Diagnostic Testing and Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

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Issue 09-12/December 2009

CONTENTS

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Judge Denies Myriad's Motions to Dismiss ACLU Gene Patents Suit

The lawsuit filed in May by the American Civil Liberties Union (ACLU; New York City) and the Public Patent Foundation (New York City) charging that patents on the cancer-associated BRCA1 and BRCA2 genes stifle valuable medical research and clinical care will continue. On Nov. 1, Judge Robert W. Sweet of the Southern District of New York ruled against the defendants' motions to dismiss. The district court is scheduled to hear the ACLU's motion for summary judgment on Dec. 11.

Defendants named in the suit are the U.S. Patent and Trademark Office and Myriad Genetics (Salt Lake City) and the University of Utah Research Foundation, which hold the patents on the BRCA genes. Myriad's BRCAnalysis test, which assesses a woman's risk of developing hereditary breast or ovarian cancer based on detection of BRCA1 and BRCA2 gene mutations, is performed exclusively in the company's CLIA-certified laboratory and costs approximately $3,120, with operating margins of nearly 50 percent. The plaintiffs argue that Myriad's gene patents are unconstitutional and should be invalidated because genes are "products of nature." The suit is the first to apply the First Amendment to a gene patent challenge.

For more about gene patents and the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS)'s new recommendations regarding gene patents and licensing practices, see *Inside the Diagnostics Industry*, p. 5.

Qiagen and Life Technologies to Acquire PCR Array Makers

Two of the world's largest biotechnology tools companies have announced deals designed to boost their offerings in the high-growth market for polymerase chain reaction (PCR) technology. On Nov. 10, Life Technologies (Carlsbad, Calif.) announced that it has agreed to acquire BioTrove (Woburn, Mass.) for an undisclosed amount. One day later, Qiagen (Venlo, the Netherlands) indicated that it will purchase privately held SABiosciences (Frederick, Md.), a developer and manufacturer of disease- and biological pathway-focused PCR arrays, in a cash deal valued at $90 million. The transactions are expected to close by January 2010.

Continued on p. 2

▲ **Qiagen and Life Technologies,** *from page 1*

Acquiring BioTrove will give Life Technologies, formed in 2008 as a roll-up of Invitrogen and Applied Biosystems, a novel platform for genetic analysis. BioTrove's OpenArray platform is a high-throughput gene expression and genotyping analysis system based on a flexible array format that enables researchers to perform up to 3,072 independent PCR or real-time PCR analyses simultaneously on up to 144 samples in a plate the size of a microscope slide.

Life Technologies plans to integrate the OpenArray platform into its Applied Biosystem offerings, namely its TaqMan assay family, which includes more than approximately 1.1 million assays for gene expression and 4.5 million for genotyping applications.

According to Life Technologies, both customer-specified and predefined panels of TaqMan assays will be available for the OpenArray platform under the Applied Biosystems brand. Applied Biosystems previously collaborated with BioTrove to commercialize its OpenArray business for genotyping applications.

The Life Technologies deal does not include BioTrove's RapidFire division, which focuses on the development of drug-discovery technologies using in vitro assays. This division will be spun out of BioTrove and operated independently of Life Technologies under the name Biocius Life Sciences.

Life Technologies' agreement to acquire BioTrove follows its July purchase of privately held Cytonix Corp. for intellectual property related to its microfluidics-based PCR technology.

Qiagen also stands to boost its PCR portfolio through acquisition. Founded in 1998 as SuperArray, SABiosciences designs and commercializes disease- and pathway-focused real-time PCR-based panel assays. These kit-based research tools are widely used to develop diagnostic tests and therapeutics.

The company's primary product line includes more than 100 real-time PCR arrays designed to analyze DNA, RNA, epigenetic, and microRNA targets in biological pathways, including those associated with diseases such as cancer, diabetes, and cardiovascular disorders. The company has approximately 100 employees.

SABiosciences' panel-based approach can facilitate biomarker discovery by allowing researchers to analyze how gene activity in a sample correlates with disease states. Qiagen intends to parlay the acquisition into biomedical and pharmaceutical collaborations, including those related to new diagnostic findings linked to prevention, profiling, and personalized health care.

The deal comes in the wake of Qiagen's September acquisition of DxS (Manchester, United Kingdom), a privately held developer and manufacturer of companion diagnostics, in a deal valued at approximately $95 million in cash plus up to an additional $35 million based on the achievement of specified milestones. Qiagen described the acquisition as part of its efforts to step up its presence in molecular diagnostic-based prevention, profiling, and personalized medicine.

Bostwick Labs Acquires Commonwealth Biotechnologies Businesses

Bostwick Laboratories (Richmond, Va.) has completed its acquisition of the bioanalytical and DNA testing business units of Commonwealth Biotechnologies (CBI; Richmond, Va.). The pathology reference lab paid $1.11 million in cash for the two units, CBI Services and Fairfax Identity Laboratory, in a deal that excluded land and buildings but included a lease commitment of five years.

Bostwick will operate CBI Services as a contract research organization under the name International Biotechnology Services (AIBioTech). It will be a division of American International Pathology Laboratories, Bostwick's anatomic pathology laboratory subsidiary. Fairfax Identity Labs will retain its name. Bostwick will operate both businesses out of the CBI building in Richmond.

The divestment of the two business units is among the conditions of CBI's June 2009 agreement to merge with GL Biochem (Shanghai, China), a global supplier of research-grade peptide products and peptide reagents. The sale of the divisions was approved by CBI's shareholders at the company's annual meeting on Oct. 9.

Having sold its discovery-phase contract research organization (CBI Services) and its DNA reference laboratory business (Fairfax Identity Laboratory), CBI is left with its Australian subsidiary (Mimotopes) and Venturepharm Asia, a contract research consortium specializing in drug discovery and development, cGMP manufacturing, and clinical trial management.

According to CBI's most recent annual report, Fairfax Identity Laboratory generated revenue of $1.9 million from genetic testing in 2008. Founded in 1990, the lab is accredited by the American Association of Blood Banks, the National Forensic Science Technology Center, and the New York State Department of Health. Clinical services, government contracts, and commercial contracts accounted for an additional $7.3 million in 2008 revenue for CBI.

Tethys Bioscience Raises $25 Million to Expand Biomarker-Based Diabetes Testing

Privately held Tethys Bioscience (Emeryville, Calif.) has raised $25 million in a Series D funding round led by Aeris Capital AG. The company will use the financing to expand commercialization of its first and only product, a biomarker-based test to identify patients at high risk of developing type 2 diabetes within the next five years.

Tethys offers its PreDx diabetes risk test exclusively through its CLIA-certified laboratory. The enzyme-linked immunosorbent assay (ELISA)-based test analyzes a fasting blood sample for a defined set of biomarkers implicated in the development of type 2 diabetes, including those related to inflammation, fat and carbohydrate metabolism, coagulation, and cell death. Using an algorithm, it provides a personalized diabetes prediction score between 1 (least risk) and 10 (highest risk). List price for the test is approximately $750.

Tethys is marketing the PreDx test to primary-care physicians. The company is also developing educational materials to assist clinicians in educating high-risk patients about lifestyle and behavioral changes that can help prevent diabetes. Tethys plans to develop biomarker-based tests to quantify an individual's risk of developing other chronic conditions, such as heart disease.

FDA Clears Nanosphere's Respiratory Virus Panel, Automated Instrument

Molecular diagnostics company Nanosphere (Northbrook, Ill.) has received 510(k) clearance from the U.S. Food and Drug Administration (FDA) to market its respiratory virus test panel. The nucleic acid test is for use on Nanosphere's Verigene SP, a fully automated instrument that was cleared along with the test.

'Our target customers are acute care hospitals, ambulatory clinics, and regional reference labs.'
William Moffitt, President and CEO, Nanosphere

The newly cleared test uses RT-PCR and Nanosphere's proprietary nanoparticle hybridization technology to detect and identify influenza A, influenza B, and respiratory syncytial virus (RSV) from nasopharyngeal swabs. It is cleared for use on the automated Verigene SP, a multiplexed, random-access, molecular diagnostic platform that allows for complementary or stand-alone integration into molecular and microbiology laboratories. The instrument is capable of performing protein analysis as well as nucleic acid testing.

In May 2009, Nanosphere received FDA clearance for a first-generation Verigene respiratory virus nucleic acid test.

The company plans to submit additional FDA applications for each of its previously 510(k)-cleared assays to allow their use on the new Verigene SP system, which will be commercially available in early December. These assays include a hypercoagulation panel, a warfarin metabolism assay, and a cystic fibrosis panel.

"Our target customers are acute-care hospitals, ambulatory clinics, and regional reference labs," said Nanosphere President and CEO William Moffitt on a Nov. 5 quarterly earnings call with investors and analysts. He went on to highlight the "four key market segments" into which Nanosphere plans to expand its test menu: human genetics, pharmacogenetics, ultrasensitive protein assays, and infectious disease.

Nanosphere recently completed clinical trials for its troponin assay and has indicated that an FDA filing is imminent. The company has also completed development of an assay for detection of cytochrome P450 2C19 gene variants that lead to diminished response to clopidogrel, the oral antiplatelet drug marketed by Bristol-Myers Squibb and Sanofi-Aventis under the trade name Plavix. In June, the FDA updated the Plavix label to include pharmacogenetic data but has not provided genotype-based dosage recommendations.

Nanosphere plans to initiate clinical trials on its 2C19 essay by the end of 2009. "We would expect clearance sometime in the middle of 2010," says Moffitt. The assay would be launched in conjunction with the company's troponin assay.

SACGHS Recommends Exemption from Gene Patent Infringement in Clinical Care

While the high-profile lawsuit against Myriad Genetics continues, the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) is moving forward with its recommendations on gene patents and licensing issues. At the SACGHS meeting held Oct. 8 and 9 in Washington, D.C., the committee reviewed the extensive public comments received on its December 2008 draft report concerning gene patents and approved a series of recommendations, including one that, if adopted, would clear the way for research and testing based on already-patented human genes without the threat of a patent infringement lawsuit.

In his presentation to SACGHS, James P. Evans, M.D., Ph.D., chair of the committee's Gene Patents and Licensing Task Force, touched on legal developments that may alter the patentability of genes, associations, and methods of detecting specific sequences. He mentioned the ongoing case against Myriad as well as Bilski v. Kappos, a U.S. Supreme Court case that could affect the patentability of processes for correlating a genotype with a phenotype.

SACGHS Recommendations on Gene Patents and Licensing Practices

- ❑ Supporting the creation of exemptions from infringement liability
- ❑ Promoting adherence to norms designed to ensure access
- ❑ Enhancing transparency in licensing
- ❑ Establishing an advisory body on the health impact of gene patenting and licensing practices
- ❑ Providing needed expertise to U.S. Patent and Trademark Office
- ❑ Ensuring equal access to clinically useful genetic tests

"It was the feeling of the task force that it is impossible to predict the outcome of these cases," said Evans. "It's better, then, to address problems that we see as pressing through recommending policy changes and statutory changes."

Evans went on to present the task force's six proposed recommendations, which were later approved by the full committee. First, SACGHS recommends that the secretary of Health and Human Services (HHS) work with the secretary of Commerce to promote statutory changes that would exempt from patent infringement liability those using patented genes for clinical testing or research. "What this seeks to do is . . . narrowly dissect the diagnostic use of gene patents from other uses and exempt that use in the medical context," explained Evans, who compared it to legislation exempting medical providers from infringement claims on a variety of procedures.

The second recommendation concerns promoting adherence to norms that are designed to ensure access. Specifically, SACGHS recommends the creation of a code of conduct that would encourage broad access to diagnostic genetic

technologies. "We'll need to have a discussion [as to whether there should] be teeth put in regulations that seek to get, for example, fundees to adhere to norms of licensing," added Evans.

SACGHS also recommends enhanced transparency in licensing. Information about patent licenses should be made more readily available to the public, advises the committee. Specifically, access should be improved to information concerning the type of license, the field of use, and the scope of technologies.

'In the realm of diagnostics, patent-enabled exclusivity results in narrowing of offering to patients and physicians.' — James P. Evans, M.D., Ph.D.

"We have advocated an advisory board that would, in an ongoing way, assess problems in the realm of gene patents," said Evans, describing the fourth recommendation. Such a group could also provide input on the implementation of any future policy changes and in this way act as a kind of fallback if other recommendations were not implemented.

Another recommendation involves collaboration with the U.S. Patent and Trademark Office (USPTO). SACGHS advises that the secretary of HHS work with the secretary of Commerce to ensure that the USPTO is kept apprised of scientific and technological developments related to genetic testing and technology. "It was felt that it might be helpful to the USPTO if an advisory committee were established to advise not only about ongoing dilemmas with the fast clip of technology advancement but also how to incorporate the legal decisions that are in the pipeline now into this changing landscape," noted Evans.

Finally, the committee addressed the issue of equal access, highlighting issues of availability and accessibility as increasingly incorporated given that genetic tests are increasingly integrated into clinical care.

Evans concluded his presentation to the committee by emphasizing that the patent system is designed to promote progress and distinguishing diagnostic tests from commodities, including therapeutics. "In the realm of drugs, strong arguments can be made that patents enable innovation, drive progress, and serve an important role because, for example, of the high, high up-front costs in investment that are required," said Evans. "In the realm of diagnostics, patent-enabled exclusivity primarily, demonstrably, and empirically results in narrowing of offering to patients and physicians."

The College of American Pathologists (CAP), which has long opposed the issuance of human health-related gene patents, applauded the most recent recommendations of SACGHS. In May, CAP signed on as a plaintiff in the lawsuit challenging the patents held by Myriad Genetics. Other plaintiffs include the Association for Molecular Pathology, the American College of Medical Genetics, the American Society for Clinical Pathology, and the College of American Pathologists.

With New Gene Patents, Myriad Genetics Developing Predictive Test for Pancreatic Cancer

Myriad Genetics (Salt Lake City) will use newly acquired gene patent rights to develop a test that can help predict an individual's risk of pancreatic cancer. The test would bolster Myriad's portfolio of predictive genetic tests, which include those for hereditary breast and ovarian cancer, colorectal and uterine cancer, colon cancer, and melanoma.

In a deal with Johns Hopkins University (JHU), the company acquired an exclusive global license to patents covering mutations in PALB2, a tumor suppressor gene that was recently identified by JHU researchers as a susceptibility gene for familial pancreatic cancer. These mutations have been shown to substantially increase an individual's risk for developing pancreatic cancer later in life.

'We have noticed a recent uptick in patient visits to the physician's office, and it looks like the economy is improving.' — Peter Meldrum, Myriad, President and CEO

Myriad plans to combine the PALB2 patents with its other patents that cover predisposition genes for pancreatic cancer (those for BRCA2 and p16) to create a novel molecular diagnostic test that can assess an individual's risk of developing hereditary pancreatic cancer. The company plans to launch the test in late 2010, following the introduction of a separate cancer diagnostic product in the first calendar quarter of 2010.

Molecular diagnostic revenue at Myriad increased 22 percent to $85.1 million in the fiscal quarter ended Sept. 30, 2009, compared with $70 million in the same period last year. This quarter is historically the company's weakest, as it includes the summer vacation months of July and August.

"We have noticed a recent uptick in patient visits to the physician's office, and it looks like the economy is improving," said Myriad President and CEO Peter Meldrum on a Nov. 3 call with analysts and investors. The company's weekly testing volume increased during the latter half of September and through October. Meldrum credited the boost in part to expanded sales and marketing efforts, including the newly accelerated direct-to-consumer (DTC) marketing campaign in the Midwest and the renewed DTC campaign in the South.

HER2-Positive Breast Cancer Puts Patients at High Risk of Recurrence

Early-stage breast cancer patients with human epidermal growth factor receptor-2 (HER2)-positive tumors 1 centimeter or smaller are at significant risk of disease recurrence, compared to those with early-stage disease whose tumor cells do not overexpress the HER2 gene, according to a study published online on Nov. 2 in the *Journal of Clinical Oncology*.

Led by researchers at the University of Texas M.D. Anderson Cancer Center (Houston),

the study calls for a change in the way women with early-stage HER2-positive breast cancer should be assessed for risk of recurrence and considered for treatment, said the study's senior author, Ana M. Gonzalez-Angulo, M.D, associate professor in M.D. Anderson's departments of Breast Medical Oncology and Systems Biology.

Approximately 20 percent of women with breast cancer have a genetic alteration in the HER2 gene that produces an increased amount of the growth factor receptor protein on the tumor cell surface and makes the cancer more aggressive. The drug trastuzumab (Herceptin) induces an antibody-dependent cell-mediated cytotoxicity against tumor cells that overexpress HER2. The drug was approved for use in 1998 in women whose advanced breast cancer expresses HER2.

"Our findings show that women with early-stage HER2-positive breast cancer have a 23 percent chance of recurrence. In contrast, the five-year survival rate of all women with such early-stage breast cancer is more than 90 percent," said Gonzalez-Angulo. "The findings indicate that physicians need to consider offering these women Herceptin-based therapy in the post-operative, or adjuvant, setting."

As technology allows for improved surveillance and earlier detection of breast cancer, the number of patients with HER2-positive tumors smaller than 1 centimeter continues to increase. Current guidelines call for no additional therapy after surgery and radiation if tumors are less than five millimeters and Herceptin-based adjuvant therapy should be discussed with patients if the tumors are from 6 to 10 millimeters.

The study retrospectively analyzed 965 patients treated at M.D. Anderson between 1990 and 2002. All of the patients' tumors were smaller than 1 centimeter. To validate the findings, a second group of 350 patients from European institutions was also analyzed.

Of the M. D. Anderson patient population, more than 10 percent, or 98 patients, had HER2-positive tumors. The five-year, recurrence-free survival was 77.1 percent; in contrast, HER2-negative patients' recurrence-free survival was 93.7 percent. Five-year distant recurrence-free survival was 86.4 percent in women with HER2-positive tumors compared to 97.2 percent in women with HER2-negative tumors. Patients with HER2-positive tumors had 2.68 times higher risk of recurrence and 5.3 times higher risk of distant recurrence than those with HER2-negative tumors.

In addition, women with HER2-positive tumors had 5.09 times the risk of recurrence and 7.81 times risk of distant recurrence than women with hormone receptor-positive tumors.

"The risk of recurrence was much higher than we suspected," said Jennifer Litton, M.D., assistant professor in M. D. Anderson Department of Breast Medical Oncology, and also an author on the study. "With this study, we now have concrete evidence to discuss with our HER2-positive patients with even the smallest of tumors, and Herceptin alone or combined with chemotherapy should be strongly considered as adjuvant therapy."

Liquid-Based Cytology Not Superior to Pap Test for Cervical Cancer Detection, *JAMA* Study Finds

A study published in the Oct. 28 issue of the *Journal of the American Medical Association* (*JAMA*) weighs in on the controversy that has long surrounded the diagnostic accuracy of liquid-based cytology as an alternative for conventional cervical cytology. The study of nearly 90,000 women found that liquid-based cytology is not superior to Papanicolaou (Pap) tests for the detection of cervical cancer precursors or cancer. These results confirm those of a meta-analysis published last year in *Obstetrics and Gynecology*.

Pap tests are considered suboptimal due to false-negative and false-positive test results that can be caused by poor sampling and preparation as well as erroneous detection and interpretation. Liquid-based cytology, which has now largely replaced Pap smears in the United States, harvests cervical cells with a traditional sampling device and then rinses them into a vial with preservation solution rather than being smeared on a slide.

Researchers led by Albertus G. Siebers of Radboud University Nijmegen Medical Centre (Nijmegen, the Netherlands) compared the screening performance of Pap tests and liquid-based cytology in terms of test positivity rates, histological detection rates, and positive predictive values (PPVs). The randomized controlled trial involved 89,784 women ages 30 to 60 who participated in a Dutch cervical screening program at 246 family practices. One hundred twenty-two practices were assigned to use liquid-based cytology and screened 49,222 patients, and 124 practices were assigned to use the conventional Pap test and screened 40,562 patients. Patients were screened for cervical intraepithelial neoplasia (CIN) and were followed up for 18 months.

The researchers found that the adjusted detection rate ratios for CIN grade 1+ was 1.01; for CIN grade 2+, 1.00; for CIN grade 3+, 1.05; and for carcinoma, 1.69. "Because of randomization, it can plausibly be assumed that the prevalence of CIN was equal in both study groups," write the researchers. "Therefore, the lack of difference in detection rates and PPV in this trial demonstrates that liquid-based cytology is neither more sensitive nor more specific in detecting cervical cancer precursors than the conventional Pap smear."

The study found no differences between the positivity rates of the two methods. At the same time, the authors caution that their cytological findings are not sufficient to claim that liquid-based cytology and conventional cervical cytology are equal in their diagnostic accuracy. "Altogether, these findings provide strong evidence that the performance of liquid-based cytology is not superior to that of the conventional Pap test when applied within a well-organized and quality-controlled cervical screening program," the authors write.

In an accompanying editorial, Mark Schiffman M.D., and Diane Solomon, M.D., of the National Cancer Institute, comment on the findings of this study. "For those designing rational cervical cancer prevention programs, Siebers et al. have convincingly simplified one aspect of a complex health policy puzzle," they write. "Physicians and other health professionals can choose either liquid-based cytology or conventional Pap smear as they discuss how cytology fits into the larger picture."

Genetic Signature Linked to Skin Cancer Prognosis

The results of a new study may pave the way for a genetic test to determine prognosis for advanced melanoma. Researchers at New York University (NYU) used DNA microarrays to analyze the activity of hundreds of genes involved in immune response and gene proliferation and found 266 genes associated with shorter or longer survival among 38 patients whose melanomas had recurred after being surgically removed. The study was published online on Nov. 13 in the early edition of the *Proceedings of the National Academy of Sciences*.

The American Cancer Society estimates that 68,729 people in the United States will develop melanoma this year, and 8,650 people are expected to die from the disease. Risk factors for melanoma include excessive exposure to sunlight, a fair complexion, and a family history of the disease. With early detection and prompt treatment, however, melanoma is highly curable.

Genetic information about prognosis may help clinicians determine the best course of treatment for patients with advanced melanoma. "If we could actually understand what was happening in those patients, within the tumor itself, perhaps we'd be able to help them in terms of what therapy they might go on," said Nina Bhardwaj, M.D., Ph.D., professor of medicine, pathology, and dermatology at NYU Langone Medical Center and the study's senior author.

The *PNAS* study offers some insight into the underlying mechanism of melanoma. "We found that patients who survived longer had gene activity consistent with an immune response," said Bhardwaj. "Patients who didn't survive as long didn't have an up-regulation of those genes but tended to have higher levels of genes associated with cell proliferation, suggesting that if your cells are growing more actively, the tumor is going to grow faster."

To help predict survival, physicians routinely assign melanoma to one of four stages, based on tumor size and location. Currently, the thickness of a melanoma at the time of diagnosis, sometimes combined with a procedure called sentinel node biopsy, is used to assess whether a patient's tumor will recur and if additional treatment with immunotherapy is warranted after the cancer is removed. Patients with early-stage melanoma, known as stage I cancer, have the thinnest lesions and are therefore the least likely to have a recurrence of their original cancer.

The prognosis usually worsens as the tumor extends deeper into the skin. By stage III, the melanoma has generally spread beyond the skin to lymph nodes draining the tumor, and five-year survival rates begin dipping below 69 percent. By the time the melanoma has metastasized to lymph nodes or organs far from the initial tumor site, considered stage IV disease, patients rarely survive more than a year.

There are some ambiguities within the staging approach. Stage III has been subdivided into three groups according to the extent of tumor growth within the lymph nodes. The latter two subgroups, IIIb and IIIc, correspond to more advanced disease but have proven nearly indistinguishable as indicators of long-term survival.

The researchers found that when genetic profile information was added to the traditional staging rubric, survival predictions improved substantially. Having found that many cell growth genes were associated with a poorer prognosis, they tested whether they could obtain similar results by staining a tumor specimen to get its mitotic index. This measure of cell proliferation not only helped distinguish between stages IIIb and IIIc but also proved to be the single strongest predictor of patient survival.

The study also found that two other measures of immune response, including the infiltration of tumors by T cell specialists or by the immune system's larger collection of white blood cells, also improved predictions when added to the traditional staging system.

"It's exciting, because we finally have some parameters that might help distinguish between these two stages in terms of survival and possibly address how these patients should be treated," Bhardwaj said. The next step is to validate the findings with a much larger, independent group of patients.

M. D. Anderson Releases New Cancer Screening Guidelines

The University of Texas M.D. Anderson Cancer Center (Houston) has released new risk-based screening guidelines for breast, cervical, and colorectal cancers. Aimed at the public, the recommendations identify risk categories and provide information about when to begin and discontinue screening exams. The new recommendations are part of the institution's new initiative to improve cancer prevention and detection through expanded screening, risk reduction, and diagnostic guidelines.

"Cancer screening is not one-size-fits-all," said Therese Bevers, M.D., medical director of M. D. Anderson's Cancer Prevention Center. "Our new risk-based recommendations are markedly more personalized and precise, offering detailed guidance than what has previously been made available to the public here or by other cancer organizations."

Until now, cancer screening recommendations were targeted largely to individuals at average risk for developing cancer based on characteristics like age, family history, or genetic predisposition. However, average risk was not previously defined and recommendations for individuals at increased or high risk were not outlined. The new screening guidelines define risk and offer recommendations for those at increased and high risk of developing cancer.

For example, the guidelines include five different sets of screening recommendations for those at increased risk for breast cancer; four categories of age-based risk recommendations for cervical cancer; and for colorectal cancer, there are three categories defining those at increased risk and three categories defining those at high risk.

The risk categories and related guidelines were developed by multidisciplinary panels of M.D. Anderson disease site experts across several areas, including medical oncology, surgical oncology, cancer prevention, and imaging. Risk-based screening guidelines for prostate, liver, skin, endometrial, and ovarian cancers are currently in development and a new online risk assessment tool integrating the new screening guidelines will be launched on the M.D. Anderson Web site in early 2010.

FDA Grants Additional EUAs for H1N1 Flu Tests

In October, the U.S. Food and Drug Administration (FDA) issued three additional emergency use authorizations (EUA) for tests that can diagnose 2009 H1N1 influenza infection. The EUAs were issued to Diatherix Laboratories (Huntsville, Ala.), Prodesse (Waukesha, Wis.), and Focus Diagnostics, the infectious disease diagnostics business of Quest Diagnostics (Madison, N.J.).

Use of the tests is authorized only for the duration of the declaration of 2009 H1N1 influenza virus as a public health emergency, which is currently set to expire on April 26, 2010.

Diatherix Laboratories was granted an EUA for its Diatherix H1N1-09 influenza test, which detects 2009 H1N1 influenza viral RNA using the company's proprietary target-enriched multiplex polymerase chain reaction (Tem-PCR) technology. The EUA authorizes use of the test on the ABI 9700 thermocycler followed by detection on the Qiagen Luminex LiquiChip 100 platform.

The test is intended for use on nasopharyngeal swabs, nasal swabs, throat swabs, and nasal aspirates from patients with symptoms of respiratory infection in conjunction with clinical risk factors. Turnaround time for the test, which is performed exclusively at Diatherix's CLIA high-complexity laboratory, is 24 hours.

Prodesse, which in October was acquired by Gen-Probe (San Diego), received an EUA for its ProFlu-ST influenza A subtyping assay. The test is to be used for the diagnosis of 2009 H1N1 influenza virus infection provided that it is aided by an algorithm that relies on seasonal influenza A/H1 virus and seasonal influenza A/H3 virus results in individuals who are diagnosed with influenza A by currently available FDA-cleared or authorized devices.

Prodesse's multiplex real-time RT-PCR assay uses fluorogenic hydrolysis (TaqMan) probes and is run on the Cepheid SmartCycler II instrument. It is authorized for use in CLIA high-complexity laboratories.

Finally, Focus Diagnostics received a second EUA for H1N1 flu testing. The most recent authorization covers the Simplexa influenza A H1N1 (2009) test for use on the 3M integrated cycler, a molecular diagnostic platform that has not been cleared or approved by the FDA. The test, which is authorized for use by CLIA high-complexity labs, is the first in a new line of molecular diagnostic tests developed by Focus for use on the 3M system.

In July, the FDA issued an EUA for the Focus Diagnostics influenza H1N1 (2009) real-time reverse transcription polymerase chain reaction (rRT-PCR) diagnostic test, which qualitatively detects 2009 H1N1 influenza viral RNA in nasopharyngeal swabs, nasal swabs, throat swabs, and nasal aspirates from patients with signs and symptoms of respiratory infection. Focus began performing the test in its Cypress, Calif., laboratory in May. It was the first commercial H1N1 test to be granted an EUA. The FDA had previously granted the Centers for Disease Control and Prevention two EUAs for diagnostic tests.

Geisinger's Proven Diagnostics to Comarket Berkeley HeartLab Tests

Proven Diagnostics (Bethlehem, Pa.), a clinical laboratory owned by Geisinger Health System, has inked a deal with Celera subsidiary Berkeley HeartLab (BHL; Alameda, Calif.) to comarket select tests offered by BHL as well as BHL's disease-management program. Financial terms of the agreements were not disclosed.

Proven Diagnostics and Geisinger Medical Center will also be the first external clinical labs to offer BHL's proprietary genetic test for the kinesin-like protein 6 (KIF6) gene, which has been associated with cardiovascular risk and statin benefit. Testing will be performed by BHL.

Launched in July 2009, Proven Diagnostics is headed by CEO Candice Miller and Rob Gilmour, vice president of sales. In addition to clinical laboratory testing, Proven Diagnostics also offers anatomic pathology testing services through its collaboration with Geisinger Medical Laboratories, which is led by Conrad Schuerch, M.D., and 17 pathologists.

Earlier this year, Proven Diagnostics announced a partnership with recently merged ViraCor-IBT Laboratories (Lenexa, Kan.) to offer selected tests on the company's allergy, immunology, and infectious disease diagnostic menu to physician offices in Pennsylvania.

The collaboration is uniquely comprehensive, explained Maureen Loftus, chief business officer of ViraCor-IBT. "This is the first collaboration where we are going to be training the sales force on the specific aspects of the ViraCor-IBT test menu," she said. "For most of the health systems that we perform testing for, whether they are outreach or hospital-based, we are an extension of their labs. In this situation with Proven Diagnostics, we are really viewing this as an extension of our sales force, as opposed to just the reference lab."

Agendia Raises $23 Million in Series E Financing

Agendia remains focused on becoming a competitive force in the breast cancer prognostic testing market long dominated by Genomic Health's Oncotype DX and now has additional financial resources to pursue this goal. A few months after opening a 3,500-foot CLIA lab in Huntington Beach, Calif., the Amsterdam-based company announced that it has raised $23 million in Series E financing. The funding round was led by an undisclosed family investment firm.

The financing will be used to accelerate the commercialization of the company's MammaPrint test in the U.S. market. The microarray-based test uses a 70-gene expression profile to assist clinicians in determining the risk of relapse for newly diagnosed breast cancer patients. In February 2007, MammaPrint became the first in vitro diagnostic multivariate index assay (IVDMIA) assay to be cleared by the U.S. Food and Drug Administration (FDA).

In 2008, Agendia launched a companion assay, TargetPrint, which measures the expression level of estrogen receptor (ER), progesterone receptor (PR), and HER2 in breast cancer tumor biopsies. The TargetPrint assay has been validated against FDA-approved immunohistochemistry assays but has not itself been cleared by the FDA.

MedPAC Recommends Laboratory Test Values as Expanded Data Collection Point

On Nov. 6, the Medicare Payment Advisory Commission (MedPAC) voted to approve eight recommendations on data collection requirements comparing quality between traditional Medicare and Medicare Advantage plans. The data points include laboratory test values.

Critics have charged that Medicare routinely pays providers without regard to outcomes and pays Medicare Advantage (MA) plans beyond the costs of traditional Medicare without proof of higher quality. In the Medicare Improvements for Patients and Providers Act of 2008, Congress required MedPAC to submit a report by March 31, 2010, on how comparable performance measures and patient experience measures can be collected among MA plans and with traditional Medicare.

Among MedPAC's recommendations to the secretary of Health and Human Services is to calculate fee-for service results from the Health care Effectiveness Data and Information Set (HEDIS) administrative measures by 2011, to begin collecting laboratory test values for fee-for-service by 2011, and to use the information to calculate intermediate outcome measures for fee-for-service as soon as it is practical.

Other recommendations address the fact that plans currently report at the level of contracts, which can cover broad and diverse geographic areas. Therefore, MedPAC advises that performance measurement results in MA be collected, calculated, and reported at the level of separate geographic units. The commission recommends that fee-for-service performance results used to compare MA and fee-for-service be calculated using the same geographic area definitions.

With forthcoming Medicare subsidies expected to accelerate the adoption of electronic health records (EHRs), MedPAC is also calling for the secretary to define the "meaningful use" of EHRs to support quality measurement. Of particular importance is the ability of EHRs to include and report patient demographic data, such as race, ethnicity, and language preference.

Catholic Health Initiatives Expands Outreach Testing By Acquiring Stake in PAML

PAML CEO and President Thomas Tiffany, Ph.D., described the deal as "an opportunity for CHI and Providence to grow the esoteric reference laboratory to better support the hospital systems' service lines."

Catholic Health Initiatives (CHI; Denver) is set to assume a 25 percent equity position in Pathology Associates Medical Laboratories (PAML; Spokane, Wash.), an industry leader in joint venture partnerships with community-based hospitals. PAML is owned by Providence Health & Services, a nonprofit health system with 27 hospitals and more than 35 non-acute-care facilities.

The deal will significantly expand PAML's outreach hospital base. CHI is the second-largest Catholic health care system in the nation and includes 78 hospitals in 20 states. As part of the agreement, PAML and CHI will work together to develop a national network of regional laboratories at select CHI hospitals. PAML will provide the financial infrastructure, connectivity capabilities, and esoteric testing menu to launch this national outreach growth strategy.

IVD Stocks Dip 2%; Affymetrix Plummets 32%

The G-2 Diagnostic Stock Index lost an average of 2 percent in the five weeks ended Nov. 6, with nine stocks up in price and seven down. The G-2 index is up 30 percent so far this year, while the Nasdaq is up 34 percent and the S&P is up 20 percent.

Shares in microarray maker **Affymetrix** (Santa Clara, Calif.) dropped 32 percent to close at $5.71 per share and a market capitalization of $395 million. The company recently posted a quarterly net loss of $8.8 million, or 13 cents per share, on $78.2 million in sales. Although the results were an improvement over the $31.8 million loss reported for the same period in 2008, they disappointed analysts, who predicted an average loss of 8 cents per share on $80.7 million in sales.

Also losing ground was **Luminex** (Austin, Texas), which was down 15 percent to a share price of $22.63 and a market capitalization of $575 million. Although quarterly revenue at the multiplex testing company was up slightly to $29.1 million, compared to $28.8 million in 2008, it was not enough to offset operating expenses, which increased to $19.3 million for the quarter, from $16.6 million in the same period of 2008. This led to a net loss of $0.6 million, compared with net income of $3.2 million for the same period last year. Luminex attributed the increased expenses to recent infrastructure investments, including employee costs. Over the past year, the company has added 42 employees, bringing its total employees to 423.

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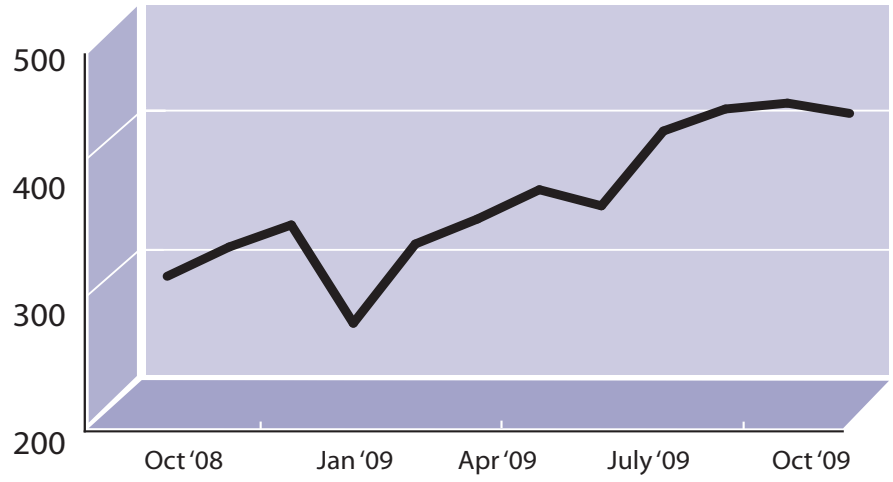
The biggest gainer of the period was **OraSure** (Bethlehem, Pa.). Shares in the oral fluid diagnostics company gained 19 percent to close at $3.50 with a market capitalization of $159 million. The company recently reported quarterly revenues of $21.6 million, compared to $16.9 million in the same period last year. OraSure noted that it has seen double-digit growth in sales of its infectious disease testing, cryosurgical systems, and insurance risk assessment testing products. These gains have been partially offset by lower sales of substance abuse testing products.

G-2 Diagnostic Stock Index



Source: The G-2 Diagnostic Stock Index is tabulated weekly by *DTTR* from the average percentage change in the stock price of 16 IVD companies.

UP	PRICE	% CHG
Abbott Labs	$51.53	3%
Becton Dickinson	70.54	5
Bio-Rad	97.34	9
Gen-Probe	41.03	1
Immucor	18.44	4
Inverness Medical	39.89	3
Johnson & Johnson	60.30	1
Nanosphere	6.77	2
OraSure	3.50	19
DOWN		
Abaxis	23.05	-11
Affymetrix	5.71	-32
Beckman Coulter	65.57	-1
Clinical Data	15.24	-8
Luminex	14.20	-15
Meridian	22.63	-6
Quidel	14.87	-5

G-2 Insider

Sales and marketing strategies are powerful tools for gaining market share in the increasingly competitive clinical laboratory market. . . . Ensure that your lab is well-positioned to compete and win by attending Washington G-2 Reports' second annual LabCompete: Laboratory Sales and Marketing Conference, Dec. 7-9 at the Sheraton Wild Horse Pass in Chandler, Arizona. Prepare to compete with the diagnostic testing giants and respond to the latest CLIA lab-driven business models with sessions including:

- ❑ "Building a Sales Strategy, Team, and Presentation That Will Dominate Any Market in Any Economy," a keynote address by author and sales trainer Jeffrey Gitomer;
- ❑ "Launching a Novel Test: Lessons from Agendia," in which Dan Forche, vice president of sales and marketing for Agendia, will explain how the company laid the groundwork for the successful launch of MammaPrint, the first in vitro diagnostic multivariate index assay (IVDMIA) to be cleared by the U.S. Food and Drug Administration;
- ❑ "Selling and Marketing Specialized Tests," a breakout session in which Genova Diagnostics Vice President Chris Smith will discuss how to build a highly successful sales force for a complex sale as well as Genova's data-driven approach to identify, attract, and retain customers; and
- ❑ "Building a Sales and Marketing Strategy to Compete With Local, Regional, and National Labs," by Robert P. Gasparini, president and chief scientific officer of NeoGenomics Laboratories.

View the complete program agenda at *www.g2reports.com/labsalesmarketing09*. Registration is available online or by contacting John Watkins at 800-401-5937 ext. 4710 or johnwatkins@ioma.com.

References

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Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by Washington G-2 Reports, 1 Washington Park, Suite 1300, Newark, NJ 07102-3130. Tel: 973-718-4700. Fax: 973-622-0595. Web site: www.g2reports.com.

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