Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Top IVD Execs Preview Prospects For 2005

To get a firsthand picture of what may be in store for the IVD industry this year, *Diagnostic Testing & Technology Report (DTTR)* interviewed top executives at 11 of the world's leading diagnostics manufacturers. For a top down look at the industry we begin with Heino von Prondzynski, head of the diagnostic division at Roche, who anticipates continued pricing pressure on routine reagents. "Only innovation will enable higher prices, but the R&D spending and regulatory demands are also increasing," he notes.

Heino von Prondzynski

Roche gained regulatory approval to sell its new AmpliChip CYP450 microarray for clinical use in Europe in September 2004. Prondzynski estimates that European sales totaled one million Swiss francs (US $870,000) in the three months the chip was available in 2004. He says Roche filed a 510K with the FDA for AmpliChip CYP450 in September and anticipates market clearance within weeks. This would mark the first time that a microarray has been approved for clinical use in the United States. In 2005, Prondzynski says Roche is aiming to get its P53 cancer resequencing microarray on the U.S. market as well as a second generation CYP450 chip.

Meanwhile, Prondzynski says Roche's Elecsys immunoassay business is growing at a 35% annual clip in the United States. New immunoassays planned for launch in 2005 include an osteoporosis test and TORCH panel. As for Abbott Diagnostics, Prondzynski says, "Repairing trust takes more than one year. They are not yet regaining market share."

Prondzynski anticipates that the worldwide diabetes self-testing market will grow by approximately 8% in 2005. New U.S. product launches will include the Accu-Chek Spirit, which will be the first Accu-Chek product coming out of Roche's acquisition of Disetronic.

What's the biggest challenge the IVD industry faces? "Making governments and payers understand that modern diagnostics can help solve their problem in healthcare cost increases," answers Prondzynski. Diagnostic reagents currently comprise about 1% of worldwide healthcare spending, and Prondzynski believes there is long-term potential to reach 2%. "Our message is starting to be heard, especially in the area of pharmacogenomics," he concludes.

Tony Bihl

Tony Bihl, senior vice president of business planning and administration and acting head of the diagnostics division at **Bayer Healthcare** (Tarrytown, NY). Bayer Diagnostics, with approximately $2.5 billion in annual worldwide revenue, is the fourth largest IVD company in the world. The company has 2,300 diagnostic employees in the United States, where its annual revenue is nearly $1 billion.

DTTR: *Can you update us on Advia Centaur placements?*
Bihl: We installed our 3,000th worldwide Advia Centaur in October and in the United States we have 1,200 installations. In 2005, we'll begin marketing the Advia Centaur CP for small and mid-sized labs. [Note: In the nine months ended Sept. 30, 2004, Bayer's revenue from Advia Centaur increased by 22% (adjusted for currency changes) to $425 million.]

The current U.S. menu for Centaur is 60 tests and BNP continues to be our fastest-growing test. New tests additions for 2005 will focus on infectious disease, especially hepatitis. We also plan additions in the cardiovascular and autoimmune areas, including cyclosporine and ANA.

DTTR: *How fast is Bayer's molecular diagnostics business growing?*
Bihl: Our Versant bDNA and Trugene product lines are growing at or above the market in molecular diagnostics. The Trugene HIV-1 Genotyping kit [added with the acquisition of Visible Genetics in late 2002] started off slow, but is now steadily growing.

The reference labs don't easily switch from their homebrew methods. One recent important win has been Specialty Laboratories, which has signed up to use Trugene. We're also seeing increasing demand from hospitals for molecular diagnostics.

Increasing the automation and throughput of our molecular diagnostics systems is a major goal at Bayer. For example, in 2006, we plan on launching the Versant 440 bDNA analyzer to more fully automate branch DNA testing.

DTTR: *How many Advia WorkCell and LabCell automation systems are now in place?*
Bihl: In October, we installed our 100th system worldwide at Pathology Associates Medical Laboratories in Spokane, Washington. We now have more than 60 installations in the United States.

Hospital labs are increasingly looking to diagnostic manufacturers to provide solutions and efficiencies to cope with continued budget pressure and rising test volumes. We're applying Six Sigma management to some of Bayer's operations and we're considering offering it to selective lab clients, especially in the area of planning for automation.

DTTR: *Where is Bayer seeing the strongest growth geographically?*
Bihl: In our Asia/Pacific region, our business is growing particularly well and we continue to see excellent opportunity in this region, including some currently untapped markets. Our business in North America also continues to outpace market growth rates.

DTTR: *What specific area of testing is most likely to shift to the point of care over the next few years?*
Bihl: This shift is already underway in the area of cardiovascular immunoassays. Customers clearly want the shift to continue, particularly if the point of care tests correlate with the central laboratory.


Jim Reid-Anderson

Jim Reid-Anderson, chairman and chief executive of **Dade Behring** (Deerfield, IL). Dade Behring, with annual revenue of more than $1.5 billion, is the sixth largest IVD company in the world. The company's biggest product line is Dimension RxL, which integrates chemistry and immunoassay on one workstation and represents $650+ million in annual worldwide revenue.

DTTR: *In which areas of the world is Dade seeing the fastest growth?*
Reid-Anderson: The United States is our biggest market, and we're currently growing by 6% here. But our fastest-growing markets include Mexico, Brazil, Eastern Europe, India, Singapore, and Taiwan. Over the past few years, Dade has grown its worldwide revenue by 8% to 12% per year. Over the next few years we project long-term revenue growth of 3% to 5% per year.

DTTR: *Describe the trend in reagent pricing?*
Reid-Anderson: It's still very competitive, especially in routine chemistry. Pricing is better in immunoassay because of the new tests coming to market. Geographically, pricing pressure is greatest in Germany and Japan.

DTTR: *What are some of the more important tests and instrument systems Dade is launching?*
Reid-Anderson: In late 2005, we plan to launch a new version of Dimension RxL for mid-sized labs. Our Dimension Vista system for high-volume labs should be on the market in early 2006. And BCS XP, an update to our high-volume coagulation analyzer, should be on the market in third-quarter 2005.

We just launched an NT-proBNP test for our Dimension instruments and we're very pleased with customer uptake. We plan to have it available for our Stratus CS for emergency room point-of-care testing in second-quarter 2005.

We also just announced an agreement with the Cleveland Clinic that gives us semi-exclusive diagnostic rights for the commercialization of automated diagnostic tests for myeloperoxidase (MPO). Researchers at Cleveland Clinic have found that MPO is useful for identifying inflammation in the walls of coronary arteries, which in turn may indicate a risk for heart disease or heart attack. We believe we could have an automated MPO test on the U.S. market within two to three years.

DTTR: *How is your StreamLab automation system doing?*
Reid-Anderson: I'm kind of astonished by the demand for StreamLab [rolled out in mid-2003]. We've now got 32 customers for StreamLab, and we were inundated with questions about the system at the last AACC conference.

DTTR: *What's your outlook on molecular diagnostics?*
Reid-Anderson: It's not clear that the financial returns, especially after you factor in the risks, will be there for molecular test developers. So other than licensing agreements, we're staying out of molecular diagnostics. However, over the very long term, the eight to 10-year range, we believe we could run proteomics-based tests on Dimension Vista in a low-cost format.

DTTR: *What is the biggest challenge the IVD industry will face over the next few years?*
Reid-Anderson: I've got two answers: 1) helping customers deal with continued cost pressure and finding appropriate employees; and 2) raising the profile of the lab industry so that the public understands that doing testing in advance lowers healthcare costs.


John Kershaw

John Kershaw, chief operating officer and managing director of **Sysmex America** Inc. (Mundelein, IL). Sysmex America, which is a subsidiary of Sysmex Corp. (Kobe, Japan), has approximately 4,600 hematology and hemostasis analyzers placed in the United States, giving it the number three market position after Beckman Coulter and Abbott Diagnostics. Sysmex America has 350 employees and posted $125 million to $130 million of U.S. revenue in 2004.

DTTR: *How does Sysmex view the U.S. market?*
Kershaw: With the United States representing a 40% to 45% share of the worldwide IVD market, Sysmex recognizes that the U.S. is its most important market. In the past, Sysmex had somewhat of an inferiority complex regarding our ability to understand the U.S. market and so in 1999 we entered into a sales and distribution agreement with Roche.

But as Sysmex became larger [$700+ million in annual worldwide sales] and the U.S. became more price competitive, the company decided it had the size to go after the higher margins that go with direct selling. In July 2003, Sysmex resumed direct sales, marketing, and service of its hematology products in the U.S.

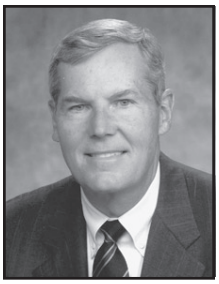
Sysmex has a 12% to 15% market share in hematology in the U.S., and a 30% to 40% share in the rest of the world. Our challenge is to get Sysmex's U.S. share up to where it is in the rest of the world. We're aiming for revenue growth of 25% to 30% per annum.

DTTR: *What are some of the new tests Sysmex will launch in the United States in 2005?*
Kershaw: We'll introduce several new extended differential parameters on our hematology analyzers, including IPF (immature platelet fraction) and RET (reticulated hemoglobin). We also plan to introduce an immunoassay-based fecal occult blood test that is already on the market in Japan.

DTTR: *What are you seeing in terms of reagent pricing trends?*
Kershaw: There's price erosion in routine testing reagents driven by competition. But the U.S. market is willing to pay higher for new analytes and molecular tests. That's different than in Europe and Japan where local governments determine pricing and are generally unwilling to provide extra financing for new tests.

DTTR: *Sysmex's customer base is almost entirely hospitals, what are you seeing out there in the market place?*
Kershaw: There's been a huge increase in outreach activity. More hospitals are now part of IDN systems, and they are creating core labs. The core labs are looking for outreach business to fill their workload capacity.

DTTR: *How does the management style in the United States differ from Japan?*
Kershaw: In the U.S. there is more individual decision making, while in Japan its consensus management. Before managers at a Japanese company make a business proposal, they talk with other executives privately and ask them what they really think of their idea. The proposal is then presented at a formal meeting. Building a consensus beforehand results in fewer changes after a decision has been reached and helps make sure decisions are followed through. In the U.S., business decisions are frequently changed after they have been put in place and that costs money. In Japan, the company is viewed like a family and loyalty is valued. In America, people change jobs every three or four years and that's how you get ahead.



Henry Nordhoff

Henry Nordhoff, chairman and chief executive of **Gen-Probe Inc.** (San Diego, CA). Gen-Probe is a leading provider of molecular diagnostics to clinical laboratories and blood screening labs. The company has nearly 900 employees and generated an estimated $263 million of revenue in 2004, including roughly $127 million from the clinical diagnostics market (primarily from its Chlamydia/gonorrhea tests).

DTTR: *Can you update us on your new molecular diagnostic for prostate cancer?*
Nordhoff: We have licensed the prostate cancer gene PCA3 from a Canadian company named DiagnoCure [see *DTTR*, November 2003, page 1]. And we are developing a diagnostic urine test for the marker that will run on our Tigris system.

Clinical studies have shown that the PCA3 gene is overexpressed 30 to 40 times in the urine of patients with malignant prostate cancer. The PCA3 marker has a positive predictive value of 75% compared with only about 38% for total PSA [*Urology*, Volume 64, Issue 2, August 2004, Pages 315-316].

Right now, Bostwick Laboratories in Virginia is performing a homebrew version of the test. Gen-Probe is developing a second-generation version of the test using our Aptima technology that will run on our Tigris system. We'll have an ASR on the market in about one year.

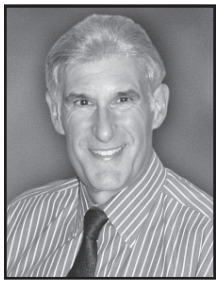
DTTR: *What is the expected pricing of your PCA3 test?*
Nordhoff: That depends on how it gets used. If used as a reflex for patients with a positive PSA level [>4.0 ng/ml] and a negative first biopsy, the test could help eliminate second biopsies. If we can eliminate the $1,000 cost of a second biopsy, then maybe we could charge $100 for our test.

DTTR: *What's the biggest challenge you face in trying to convince labs to use your Tigris system for molecular diagnostics versus Roche's Amplicor or Lightcycler?*
Nordhoff: Our Aptima Combo 2 assay for Chlamydia/gonorrhea is more expensive, but it's more sensitive. We also need to add more tests to the menu. But Tigris has higher throughput. Each Tigris can perform 500 tests per eight-hour shift and one tech can run two to three Tigris's at a time. That's 1,000 to 1,500 tests per shift per tech.

DTTR: *Is molecular testing migrating to local labs?*
Nordhoff: It's happening. A lot of tests are becoming easier to perform and smaller labs want the higher reimbursement associated with molecular diagnostics.

DTTR: *What are some of the new tests you're developing for Tigris?*
Nordhoff: In addition to PCA3, we're looking for sources of licenses so that we can offer an HPV test. I expect to work out a solution to the HPV licensing issue fairly soon. We'd like to create a women's health panel for Tigris that includes Chlamydia/ gonorrhea and HPV that can be performed from liquid Pap specimens. We're also developing a trichomoniasis test. Longer term, we'll be moving into the area of pharmacogenomics.

DTTR: *Will drug companies fight the move toward personalized medicine?*
Nordhoff: Today, healthcare spending accounts for 14.9% of GDP. Prescription drugs account for a big portion of overall healthcare spending, but only one-third of drugs have the desired effect on the patients that take them. There's going to be a lot of economic pressure to move toward personalized medicine. Pharmacogenomics will give drug companies the opportunity to have a higher share of a smaller market. It will also mean easier and cheaper clinical trials.


Stephen Wasserman

Stephen Wasserman, group vice president for diagnostic systems at **Olympus America** (Melville, NY). Olympus America is a unit of Olympus Corporation (Tokyo, Japan). Olympus generated 37.4 billion yen, or $340 million, from worldwide diagnostic sales in the fiscal year ending March 31, 2004, including $104 million in U.S. sales. Olympus has 240 diagnostic employees in the United States, and its chemistry analyzers are used in approximately 1,200 hospital, commercial, and physician office labs.

DTTR: *Which new products will you bring to market in 2005?*
Wasserman: We believe there will be two major areas of opportunity for Olympus in 2005—the immunoassay market and automated blood banking.

We previewed our new AU3000i automated immunoassay system at the American Association for Clinical Chemistry annual meeting this past summer and at the Medica conference in Germany this fall.

We will begin placing the AU3000i at customer sites in Europe late next year and in the United States in early 2006. In the first year of launch, we'll have a 20-test menu and up to 30 tests by the second year. The target market for the AU3000i is mid-to-high volume labs where we expect to leverage our business and growth in chemistry analyzers. In conjunction with the AU3000i launch, we will be launching the Olympus AU-Connector, which allows up to four Olympus clinical chemistry and immunoassay systems to be integrated into a single consolidated workcell.

We will also be introducing the fully automated Tango benchtop blood bank analyzer, which is designed for transfusion services, donor centers, and reference laboratories performing ABO/Rh testing and antibody screening.

Finally, the Olympus SupportVision system for Internet-based real-time monitoring of instruments will be shipped with all AU400^{e} and AU640^{e}'s in January, and AU2700 and AU5400's a month later.

DTTR: *What's the latest news on lab automation at Olympus?*
Wasserman: Our OLA2500 [decaps, sorts, and aliquots 650 tubes/hour] and OLA2500 High Speed Sorter [decaps and sorts 1,200 tubes/hour] systems are now installed in nearly 100 labs in the U.S. and Europe. We're working hard to sell the benefits of a standalone workstation that sorts multiple sample tubes to any analyzer rack. At the same time, we're developing a robotic interface to connect our chemistry analyzers to lab automation track systems.

DTTR: *What is the current trend in reagent pricing in the United States?*
Wasserman: Reagent pricing for routine tests is stable, but pricing for some of the newer tests like Hemoglobin A1c, HDL, and high-sensitivity CRP is under pressure.

DTTR: *How fast is the U.S. diagnostics business at Olympus growing?*
Wasserman: We've grown at an average annualized rate of 14% over the past seven years and should continue to grow in the double-digits for the next few years. Olympus views the United States as a growth market.

DTTR: *Who do you think will win market share over the long term: hospital labs, national labs (Quest & LabCorp), independent regional labs, or POLs?*
Wasserman: I believe hospitals will maintain larger market share because they will create large core labs that can compete with commercial labs.

Christopher Gleason

Christopher Gleason, president and chief executive of **Ventana Medical Systems** (Tucson, AZ). Ventana, which has 618 employees and 2003 revenue of $132.4 million, makes instrument-reagent systems that automate slide staining in anatomical pathology.

DTTR: *What's the size of the market for instruments and reagents for anatomic pathology?*
Gleason: The worldwide market is roughly $1.5 billion and is growing by more than 15% per year, including roughly 7% to 10% each from volume growth and higher prices for new automated systems that lower labor costs. The U.S. market is about $600 million to $700 million and also growing by greater than 15%.

DTTR: *What are Ventana's goals for growth?*
Gleason: We've projected $161 million to $162.5 million for 2004, up 22% to 23% from $132.4 million in 2003. Over the next five years, we expect average annual growth of 20%.

DTTR: *What are Ventana's fastest-growing products?*
Gleason: The adoption of our BenchMark Series platform has been the fastest growing in the history of pathology. [BenchMark is an automated slide-staining system.]

Our fastest-growing tests include our Inform HPV test for tissue specimens. Inform HPV allows the pathologist to visualize the presence of HPV. We currently sell the test in ASR form, but plan an FDA submission sometime in 2005.

Our TheraDx C-kit diagnostic test, which has been cleared by the FDA, is rapidly growing. We began marketing this test in mid-2004 and it has exceeded our expectations. This test is for the qualitative detection of the c-KIT protein in gastrointestinal stromal tumors to help identify patients who will respond to Novartis' Gleevec. As the utility for Gleevec is expanded, the market for our test will get bigger.

Finally, our Confirm EGFR assay is also growing fast. We currently have an ASR on the market and plan a PMA submission to the FDA in 2005. [Colorectal cancer patients with EGFR-expressing tumors are eligible for Imclone's Erbitux treatment.]

DTTR: *What's in the pipeline?*
Gleason: Symphony, the first fully automated system for initial screening of tissue biopsies will come to market in the first half of 2005. This launch will take us into the largest segment of tissue sample testing and a segment where Ventana does not compete today.

DTTR: *What are the biggest changes coming to the anatomic pathology field?*
Gleason: The growth in the number of cancer patients will be substantial. The incidence of cancer is three times greater for people 50 years or older. Today there are about 75 million people in North America age 50 or older. Over the next 15 years this number will increase to 120 million. There will be a corresponding increase in the volume of testing and a need to increase automation. There will be new methods that utilize serum and blood samples, but the ultimate diagnosis will always be looking at the cell through a microscope.

DTTR: *What activity do you see from Quest Diagnostics and LabCorp in anatomic pathology?*
Gleason: Quest Diagnostics and LabCorp have made a significant investment in expanding their AP services. They are looking for ways to bring cost-effective, high volume, and standardized methods to anatomic pathology for hospitals that want to outsource their labs.

Evan Jones

Evan Jones, chairman and chief executive of **Digene Corp.** (Gaithersburg, MD). Digene makes the Hybrid Capture 2 HPV DNA Test, the only FDA-cleared test for detecting human papillomavirus (HPV), which has been shown to be the cause of greater than 99% of all cervical cancer cases. The Hybrid Capture system is installed at approximately 340 lab sites in the United States and 500 in Europe.

DTTR: *What should doctors do when a patient gets a negative Pap and a positive HPV test?*
Jones: Guidelines published in the February 2004 issue of *Obstetrics & Gynecology* recommended that if a woman tests positive for HPV, but has a negative Pap, the two tests should be repeated in six to 12 months. A second positive HPV test should be followed up with a colposcopy.

DTTR: *Describe the economics behind your HPV DNA test?*
Jones: We sell the high-risk test, which tests for 13 HPV types, to labs at an average price of $21 to $22. Medicare reimburses the test at $49.04. Managed care and other third-party payers reimburse labs an average of about $50 per test.

DTTR: *How do you market the test?*
Jones: We've currently got a total of 150 people in sales and technical support in the United States, including 14 sales reps focused on labs and 35 physician office detail reps. By the spring of 2005, we plan to add another 30 physician office detail reps.

DTTR: *What the status of your new automated system?*
Jones: We recently began marketing our automated Rapid Capture system, which allows 350 specimens to be tested per shift versus 90 to 180 specimens for our manual system. We've placed 30 Rapid Capture systems in the U.S. to date.

DTTR: *What kind of growth do you anticipate in 2005?*
Jones: We grew our worldwide revenue by 43% to $90 million in fiscal 2004 (ended June 30, 2004). Worldwide revenue is expected to increase to between $115 million and $120 million in fiscal 2005, including 40% to 50% growth in the U.S. to reach $81 million to $87 million.

Currently 70% of all ASCUS Pap tests in the U.S. have an HPV test follow up, while under 10% of initial cervical cancer screens are for the DNA Pap test [i.e., traditional Pap test plus HPV DNA test]. Our goal is to establish the DNA Pap test as the standard of care over the next 12 to 24 months.

DTTR: *What about the threat of a vaccine for HPV coming to market?*
Jones: Merck and SmithKline are each working on vaccines, and SmithKline has said it plans to submit a filing for regulatory approval in 2006. But the SmithKline vaccine is good for only two strains of HPV [representing 70% of all cervical cancer cases]. Our test covers 13 HPV types. In the long term, there will be HPV vaccines, but they'll be used in conjunction with testing.

DTTR: *What's the outlook for acquisitions?*
Jones: Now that we're profitable [pretax income of $7.2 million in fiscal 2004], we're in a position to make strategic acquisitions. We would like to make one per year over the next several years, with the focus on women's health. We're also looking for licensing agreements so we can distribute promising tests. We have the expertise in getting FDA approval, reimbursement, and educating physicians to create a marketplace for new tests.

Larry Cohen

Larry Cohen, president of **International Technidyne Corp. (**ITC—Edison, NJ). ITC posted revenue of $51.5 million in the nine months ended Sept. 30, 2004, up 33% (up 18% excluding the acquisition of Diametrics) from the same period a year earlier. The company, which is a subsidiary of Thoratec Corp. (Pleasanton, CA), is focused on point-of-care testing. Its ProTime Microcoagulation system (15,000+ worldwide placements) is for prothrombin time testing, while its Hemochron line of analyzers (20,000+ worldwide placements) is used to monitor heparin therapy.

DTTR: *How has the integration of your acquisition of Diametrics gone? [ITC purchased Diametrics and its blood gases/electrolytes point-of-care testing business, "IRMA," in October 2003 for $5 million.]*
Cohen: We have maintained their manufacturing and research and development operations in Roseville, Minnesota, and consolidated sales, technical support, and administrative functions at our headquarters in New Jersey. We've kept a large majority of Diametrics' customers and are now working to develop a system that integrates our Hemochron analyzers with Diametrics' IRMA analyzers.

DTTR: *What's happened since Medicare began covering at-home testing for prothrombin?*
Cohen: It's helped, but there hasn't been a tidal wave of demand. Currently, there are about 3,000 patients using our ProTime system for self testing. It takes time to educate physicians and patients on the reimbursement and technical aspects of at-home testing.

DTTR: *What are some of the key new products ITC will launch next year?*
Cohen: In the first quarter we'll launch our Hemochron Signature Elite, which will include a barcode reader built right into the unit that can scan patient IDs, user IDs, reagent lot number, and expiration date. Tracking testing has become a huge requirement for hospital quality control programs.

In mid-year 2005, we'll add a creatinine test to our IRMA menu for screening patients before getting contrast media for diagnostic imaging procedures. For our Hemochron analyzers, we'll be launching a test for low molecular weight heparin and another for monitoring Angiomax treatment.

DTTR: *What's the current trend in reagent pricing?*
Cohen: Reagent prices in our point-of-care markets are stable. But reimbursement will continue to be the biggest challenge in introducing new point-of-care and self-tests. You've got to be able to demonstrate to CMS why your test results in better outcomes and lower costs over time.

DTTR: *Who will win market share over the long run: hospital labs, commercial labs (Quest and LabCorp), independent regional labs, or POLs?*
Cohen: It's cyclical. Right now it looks like hospitals labs are regaining some of the ground they lost to commercial labs in the past. Over the long term, I believe routine testing will be consolidated at hospitals and commercial labs. Independent labs will continue to exist and prosper, but they're going to need to offer more specialized [i.e., esoteric] tests. Growth in the POL market will depend on reimbursement issues. Tests with the potential to shift more to the point of care in the near term include glycated hemoglobin [HbA1c], prothrombin time, and cardiac markers.

John Puisis

John Puisis, chairman and chief executive of **Third Wave Technologies** (Madison, WI). Third Wave offers a menu of 12 molecular tests in an ASR format for its Invader system for genetic testing. Its highest volume tests are Factor V Leiden and Factor II prothrombin.

DTTR: *How many labs in the United States use Third Wave's Invader technology for clinical testing?*
Puisis: About 115 labs currently and we're adding fifteen to twenty new labs per year. Most of our customers are reference labs. We estimate that the top 150 reference labs perform 80% to 90% of all molecular testing in the United States, but more and more mid-size labs are moving toward molecular diagnostics.

DTTR: *What's in the pipeline for 2005?*
Puisis: Later this month [December 2004], we'll introduce HPV detection reagents as an ASR and next year [2005] we plan to seek FDA approval. We'll also begin the submission process to get our Factor V and Factor II assays cleared for sale in kit form next year.

Other infectious disease tests we plan to bring to market in ASR form in 2005 include herpes simplex viruses 1 and 2, Varicella-Zoster virus [causes Chickenpox and shingles], and cytomegalovirus.

We'll also bring a cystic fibrosis microfluidic card to the market. This will be Third Wave's first product coming out of our partnership with 3M. Microfluidic technology will enable labs to forgo numerous liquid-handling steps and shorten the time to test results.

We expect clinical molecular diagnostic revenue of between $23 million and $26 million in 2005, up from approximately $15 million in 2004.

DTTR: *What are the typical cost savings when a local or regional lab brings a gene-based test inhouse?*
Puisis: That depends on the test and the size of the lab performing it, but most of our customers have a two to three times advantage when they perform a send-out test themselves. In other words, it might cost them $25 to perform a certain molecular test inhouse, but they get reimbursement of $100.

DTTR: *Some of Roche's PCR patents will expire in 2005. What does this mean for Third Wave?*
Puisis: The upcoming expiration of basic PCR patents will allow Third Wave to begin integrating our Invader chemistry system and PCR as early as mid-2005. We believe the combination will provide customers with a highly sensitive, accurate and rapid solution that is even more robust than either of them alone.

DTTR: *What's your outlook for the growth of pharmacogenomics?*
Puisis: This is still a young market, but situations like Vioxx illustrate the need for personalized medicine. [Note: Merck pulled its $2.5 billion a year Vioxx arthritis drug from the market on September 30 after a study showed it doubled the risk of heart attack and stroke in long-term users.] We're definitely seeing more discussion at the government level and with pharmaceutical companies about personalized medicines. Drug companies face the risk of having to pull drugs from the market, or they can get smarter in how they target the appropriate patients for prescriptions.

Stephen Chubb

Stephen Chubb, Chairman and chief executive of **Matritech** (Newton, MA). Matritech sells the NMP22 BladderChek test, a CLIA-waived point-of-care test. Using technology licensed from the Massachusetts Institute of Technology, BladderChek detects levels of the nuclear matrix protein marker NMP22 in urine. NMP22 is elevated in bladder cancer cells by 20- to 80-fold and is released in the urine of bladder cancer patients.

DTTR: *How many physicians in the United States use your BladderChek test?*
Chubb: Approximately 1,000 of the 7,200 urologists that treat bladder cancer have ordered a BladderChek test, and well more than half reorder it.

DTTR: *What's the clinical benefit of BladderChek?*
Chubb: The American Cancer Society estimates that 60,240 new cases of bladder cancer were diagnosed in the United States in 2004 and more than 12,000 people die from the disease each year. If diagnosed in its early stages, the five-year survival rate for bladder cancer exceeds 90%.

In conjunction with a cytoscope examination, BladderChek detects 90% to 95% of tumors. This compares with 80% to 85% for the combination of cytoscope and a urine cytology microscope exam. In addition, BladderChek provides qualitative results in 30 minutes, while a urine cytology is a lab-based test.

We also have a test kit version of BladderChek that provides quantitative results for the level of NMP22 in urine.

DTTR: *What are the economics behind BladderChek?*
Chubb: We have a 15-person direct salesforce that sells the test for $15 to $20 each. Medicare reimburses the test under CPT code 86294 at $25 to $30 depending on the carrier. We're working to get managed care coverage, but that's a slow process.

DTTR: *What's the biggest challenge in getting greater physician adoption?*
Chubb: Physician inertia. Changing practicing patterns isn't easy.

DTTR: *What are some of the new tests Matritech is working on?*
Chubb: Sysmex is developing an automated cervical cancer screening system using our NMP179 precancer protein marker. Sysmex will screen for NMP179 using their flow cytometry technology. The goal is for an 80% automated sort rate, which is about three to four times more than the automated cervical cancer screening systems that are on the market today. Sysmex is anticipating they'll have the system on the U.S. market in 2006.

We also have an agreement with Mitsubishi Kagaku Medical in Japan for the development of our NMP66 protein marker for breast cancer. Preclinical trials are underway, and we could have a test on the market in 2006. This time line could be speeded up if we team up with one of the larger commercial labs, which could then offer the test on a homebrew basis.

DTTR: *When will Matritech achieve breakeven operating results?*
Chubb: We need to reach about $15 million to $25 million in annual revenue to break even with our current operating structure. We recorded $4.4 million of revenue in 2003, approximately $8 million in 2004, and are aiming for over $10 million in 2005. About half of our current sales come from the United States and half from Germany.

G-2 Insider

Cardinal Health throws in the towel on Lab-InterLink. Less than six months after purchasing Lab-InterLink (Omaha, NE) out of bankruptcy for $3.25 million, Cardinal Health (Dublin, OH) has decided it's not worth the time or money to try to rejuvenate the troubled maker of lab automation systems, *DTTR* has learned. Instead, Cardinal has given away Lab-InterLink's assets, intellectual property, and inventory to the University of Nebraska in the form of a charitable donation.

By donating Lab-InterLink, Cardinal, which is under investigation by the Securities & Exchange Commission for previous acquisition-related accounting, will avoid a capital loss and get a larger tax deduction.

Initially, Cardinal had aimed to combine Lab-InterLink with its Pyxis division (San Diego), which sells automated medication dispensing systems to hospitals. But these plans were scrapped after Cardinal acquired Alaris Medical Systems (San Diego), which makes systems that deliver drugs intravenously, in October for $1.6 billion. Cardinal is now working to integrate Alaris with Pyxis and has decided that Lab-InterLink would have been a money-losing distraction.

Meanwhile, *DTTR* hears that the University of Nebraska, which had served as an incubator for Lab-InterLink and its founder Dr. Rodney Markin, is now hoping to sell Lab-Interlink. The only requirement is that the company not be bought and then automatically shut down as Beckman Coulter had tried to do during the initial bankruptcy auction (see *DTTR*, June 2004, page 1). That leaves Abbott, Dade Behring, and Olympus as potential buyers, *DTTR* speculates.

Company References

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914-631-8000

Dade Behring
847-267-5300

Digene 301-944-7000

Gen-Probe 858-410-8000

International Technidyne
800-631-5945

Matritech 617-928-0820

Olympus America
631-844-5690

Roche Diagnostics
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Sysmex America
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