treatment failures—those that have genetic roots. Still, the numbers are so large that even a small improvement in targeting could save billions of dollars," said Dr. Barbara Evans, director of the Pharmacogenomics, Ethics, and Public Policy Program at the Indiana University Center for Bioethics.

Certainly, investors are predicting an increasing role for diagnostic tests and laboratories relative to the pharmaceutical industry. After decades of sporting above-market valuations, major drug companies are now trading at price-to-earnings ratios that fall below those of both laboratory and IVD stocks.

Company References

Affymetrix 408-731-5000
Biosite 858-455-4808
Decode Genetics 781-464-0905
Exact Sciences 508-683-1200
Genomic Health 650-556-9300
Immucor 770-441-2051
Roche Diagnostics 317-849-9350
XDx 650-624-0120
Xenomics 212-297-0808

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. Website: *www.g2reports.com*

Jondavid Klipp, Managing Editor; Dennis Weissman, Executive Editor; Janice Prescott, Sr. Production Editor; Perry Patterson, Vice President and Group 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 212-244-0360, ext. 2.