

Diagnostic Testing and Healthcare Industry News Update

July 20, 2010

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Who We Are

The Emmes Group is a strategic consulting, information and knowledge provider whose core competency is conceiving and implementing proprietary research-based investigations that fulfill clients' explicit needs.

What We Do

We specialize in obtaining vital market facts, judgments, preferences and perceptions -- without delay, and converting this information into applicable knowledge. We deliver unique understandings whose depth and breadth provides our clients with enhanced insights and wisdom.

Who We Support

The Emmes Group counsels and supports managers who are seeking greater understanding and desire better results. Our practice is concentrated on the essential characteristics of healthcare, including diagnostics, medical information management/technology, biotechnology, medical devices, and lab instruments.

Our Credentials

The methods, skill sets, and analyses we offer are based upon decades of first-hand experience and success, not only in research, but also in significant operational roles for industry leaders. Thus, in any project we undertake for you, we can foreshorten the learning curve and help you to be better informed.

Contact Us

For more information please contact Edward Weiner at **(508) 358-2221** or e-mail us at: **EMMES@aol.com**



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The Emmes Group, a leading provider of essential IVD market information and insights for over 25 years will be at the 2010 AACC meeting in Anaheim next week providing free demonstrations of its highly acclaimed 2010 Molecular Testing Database.

Molecular diagnostics is becoming a dominant platform in clinical medicine and represents one of the fastest growing segments of the diagnostics market. For anyone interested in better understanding the specifics of this market segment, the Emmes Molecular Testing Database is an invaluable management resource.

Extraordinarily useful for marketing, sales management, business development, strategic planning, competitive analysis, financial assessments and customer service, the Emmes Molecular Testing Database is easy to use, comprehensive, efficient and interconnected. It holds promise beyond its fundamental elements, allowing users to apply advanced analytics to improve decision-making and leading to better results.

An authentic profile of one of the 1,000 laboratories that comprise the 2010 Emmes Molecular Testing Database is shown on the next page. This is followed with an actual summary table (based on the feedback from 500 MDx labs) from the 2010 database illustrating the exceptional detail provided to subscribers.

To arrange for a free in-person (at 2010 AACC) demonstration of the 2010 MDx database (or, if you are unavailable at AACC but would like to arrange for a free online demo please contact me as soon as possible at:

Edward Weiner
Tel: 508-328-6800
E-Mail: Emmes@aol.com

Emmes 2010 Molecular Dx Testing Database

Account: Health Network Laboratory Address: 2024 Leigh St. City: Allentown State: PA Zip: 18103 Telephone: 610-402-5032 Respondent: Carol Beckwith Title: Molecular Manager	Type of Institution: Reference Testing Lab Hospital Size: Reference Labs Performing MDx Testing: <input checked="" type="checkbox"/> Molecular <input type="checkbox"/> Microbiology Interview Number: 606 Number of Beds: n/a	Month of Interview: March Year of Interview: 2010
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Test	Perform	Annual Volume	Trend +/- %	Commercial, ASR, Homebrew	Manufactured Platform	Will Change	Reason Why Considering Change	Lab in Which Testing is Performed	Plan To Add
Chlamydia	YES	20,000	5%	Commercial	Gen-Probe - Aptima	YES	Looking to add HPV Geno in one system	Molecular	n/a
Gonorrhea	YES	12,000	5%	Commercial	BD - GeneOhm	no	n/a	Microbiology	n/a
MRSA	YES	8,000	2%	Commercial	Qiagen - HC2	YES	Looking to add HPV Geno in one system	Molecular	n/a
HPV	no								YES
HPV Genotyping	no								no
HIV Viral Load	YES	2,500	2%	Commercial	Roche - Cobas TaqMan	no	n/a	Molecular	n/a
HIV Genotyping	no								no
HCV Viral Load	YES	1,500	2%	Commercial	Roche - Cobas TaqMan	no	n/a	Molecular	n/a
HCV Genotyping	no								no
Herpes (HSV)	YES	420	1%	ASR	Roche - LightCycler	no	n/a	Molecular	n/a
Group A Strep	no								no
Group B Strep	YES	8,300	1%	Commercial	Cepheid - SmartCycler	no	n/a	Microbiology	n/a
CMV	no								YES
Bordetella	YES	700	1%	ASR	Roche - LightCycler	no	n/a	Molecular	n/a
Influenza A/B	YES	500	Same	Commercial	Luminex	no	n/a	Molecular	n/a
Factor V Leiden	YES	600	Same	Commercial	Roche - LightCycler	no	n/a	Microbiology	n/a
Factor II/ Prothrombin	YES	300	Same	Commercial	Roche - LightCycler	no	n/a	Molecular	n/a

Acct: **Health Network Laboratory** City/State: **Allentown, PA** **Emmes 2010 Molecular Dx Testing Database** Type: **Reference Testing Lab**
Interview Number: **606**

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Test	Perform	Annual Volume	Trend +/- %	Commercial, ASR, Homebrew	Manufactured Platform	Will Change	Reason Why Considering Change	Lab in Which Testing is Performed	Plan To Add
CF	no								YES
Tuberculosis	no								no
Enterovirus	YES	200	Same	ASR	Roche - LightCycler	no	n/a	Molecular	n/a
MTHFR	no								no
EBV	no								no
HBV Viral Load	no								no
BCR/ABL	YES	60	Same	ASR	Luminex	no	n/a	Molecular	n/a
Norovirus	no								YES
EGFR	no								YES
VRE	no								no
C. Diff	YES	100,000	10%	Commercial	Cepheid - SmartCycler	no	n/a	Microbiology	n/a
Respiratory Virus	YES	500	Same	ASR	Roche - LightCycler	no	n/a	Molecular	n/a
BK Virus	no								no
K-RAS	YES	50	Same	Homebrew	Roche - LightCycler	no	n/a	Molecular	n/a
VZV	no								no

Which Molecular Tests, if Any, Does Your Lab Send Out Rather Than Perform In-House

CMV (Cytomegalovirus)	EBV (Epstein-Barr)	VZV	
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Other Molecular Tests Your Lab Would Like To Add To Its Test Menu: Bladder Cancer	Any Molecular Tests You Perform For Which We Did Not Inquire: JAK
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Emmes 2010 Molecular Testing Database Detailed Statistical Summary

Search Criteria		Assay <i>(Click on List Below)</i>	Vendor <i>(Optional)</i>			HOSPITAL SIZE DEFINITION	
<input type="button" value="Clear"/>		Chlamydia/Gonorrhea				Large Hospitals - Bed Size Greater than 400 Beds Medium Hospitals - Bed Size of 200-400 Beds Small Hospitals - Bed Size of Less than 200 Beds	
Composition of the Database							
Total Labs	All Hospital Labs	<i>Large Hospitals</i>	<i>Medium Hospitals</i>	<i>Small Hospital</i>	Reference Lab	Public Health Lab	
500	411	168	198	45	71	18	
100%	82%	41%	48%	11%	14%	4%	
Detailed Analysis							
ALL Labs in Database Meeting Search Criteria	All Hospital Labs Meeting Search Criteria	<i>Large Hospitals Meeting Search Criteria</i>	<i>Medium Hospitals Meeting Search Criteria</i>	<i>Small Hospitals Meeting Search Criteria</i>	Reference Labs Meeting Search Criteria	Public Health Labs Meeting Search Criteria	
419	336	147	158	31	66	17	
Percent of the Database	Percent of All Hospital Labs in the Database	<i>As Percent of Large Hospitals In Database</i>	<i>As Percent of Medium Hospitals In Database</i>	<i>As Percent of Small Hospitals In Database</i>	Percent of Reference Labs in Database	Percent of Public Health Labs in Database	
84%	82%	88%	80%	69%	93%	94%	
Percent of ALL Labs Testing For This Assay	% Meeting Search Criteria that are Hospital Labs	<i>% of Large Hospitals Meeting Search Criteria</i>	<i>% of Medium Hospitals Meeting Search Criteria</i>	<i>% of Small Hospitals Meeting Search Criteria</i>	% Meeting Search Criteria that are Reference Labs	% Meeting Search Criteria that are Public Health Labs	
100%	80%	44%	47%	9%	16%	4%	
Testing Volumes							
Aggregate Annual Volume for These Labs	Aggregate Annual Volume for These Hospital Labs	<i>Annual Volume for Large Hospitals</i>	<i>Annual Volume for Medium Hospitals</i>	<i>Annual Volume for Small Hospitals</i>	Aggregate Annual Volume for These Reference Labs	Aggregate Annual Vol. for these Public Health Labs	
6,648,648	3,804,618	2,321,934	1,297,814	184,870	1,960,870	883,160	
Average Annual Volume for These Hospital Labs	Average Annual Volume for These Hospital Labs	<i>Average Volume for Large Hospitals</i>	<i>Average Volume for Medium Hospitals</i>	<i>Average Volume for Small Hospitals</i>	Average Annual Volume for These Reference Labs	Average Annual Vol. for these Public Health Labs	
15,868	11,323	15,795	8,214	5,964	29,710	51,951	

The data shown here (for CT/GC) can be further broken out by vendor and/or specific vendor platform. It is but one of hundreds of possible ways in which to access and summarize data in the 2010 Emmes MDx database.

To arrange for a free in-person (at 2010 AACC) demonstration of the 2010 MDx database (or, if you are unavailable at AACC but would like to arrange for a free online demo please contact me as soon as possible at:

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 Tel: 508-328-6800
 E-Mail: Emmes@aol.com

July 8, 2010

FDA Clears Roche's LightCycler MRSA Advanced Test for Use in the U.S.

Roche Molecular Systems, announced today that the U.S. Food & Drug Administration (FDA) cleared its new LightCycler® MRSA Advanced Test for the detection of methicillin-resistant *Staphylococcus aureus* (MRSA) for clinical use in the United States. The LightCycler® MRSA Advanced Test is a qualitative in-vitro diagnostic test for the direct detection of nasal colonization with bacterial MRSA, and it is designed to aid in the prevention and control of MRSA infections in healthcare settings. Roche's new real-time polymerase chain reaction (PCR) test delivers rapid results (within two hours) and appears to have better sensitivity compared to direct culture-based methods.

"It is important that healthcare professionals have access to MRSA testing technology that provides rapid and reliable results, allowing faster implementation of appropriate infection control measures," said Paul Brown, Ph.D., president and CEO, Roche Molecular Diagnostics. "Roche's new LightCycler® MRSA Advanced Test is designed to offer a simple, flexible, and reliable method for MRSA screening to support hospitals in the prevention of MRSA infections."

High rates of infection, mortality, and high costs of treatment due to healthcare-associated infections (HAIs) caused by MRSA are a critical issue for healthcare facilities worldwide. In addition, community-associated MRSA (CA-MRSA) infection has spread in the U.S., feeding the pipeline of infection in hospitals, and underscoring the need for comprehensive infection control programs along with more rapid and reliable MRSA screening methods. In response to this public health issue, an increasing number of states have passed legislation requiring mandatory reporting and/or screening for HAI's.

"The introduction of this new advanced test will expand the options healthcare facilities have for MRSA screening using molecular diagnostic methods," said Lance Peterson, M.D., FASCP, epidemiologist and a founder of the MRSA screening program at North Shore University Health System in Evanston, Illinois. "The test showed good sensitivity with minimal hands-on time. Technicians now have the ability to have flexible batch sizes which could make it the cost-effective choice for many hospital laboratories."

The LightCycler® MRSA Advanced Test is performed on Roche's LightCycler® 2.0 Instrument with nasal swab specimens from patients suspected of MRSA colonization. Offered in a convenient, ready-to-use format and designed for flexible batch sizes, the test is intended to help ensure the safety and productivity of laboratory staff and provides flexible throughput with accurate, reliable results. The combined capabilities of the LightCycler® 2.0 Instrument with the flexible design and reliable detection of the

LightCycler® MRSA Advanced Test are intended to provide a versatile, cost-effective medically valuable tool to support healthcare institutions in their efforts to prevent and contain the spread of MRSA infection. Roche's LightCycler® 2.0 Instrument remains among the most widely used real-time amplification systems available worldwide.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of bacterium that is resistant to certain antibiotics, such as methicillin, oxacillin, penicillin and amoxicillin. *Staphylococcus aureus* is one of the most frequently isolated bacteria from patients with healthcare-associated infections (HAIs). Estimates suggest that 2 million HAIs and 90,000 deaths are attributable to these infections each year in the U.S., and that between 5% and 10% of inpatients in U.S. hospitals acquire an HAI.

Antimicrobial resistance and HAIs, either combined or separately, constitute a major infectious disease problem in the U.S. and show signs of becoming more prevalent in the future. MRSA infections are a tremendous burden for healthcare systems and hospitals and are associated with significant healthcare costs. In 2007, the Centers for Disease Control and Prevention (CDC) estimated that HAIs were responsible for \$4.5 to \$5.7 billion in added healthcare costs each year.⁽¹⁾ Experts generally believe that at least 20-30% of such infections are preventable, and molecular-based diagnostic tests to detect HAIs offer faster, sensitive methods to detect infections and prevent their spread. In the U.S. it is estimated that the market for molecular-based MRSA screening is estimated to be worth approximately \$125 million in 2010 and growing at 20% per annum.

July 13, 2010

FDA Approves Meridian Diagnostic System

Recently, Meridian Biosciences received approval from the U.S. Food and Drug Administration (FDA) for its molecular diagnostic system, "*illumigene C. difficile*", to diagnose serious and infectious diseases.

The molecular diagnostic system was recently launched successfully in Europe in the first quarter 2010. Its approval in the U.S. expands the company's existing portfolio of molecular diagnostic assays further, now catering to the needs of both the domestic and international customers.

Meridian Biosciences is an integrated life science company that engages in the development, manufacture, sale, and distribution of diagnostic test kits, primarily for respiratory, gastrointestinal, viral, and parasitic infectious diseases.

Within Meridian Biosciences' U.S. and European diagnostic segments, sales of *C. difficile* products decreased 29% year over year during the first quarter of fiscal 2010 and were flat during the second quarter of fiscal 2010. Sales were affected by the distributor-buying pattern as well as due to the stiff competition faced for such products.

Meridian Biosciences reported a 1% year over year decrease in the research and development expenses for the US Diagnostics operating segment to \$2.3 million in the second quarter, primarily due to the decrease in development costs associated with the molecular diagnostic system. Further, the increase in the cost related to the *illumigene* launch led to an increase in the selling and distribution expenses by 7% year over year in the second quarter.

Meridian Biosciences expects to combat competitive pressures with its strong position in toxin testing and with the newly launched molecular amplification assay, which is simple to use, cost effective and easily accessible for the customers.

July 20, 2010

Roche Launches New Cobas e 602 Immunoassay Module For Large Volume Laboratories

Roche announced today the launch of the cobas e 602 module for immunoassay testing as the latest addition to its cobas 8000 platform. This product is now available in Europe as well as in all countries recognizing the CE Mark in the Latin America and Asia-Pacific regions.

Including Roche's latest biomarker tests, the immunoassay module runs more than 80 different immunoassays – from high medical value tests for cardiac and infectious diseases to bone markers, rheumatoid arthritis, tumor markers and tests for maternal care – with a throughput of 170 tests / hour. Roche now offers 7 additional configurations to the cobas 8000 modular analyzer series.

"With the recent launch of the clinical chemistry modules cobas c 701 and c502, we set a new standard in efficiency for high volume testing. The e602 module will further enhance our customers testing capability by seamlessly integrating clinical chemistry and immunoassay tests in one system," said Daniel O'Day, Chief Operating Officer of Roche Diagnostics. "Thanks to its broad test menu, combined with an optimized workflow, the new cobas e 602 module will further strengthen our offering in the serum work area segment."

The cobas 8000 modular analyzer series is the newest member of Roche's cobas modular platform family. It is designed to meet the needs of high volume laboratories with about 3 to 15 million test per year to deliver high quality results fast and efficiently from a single patient sample. cobas 8000 compliments the cobas 6000 modular analyzer for medium-sized laboratories and the cobas 4000 systems for small workloads.

At around 15 billion USD, the serum work area market is one of the largest segments in in vitro diagnostics.

With the launch of the high volume immunochemistry module, customers can consolidate clinical chemistry and immunochemistry testing in many different ways into one single configuration. Not only does cobas 8000 modular analyzer series offer 19 different configurations, it has many innovative design and process elements such as the Module Sample Buffer in each module, independent transport and return lines, switch gates and many more features optimizing sample routing to achieve maximum efficiency and productivity. Also this newest member of the cobas modular platform family uses the same operator interface, detection technologies and reagents as other cobas instruments, enabling standardization of results between different analyzers.

In the coming months, Roche will continue to enhance the cobas 8000 modular analyzer series by introducing a new clinical chemistry module, the cobas c 702 module and offering even more configurations. The cobas c 702 module incorporates an innovative reagent manager allowing for intelligent continuous reagent cassette management without interruption of the workflow for even more efficiency and productivity in high volume laboratories.

July 13, 2010

Asuragen and Life Technologies Launch CE-Marked BCR/ABL1 Quant Leukemia Test in Europe

Asuragen, Inc. and announced today that they have achieved CE-marking and commercial launch in Europe of the BCR/ABL1 Quant™ Test, Asuragen's clinically validated and cGMP manufactured test intended to aid clinicians in the monitoring and treatment of individuals afflicted with chronic myeloid leukemia (CML). Asuragen manufacturers the monitoring test, which is exclusively distributed by Life Technologies and runs on the company's Applied Biosystems CE-marked 7500 Fast Dx Real-Time PCR Instrument™.

The CE-marked BCR/ABL1 Quant Test for leukemia progression is a quantitative in vitro diagnostic test to help doctors determine the most effective treatment options for CML. The test monitors the BCR-ABL1 to ABL1 ratio by reverse transcription quantitative polymerase chain reaction (RT-qPCR) on whole blood or bone marrow of diagnosed Philadelphia chromosome positive chronic myeloid leukemia (CML) patients expressing b2a2, b3a2 or e1a2 fusion transcripts. The test is intended as an aid in the assessment of complete cytogenetic response (CCyR), major molecular response (MMR), minimal residual disease and relapse in CML patients.

“The BCR/ABL1 Quant Test provides several advantages over current methods by enabling multiplex detection of all targets in a single reaction and providing unmatched standardization through the use of our proprietary Armored RNA Quant® technology for external calibrators and process controls,” said Rollie Carlson, President of Asuragen.

“Life Technologies is committed to providing versatile molecular diagnostic platforms which simplify the development of sensitive and specific diagnostic assays, and have the potential to impact the way patients are treated,” said Kimberlee Caple, Head of Molecular Medicine Products for Life Technologies. “Using genetic markers such as these to aid clinicians in monitoring disease progression is an important step in the evolution of personalized medicine.”

The BCR-ABL1 fusion gene arises from a specific chromosome translocation, known as the Philadelphia chromosome or t(9:22). The resulting BCR/ABL1 fusion transcripts are present in approximately 95% of CML. If present, the expression level of the fusion transcript or its ratio to a reference transcript may be used to monitor disease progress. Monitoring the level of BCR/ABL1 may be helpful for both prognosis and management of Gleevec®, Tasigna®, Sutent® and Sprycell® kinase therapies in patients with leukemia disease.

Asuragen and Life Technologies have plans to pursue future regulatory clearance for a BCR/ABL1 Quant test in the United States.

Asuragen is a fully integrated diagnostic development company and pharmaceutical services provider. The Company’s diagnostic product portfolio consists of the first-ever validated microRNA diagnostic assay for pancreatic cancer, quantitative RNA tests for leukemia gene translocations, and the Signature® Oncology and Genetic Testing products. Asuragen is empowered with a high level of scientific expertise and assay development capabilities, CLIA and GLP testing services, and an established cGMP manufacturing facility, which allow it to span the spectrum of discovery, testing, production and commercialization.

Life Technologies Corporation (NASDAQ: LIFE) is a global biotechnology tools company dedicated to improving the human condition. Our systems, consumables and services enable researchers to accelerate scientific exploration, driving to discoveries

and developments that make life even better. Life Technologies customers do their work across the biological spectrum, working to advance personalized medicine, regenerative science, molecular diagnostics, agricultural and environmental research, and 21st century forensics. Life Technologies had sales of \$3.3 billion in 2009, employs approximately 9,000 people, has a presence in approximately 160 countries, and possesses a rapidly growing intellectual property estate of approximately 3,900 patents and exclusive licenses. Life Technologies was created by the combination of Invitrogen Corporation and Applied Biosystems Inc., and manufactures both in-vitro diagnostic products and research use only-labeled products.

July 7, 2010

Hologic to Acquire Sentinelle Medical for \$85M

Hologic, a leading developer, manufacturer and supplier of premium diagnostics, medical imaging systems and surgical products dedicated to serving the healthcare needs of women, announced today that it has entered into a definitive agreement to acquire Sentinelle Medical Inc. (Sentinelle Medical), a leading provider of Magnetic Resonance Imaging (MRI) breast coils, tables and visualization software.

The purchase price for the transaction will be \$85 million, plus a two-year contingent earn out. The earn out will be payable in cash installments equal to a multiple of the incremental revenue growth in Sentinelle Medical's business in the two years following the closing. This transaction is expected to close during the third calendar quarter and is subject to customary closing conditions, including, among others, Sentinelle Medical stockholder approval and Canadian judicial approval.

Sentinelle Medical, a privately-held medical imaging company headquartered in Toronto, Canada, is dedicated to developing advanced breast imaging technologies using high-field strength MRI that will help in the earlier detection and better treatment of breast cancer.

"The agreement to acquire Sentinelle Medical is a further example of our strategy to maintain a leadership position in women's healthcare," said Rob Cascella, President and Chief Executive Officer. "Magnetic Resonance (MR) is rapidly becoming a standard of care for breast cancer screening of women indicated as having a high risk of developing the disease. This acquisition should further strengthen our comprehensive portfolio of product offerings in the areas of breast cancer detection and intervention."

Sentinelle Medical's revenue in calendar 2009 was approximately \$15 million. Hologic expects this acquisition to be neutral to earnings in fiscal 2011, absent the amortization

of intangibles related to the transaction and other acquisition-related charges. "We are proud of the innovations we have introduced with our MRI solutions and are very pleased with our accomplishments to date," said Cameron Piron, President and CEO of Sentinelle Medical. "This merger is a natural fit. Our expertise in MR breast imaging combined with Hologic's resources should further accelerate the adoption of our technology and ultimately benefit physicians and improve patient care."

The anticipated strategic benefits of the transaction include, among others:

- Broadens Hologic's presence in women's health by offering additional products through existing sales channels. Current sales force is uniquely positioned to capitalize on the growing interest in high-performance MR coils for breast imaging.
- Leverages best-in-class coil technology for leading MR systems across other anatomy-specific applications.
- Complements Hologic's efforts in bringing beneficial imaging modalities to market through advanced research and development capabilities. This combination is expected to expedite new advances in breast imaging.

July 6, 2010

On-Q-ity, Dx Startup, Takes on "Diagnostic Black Hole" in Cancer

Cancer survivors could have tumor cells circulating in their blood stream and not know it, because imaging exams don't detect these indicators of potential malignancies, says Mara Aspinall, the chief executive of On-Q-ity.

On-Q-ity, a diagnostics startup based in Waltham, MA, wants to find these circulating tumor cells in patients' blood and use biomarkers to shed more light on their cancer. The company formed in 2009 through the merger of Silicon Valley's Collective Dx and The DNA Repair Company in the Boston area.

Aspinall led On-Q-ity's efforts to raise \$26 million in a Series A round of venture capital last year. She is a big name in the diagnostics world, given her previous role as president of the genetic testing unit of Cambridge, MA-based biotech giant Genzyme and she's moved her new company into the center of the discussion about the future role of molecular diagnostics in cancer treatment.

Aspinall says that one area of opportunity for her company is in tracking breast cancer relapses (yet she sees applications of the technology at multiple stages of cancer treatment and for many different types of tumors.) Breast cancer is the most common cancer among American women after skin cancer, according to the National Institutes

of Health. A lurking danger for these women, after they complete treatments to wipe out their breast cancer, is that the gold standard imaging exams like MRIs and CT scans only catch tumors of a certain size. That means some percentage of recurring tumors go unnoticed, Aspinall says.

She compared this chilling scenario to a black hole in outer space.

“The patient is told that we don’t see anything abnormal. We see no lumps. We see no re-growth,” Aspinall says. “But the reality is, and this is what we call the Diagnostic Black Hole, is these patients are being told that they are in remission, but they may not be. The tumor is just too small to be seen.”

While On-Q-ity’s technology is still in development, it’s not tough to imagine how the company could address this problem in breast tumor detection and other cancers. It’s working on a microfluidic chip the size of a microscope plate. A blood sample would flow through the chip, in which thousands of antibodies attached to microscopic posts would capture the tumor cells. The tumor cells from the patient’s blood could then be analyzed and counted, Aspinall says. The CEO envisions the firm’s microfluidic chips being used as the foundation for capturing molecules in the blood for many types of diagnostic tests. Yet cancer is the primary focus of her firm at the moment.

The startup is developing its own biomarkers that indicate whether the cancer has resistance against certain cancer treatments such as chemotherapy. Such biomarkers could be used to help guide decisions about which cancer treatments to use on patients. The biomarkers might also enable doctors to monitor changes in tumors during treatment to show, say, whether the tumor is building resistance to a particular therapy.

The company faces some stiff competition in the market for technology to gather circulating tumor cells. Veridex, a unit of the health products giant Johnson & Johnson is already marketing a kit with antibodies and chips for collecting tumor cells in the blood. Quest Diagnostics, one of the largest operators of diagnostics labs in the world, has adopted the Veridex system, according to its website.

But On-Q-ity aims to improve not only the accuracy of tumor cell counts but also the ability to analyze them. “First generation [circulating tumor cell] technology is limited in practice to just enumeration of cells, and it suffers from both poor sensitivity and specificity,” said Bruce Booth, a partner at Atlas Venture in Waltham, and a board member at On-Q-ity, in an e-mail. “On-Q-ity’s next generation platform offers not only better enumeration metrics, but also opens up the opportunity to characterize [circulating tumor cells] at a genomic and proteomic level.”

On-Q-ity owes its technology to its Silicon Valley and Boston roots. The merged company got its microfluidic chip technology for capturing tumor cells from Mountain View, CA-based Collective, where Aspinall had been CEO between her leaving

Genzyme in 2008 and the merger with The DNA Repair Company last year. (Collective closed its Silicon Valley office and move its operations to Waltham last year.) Mehmet Toner, an engineer at Massachusetts General Hospital in Boston, is one of the inventors of the microfluidic chip. (Toner also invented the core technology at Cambridge, MA-based Daktari Diagnostics.)

The DNA Repair Company, which Xconomy profiled back in December 2007, brought On-Q-ity expertise in biomarkers that might be used to predict tumor resistance to certain cancer treatments. On-Q-ity is in the process of testing those biomarkers to determine whether they could be used to help guide doctors in treating breast and lung cancers, Aspinall says. The biomarker know-how came from the labs of Alan D'Andrea of the Dana-Farber Cancer Institute in Boston and Michael Yaffe at MIT.

Investors have now bet more than \$50 million on On-Q-ity's technology. Collective and DNA Repair raised a combined sum of about \$30 million prior to their 2009 merger, and then On-Q-ity raised \$26 million in first-round financing from Atlas Venture, Bessemer Venture Partners, Mohr Davidow Ventures, Northgate Capital, and Physis Ventures last year. Mohr Davidow was a previous investor in both Collective and DNA Repair.

June 30, 2010

Immunodiagnostic Systems Receives US FDA 510(k) Clearance For IDS-iSYS 25-Hydroxy Vitamin D Kit

Immunodiagnostic Systems Holdings plc ("IDS"), parent company of U.S.-based Immunodiagnostic Systems Inc. and a leading producer of diagnostic testing kits for the clinical and research markets, is pleased to announce the receipt of 510(k) clearances* from the United States Food and Drug Administration (U.S.FDA) for both the IDS-iSYS immunoassay analyzer and the automated IDS-iSYS 25-Hydroxy Vitamin D immunoassay kit.

The receipt of 510(k) clearances enables IDS to market the IDS-iSYS, a fully-automated 'closed system' analyzer and its flagship product, 25-Hydroxy Vitamin D, in laboratories undertaking analysis for human diagnostic purposes. It also clears the way to market automated assays for human growth hormone (hGH) and insulin-like growth factor I (IGF-I) since these are not required to be subjected to the pre-market 510(k) process.

IDS has enjoyed sustained growth in U.S. sales, delivering a 116% increase in revenues in FY 2008/9 and more than doubling year-on-year H1 sales in FY 2009/10. This has been achieved with 'manual' products, i.e., non-automated tests that must be

performed by skilled personnel working at the laboratory bench. Much of this growth has been driven by increasing demand for vitamin D testing, and sales of the Company's previously FDA cleared manual 25-Hydroxy Vitamin D EIA kit have more than doubled in each of the last two years.

The majority of clinical diagnostic testing in the U.S. is highly automated, frequently decentralized reference and large hospital laboratories. IDS has previously been unable to address accounts of this size and nature effectively, but the entry of the IDS-iSYS fully automated products into the U.S. will provide powerful tools to change this and allow IDS to compete more readily with our closest competitor.

The IDS-iSYS was launched outside of the U.S. in February, 2009 with more than 100 systems having already been installed. The IDS-iSYS currently offers the Bone Panel of 25-Hydroxy Vitamin D, Intact PINP, Intact PTH and N-Mid® Osteocalcin and the Growth Panel including hGH and IGF-I. Further IDS-iSYS -specific products are due to launch throughout 2010/11, including CTX-I, IGFBP-3, Bone-Specific Alkaline Phosphatase (BAP), BoneTRAP (TRACP 5b), Renin and Aldosterone. Those requiring pre-market notification will be duly submitted to the U.S. FDA for 510(k) clearance.

Dr. Roger Duggan, CEO of IDS plc, said: "This is a true milestone in the history of IDS, spearheading our entry into the automated sector of the largest IVD market in the world. We have steadily built a solid foundation at IDS Inc. in readiness for the launch of the IDS-iSYS, and Kenneth Gibbs has created an impressive team of highly experienced professionals to handle all aspects of IDS-iSYS sales, installation, training, and technical support. U.S. launch comes a little later than originally anticipated, but now we can get underway with unbridled enthusiasm."

June 28, 2010

Panel Suggests New Criteria for Gestational Diabetes

A recent article from an international panel of experts, known as the International Association of Diabetes and Pregnancy Study Group (IADPSG), has suggested new guidelines for diagnosing gestational diabetes. Gestational diabetes is diabetes that develops in pregnancy. Although these experts propose that the new recommendations will prevent risks to babies, the suggested guidelines have yet to be endorsed by any major medical associations and are not likely to have an impact until they are fully reviewed and evaluated by more widely recognized organizations.

A large study of about 27,000 pregnant women, termed the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) trial, evaluated risks of high blood sugar (hyperglycemia) that developed during pregnancy. The HAPO study found that risk to

babies increases gradually as glucose levels increase, even at values that are lower than those currently used to diagnose gestational diabetes. Based largely on the results of the HAPO study, IADPSG developed new guidelines for screening and diagnosis of gestational diabetes and published their recommendations in the March issue of *Diabetes Care*.

The current guidelines of the American Diabetes Association (ADA) recommend screening women in the second trimester of pregnancy (after about 20-24 weeks of pregnancy) by measuring their blood sugar after giving a small amount of glucose; if the levels are too high, a full glucose tolerance test, using a larger amount of glucose is given. Diabetes is diagnosed if two or more of the values in the glucose tolerance test are abnormal.

The IADPSG guidelines suggest a different approach than the current ADA guidelines. The IADPSG guidelines recommend screening all women at their first doctor's visit early in pregnancy, using the current criteria to diagnose diabetes in the general population. The goal here is to identify diabetes that is already present but not diagnosed. These women are already diabetic, and care should be started to control their blood sugar. The guidelines then suggest doing a full glucose tolerance test in the second trimester of pregnancy, without doing the screen with the small amount of glucose first.

The other major change in the IADPSG guidelines is that only one of the values has to be abnormal to diagnose diabetes, instead of two using the ADA criteria. Some of the cut-off values are slightly lower in the IADPSG guidelines as well. The lower cut-offs were selected as the values at which the risk of a baby having diabetes-related complications during pregnancy increased by 75%.

The expected benefit of the new guidelines is that it might reduce the number of babies who have problems related to high blood sugar in their mothers. These problems include premature birth and death, low blood sugar (hypoglycemia) after birth, and being larger, fatter babies. Several studies have shown that women diagnosed using the ADA criteria and treated for diabetes have babies with fewer of these complications. The HAPO trial showed that risk of having babies with these complications rises at glucose values even lower than those used currently, but did not provide any evidence that treating these can reduce complications. Estimates from the HAPO study are that about twice as many women would be diagnosed as having gestational diabetes based on the IADPSG criteria than are diagnosed using the ADA criteria.

Physicians and women might welcome the new guidelines because they offer convenience by eliminating the need for women to return to doctors' offices for a second glucose test, says an accompanying editorial by Robert G. Moses, MD, of the South Eastern Sydney and Illawarra Area Health Service. But the costs associated with the additional diagnoses might present a hurdle to widespread adoption of the guidelines. Under the criteria in the new guidelines, the proportion of pregnant women

with gestational diabetes would be an estimated 18%, about double the current figures. "Clearly the implications of this doubling will need serious consideration," Moses writes.

These proposed new guidelines have already provoked a number of professional organizations to consider whether or not to change their criteria for diagnosing diabetes. Until these decisions are made, it is unlikely that the proposed new guidelines will actually be used by most physicians caring for pregnant women.

June 28, 2010

Abbott Receives FDA Clearance for MDx Test for Detection of Chlamydia and Gonorrhea Infections

Abbott announced today that it has received 510(k) clearance from the U.S. Food and Drug Administration to market a new, sensitive molecular diagnostic test and instrument to simultaneously detect two of the nation's most prevalent sexually transmitted diseases (STDs), gonorrhea and chlamydia, including a new variant strain of chlamydia recently discovered in Sweden.

Abbott received independent 510(k) clearances for both the Abbott RealTime Chlamydia trachomatis/Neisseria gonorrhoeae (CT/NG) assay and the Abbott *m2000* System. They are required to be used together as a system for the detection of CT/NG from multiple specimen types including urine, urethral, vaginal and endocervical swabs. Also cleared was the Abbott *multi-Collect* Specimen Collection Kit, a unique device for collection and room-temperature transportation of multiple samples, including urine samples and endocervical, vaginal and male urethral swab specimens, in one collection device.

"Because many people with chlamydia are co-infected with gonorrhea, it's important to test for both diseases simultaneously," said Klara Abravaya, Ph.D., senior director, research and development, Abbott Molecular. "Left untreated, chlamydia and gonorrhea can lead to pelvic inflammatory disease, urethritis and sterility."

Abbott worked in collaboration with leading international STD researchers to develop the chlamydia test, which was introduced in the European Union in 2008 to address a newly discovered variant strain of the bacteria initially identified in Sweden.

"New tests were needed to target additional parts of the chlamydia bacteria, and Abbott responded fast to our request for research test kits that would pick up the variant strain," said Torvald Ripa, M.D., Ph.D., assistant professor, Department of

Clinical Microbiology and Infection Control, Hospital of Halmstad, Sweden, who discovered the new strain.

While there have been no reports of the variant strain in the United States, chlamydia remains the nation's most frequently reported bacterial sexually transmitted disease (STD), according to the Centers of Disease Control and Prevention (CDC). In 2008, more than 1.2 million chlamydial infections were reported to the CDC, an increase of 9 percent over the previous year.

Under-reporting is substantial because many people with chlamydia are not aware of their infections and do not seek testing. By contrast, gonorrhea incidence has remained relatively stable, although the CDC has reported slight overall declines in the rate of infection in recent years. Public health officials nationwide are particularly concerned by the even steeper increases in chlamydia in teens and young adults.

For example, a recent voluntary chlamydia screening conducted at one high school in Michigan showed that 10 percent of students were infected, according to the county health department. Routine screening of high-risk populations is viewed by infectious disease experts as essential for controlling the U.S. chlamydia epidemic because the disease can be asymptomatic.

Molecular or nucleic acid amplification tests (NAAT) are currently the standard method for detecting chlamydia and gonorrhea infections, and are widely used. The advantage of NAAT over traditional culture methods is that they are generally more sensitive and specific and can identify more positive specimens.

The Abbott RealTime CT/NG assay is an in vitro polymerase chain reaction (PCR) assay for the direct, qualitative detection of the plasmid DNA of CT and the genomic DNA of NG.

The assay may be used to test the following specimens from symptomatic individuals: female endocervical swab, clinician-collected vaginal swab, and patient-collected vaginal swab specimens; male urethral swab specimens; and female and male urine specimens. The assay may be used to test the following specimens from asymptomatic individuals: clinician-collected vaginal swab and patient-collected vaginal swab specimens; female and male urine specimens.

Abbott Molecular (abbottmolecular.com) is an emerging leader in molecular diagnostics - the analysis of DNA, RNA, and proteins at the molecular level.

Abbott Molecular's instruments and reagents detect pathogens and subtle, but key changes in patients' genes and chromosomes, which permit earlier diagnoses, the selection of appropriate therapies and improved monitoring of disease progression.

July 12, 2010

Roche Obtains Co-Exclusive License To Develop Pcr Assays Detecting Mutations In The Pi3k Oncogene

Roche announced today that the company has obtained a worldwide co-exclusive license for the biomarker PI3K (phosphoinositide 3-kinase) from QIAGEN to develop real-time and endpoint PCR diagnostic assays. Johns Hopkins University owns the patent for the PI3K biomarker and has previously granted an exclusive license to QIAGEN's wholly owned subsidiary DxS, now QIAGEN Manchester. Financial details were not disclosed.

The PI3K pathway is mutated in more cancer patients than any other(1), playing a significant role in colorectal, gastric, breast and endometrial tumors, among others. Drugs that inhibit PI3K are a significant focus of current cancer drug development. Genentech, a member of the Roche Group, has several molecules in early development targeting various points along this pathway, in a variety of tumor types.

Multiple scientific papers have shown that PI3K has the potential to be a clinically relevant biomarker for the prediction of individual response to specific cancer therapies. "There is abundant clinical evidence that the PI3K biomarker will play a significant role in the future of oncology treatment," said Paul Brown, president and CEO, Roche Molecular Diagnostics. "Diagnostic assays that detect mutations in PI3K will be an essential component of cancer drug development and personalized healthcare."

Roche has an ongoing program to develop a real-time PCR assay that detects mutations in the PI3K oncogene. The assay will run on Roche's cobas® 4800 System. Roche intends to make the PI3K PCR assay available to internal and external pharmaceutical partners for use in clinical drug trials.

The PI3K assay will complement Roche's extensive menu in development of assays for validated biomarkers, including the B-RAF V600E mutation, found in greater than 50 percent of melanomas.

"Given the demonstrated predictive value of these biomarkers, developing assays that identify clinically relevant mutations is an area of high priority for Roche," said Brown. "By applying our vast, global experience in both cancer drug development and molecular diagnostics, we believe we can quickly generate new assays that will provide value to both drug developers and oncology medical professionals."

The cobas® 4800 System is designed to deliver new standards in laboratory testing efficiency and medically relevant diagnostic information with increased testing throughput. The system combines state-of-the-art sample preparation with Roche's

proprietary real-time PCR technology for the amplification and detection of genetic material (deoxyribonucleic acid or DNA). The intuitive, easy-to-use software integrates sample preparation, amplification and detection, and results management.

July 1, 2010

NanoString Hires Genzyme Vet as CEO to Lead Foray Into Molecular Diagnostics

Seattle-based NanoString Technologies hasn't had a permanent CEO for more than a year, and now the search has ended in Boston. The company, which makes instruments to help scientists perform sophisticated genetic analyses, has named Brad Gray, the former vice president of product and business development for Cambridge, MA-based Genzyme Genetics, as its new president and CEO.

Gray comes to the job after almost six years at Genzyme, where he got experience in the pharmaceutical, venture capital, and diagnostics operations inside the biotech giant (NASDAQ: [GENZ](#)). Before that, he spent four years working with healthcare clients at McKinsey & Co. He's got a bachelor's in economics and management from the University of Oxford in the U.K., and a bachelor's in chemical engineering from MIT. Gray, a first-time CEO, was still getting settled into his new office in Seattle's South Lake Union neighborhood when I stopped by for an interview yesterday.

NanoString's new leader joins at a pivotal moment for the company, as it seeks to grow into a stronger commercial enterprise. NanoString, founded in 2004 with technology from the Institute for Systems Biology, introduced its first commercial product in July 2008. It's a digital instrument for academic biologists to help them determine the extent to which many genes are dialed on or off in a sample—what's known as gene expression analysis. The company has built a base of academic customers at top institutions like the [Broad Institute of MIT and Harvard](#), Caltech, and the University of Washington. While the company [raised \\$30 million in a round led by Clarus Ventures](#) a year ago, it hasn't yet turned profitable, and it has been operating without a permanent CEO [since Perry Fell resigned more than a year ago](#).

NanoString executive chairman Bill Young, an industry leader who's currently the chairman of Biogen Idec, said [when he joined NanoString in February](#) that the company has some very good people, but it needs "consistent leadership that can take the company to the next level."

Gray says he envisions NanoString growing into a "very valuable company."

"I want this to be a company that helps researchers make important biomedical discoveries, and helps physicians to translate those discoveries," Gray says.

NanoString first hit Gray's radar screen about a year ago, when he was running the diagnostics operation inside Genzyme. Scientists inside Genzyme told him about the NanoString instrument, called nCounter, and noted that its ability to generate digital readouts on hundreds of genes in a relatively small sample could be useful inside Genzyme. Gray noticed the company again in February when Young was named executive chairman of NanoString. Young, who formerly ran Monogram Biosciences, had noticed Gray's work at Genzyme, where he ran a \$370 million business in 2009, essentially one of the top five diagnostic service providers in the U.S., Gray says.

"We had a few interactions when Bill was at Monogram, and we had a good rapport," Gray says.

That got Gray to listen when the recruiter called. But when he started taking a closer look, he found the opportunity more and more attractive. He liked the fact that NanoString's instrument has broad ability to do "multi-plexed" experiments that, instead of looking at one gene, are able to analyze hundreds of genes in a sample to look at a symphony of what might be going wrong in complex diseases like cancer, diabetes, or inflammation. He liked the digital precision of the NanoString results. And, based on his experience in diagnostics, he really liked that the NanoString tool isn't thrown off track by Formalin-Fixed, Paraffin-Embedded preservation techniques that are commonly used in medical facilities, but sometimes cause problems for competing devices.

Still, this was a big decision to make personally and professionally. Gray, a native of Columbia, SC, had never even been to Seattle until he flew here to interview for the NanoString job. He is married, with a two-year-old son and a newborn, six-week-old daughter. It was no small thing to consider moving his family across the country. For a few more weeks anyway, his family is still in Boston, although they are planning to move to Bellevue, WA, before the end of July, Gray says.

While Young told me back in February that he was willing to consider establishing NanoString's headquarters somewhere else to recruit the right CEO, Gray said he felt that he needed to be in Seattle to be effective, and "close to the company center of gravity." It probably didn't hurt that we had our conversation on a beautiful summer afternoon in Seattle, but Gray said he's thrilled to be here.

"NanoString was exciting enough that I probably would have gone somewhere less exciting than Seattle just to be a part of it," Gray says.

Three things stand out for Gray on his to-do list as he gets up and running. The company must continue to build sales momentum for the nCounter system among its customer base of academic researchers, who use the tool to publish high-impact

scientific papers. Second, he's going to whittle down the company's long list of market opportunities to bring more focus on a couple of top priorities. And third, he's going to recruit a senior management team with the skills NanoString will need to make the transition from selling a tool to academic researchers into the completely different market of clinical diagnostics.

It sounds like he's got some serious recruiting to do. NanoString has about 75 employees now, but it will look to add some key posts, like a head of R&D, a chief commercial officer, a chief medical officer, and people with experience in regulatory affairs—which is necessary for a diagnostic application.

The diagnostics market is something Gray knows well from his Genzyme days, and both he and Young have contacts in Big Pharma companies who may be interested in using the NanoString technology to develop companion diagnostics that will help select which patients are more likely to benefit from a new drug than others. This is one of the big trends at work in the era of cost-containment, particularly with cancer drugs, where many drugs only help one-fourth of patients, and huge amounts of money are spent treating people who won't see any benefit.

Exactly how NanoString plans to tackle this market is still to be determined. It could form a partnership to develop a companion diagnostic tool with a Big Pharma company, develop the application on its own and lean on someone else's distribution network, or go it alone, Gray says. If NanoString chooses the latter route, it will need to raise more venture capital. Running the kind of experiments that will win over diagnostic customers won't come cheap.

"You want to prove that the tool is valuable before you try to sell it," Gray says. "We will continue to need to raise money to succeed if we choose to go it alone in molecular diagnostics."

July 1, 2010

IRIS Submits 510(k) Application to FDA for Automated Urine Chemistry Analyzer and Urinalysis Workstation

IRIS International, a leading manufacturer of automated in-vitro diagnostics systems and consumables for use in hospitals and commercial laboratories worldwide, announced today that its IRIS Diagnostics Division submitted on June 30, 2010, a 510(k) pre-market notification application to the U.S. Food and Drug Administration (FDA) requesting regulatory clearance for its iChem(R)Velocity(TM) Automated Urine Chemistry Analyzer and iRICELL(R) Urinalysis Workstation.

"Following the collection of additional data and expanded clinical studies and a Pre-IDE review by the FDA, we are pleased to submit our 510(k) application for clearance of the iChemVELOCITY and iRICELL urinalysis workstation," stated Cesar Garcia, a, Chairman, President and CEO of IRIS International. "Based upon our extensive clinical studies, testing and validation of the instrument improvements, we feel confident this new 510(k) submission addresses the issues raised by the FDA in our previous submission and in its recent Pre-IDE review," he added.

"While pursuing U.S. regulatory clearance, IRIS launched the iChemVELOCITY to the international market in September 2008, and since that time has sold over 250 instruments with high customer satisfaction, following implementation of certain product enhancements, design improvements and retrofits based on initial customer feedback," Mr. Garcia said.

The iChemVELOCITY system is designed to deliver improved productivity and clinical utility in the medium to high volume hospital and clinical reference labs.

"The iChemVELOCITY represents a critical element of Iris's strategy to provide both stand-alone automated urine chemistry analyzers and our fully integrated urinalysis workstation, iRICELL, globally. Upon FDA clearance, the iChemVELOCITY will allow IRIS and its global distribution partners to best meet our customer's needs in the automated urinalysis segment," stated Tom Warekois, President of the IRIS Diagnostics Division. "The global availability of iChemVELOCITY uniquely positions IRIS to supply a proprietary bench top automated urinalysis system from a single-source provider," Mr. Warekois said.

The iChemVELOCITY combined with the Company's series of iQ(R)200 automated urine microscopy analyzers, forms the portfolio of iRICELL Complete Urinalysis Workstations.

July 2, 2010

More Physicians Using Smart Phones to Access Lab Test Results and Other Clinical Information

With the advent of data-capable smart phones, disease management is taking a giant step forward. That has important implications for pathologists and clinical laboratory manager, who need to ensure that their medical laboratory information systems are ready for access by smart phones and other wireless devices used by clinicians.

Recent surveys show that physicians increasingly use their smart phones and other mobile devices to view test results and communicate with patients. In fact, in a recent

report, Manhattan Research predicted that, by 2012, about 82% of physicians will have smart phones and more than half that number will use them for such tasks as administrative work, continuing medical education, and patient care.

Another March study by healthcare marketing firm SDI found that 30% of physicians already use some form of mobile device to access patient records. Physicians and nurses also use smart phones to access decision-support tools, reference materials, and mobile CME courses.

Physicians are not the only ones using mobile devices to access medical information. The Cleveland Clinic and other hospitals around the nation—recognizing how physicians are using smart phones and similar wireless devices—now offer smart phone applications that access physician referral services and information about the hospital. Some even offer a tool that lets patients request a medical appointment from their phone or other mobile device.

For example, the Hospital of Central Connecticut developed an iPhone application that gives patients access to real-time emergency room wait times. Another company took this idea a step further with ER Texting. This application lets patients enter their zip codes and receive wait times for the emergency rooms of hospitals in their areas.

Four years ago, the New York City health agency responsible for running its hospitals and clinics introduced a phone-based glucose monitoring system to keep track of diabetic patients' blood sugar levels. Several times a day, the patient sends glucose data via modem to a nurse. If the reading is too high or too low, the nurse makes a call to find out what triggered the out-of-range diagnostic test result.

This real-time feedback helps patients make the connection between their actions and their glucose levels. According to Ann Frisch, Executive Director of New York's home care division, more than 85% of diabetics in this program have seen significant improvement. Though the current system uses landline phones to transmit the data, a new, mobile version of the monitor is now available. The city will use the new mobile device with patients who do not have a landline.

There is new phone-based technology that has application in dermatopathology. This technology allows both patients and physicians to photograph suspicious lesions and send the images to a remote pathologist for analysis. The patient application makes it possible for a consumer to photograph a skin irregularity, then transmit the image to a computer which uses algorithms to evaluate the lesion.

A more sophisticated version of that idea uses a quarter-sized device that attaches to a cell phone camera lens. A fluid-sample slide can be placed over the device to create an image that is transmitted to a pathologist for analysis.

While these devices are not quite as advanced as the visionary “tricorder” introduced in the Star Trek television show more than forty years ago, the trend is definitely toward using mobile devices to transmit medical data. As the number of young physicians entering the work force increases, the trend will accelerate. Raised with computers and cell phones as ubiquitous tools of life, this generation of physicians will demand a high level of communication sophistication from their medical partners, including pathology groups and clinical laboratories.

The ever-increasing use of smart phones and wireless devices by physicians and nurses means that it won’t be long before significant numbers of providers want to use their smart phones to access and view clinical laboratory test data. First-mover pathologists and medical laboratory managers are responding to this nascent trend by developing the capability for their LIS (laboratory information system) to feed data in a secure fashion to the smart phones of client physicians.

For laboratory managers looking toward the future of the information systems, mobile-friendly formats should be as high a priority as electronic medical records compatibility. Those pathology groups and clinical laboratories which invest in technology solutions that support how physicians are using smart phones and similar wireless devices are likely to gain significant competitive advantage.

June 26, 2010

Claros Diagnostics Receives CE Mark Approval for Point-of-Care PSA System

Claros Diagnostics, a developer of novel point-of-care *in vitro* diagnostic systems, today announced the CE Mark approval for its rapid quantitative point-of-care diagnostic platform, which can now be used for prostate specific antigen (PSA) testing throughout the European Union. The approved system consists of a small portable analyzer and credit card-sized disposable.

“This approval represents a significant milestone of our overall strategy to create a suite of products for the point-of-care market”

Claros is preparing for the European launch of its urology product and continuing the process to attain regulatory clearance in other markets, including the U.S. “This approval represents a significant milestone of our overall strategy to create a suite of products for the point-of-care market,” said Michael J. Magliochetti, Ph.D., President and CEO of Claros. “We will continue to expand the menu within urology and leverage the differentiation of our platform technology across other verticals as a vehicle to

transition virtually any complex immunoassay from the reference laboratory to the point-of-care. This CE Mark approval will facilitate the commercial rollout of the system in all of the major world markets that we will pursue.”

This approval follows the announcement late last year of the receipt of corporate ISO 13485 and CMDCAS certificates of registration by Claros subsequent to its establishment of a new manufacturing facility in 2009 for its microfluidic disposable test cassettes to support clinical trials and market launch. The Claros point-of-care system for PSA provides physicians and patients with accurate, laboratory-quality rapid results during their clinical visit. Healthcare providers experience more efficient clinical workflows and direct reimbursement, while stakeholders enjoy lower total cost of operation and enhanced customer experience.

Claros Diagnostics’ point-of-care system consists of disposable test cassettes and a small (desktop or handheld) analyzer, which delivers high performance quantitative laboratory blood test results with significant ease-of-use allowing the transition of complex immunoassays and other tests from the centralized reference laboratory to the point-of-care (bedside, physician’s office, etc.). Attractive attributes of the technology include the ability to use a finger-stick of whole blood, automation of all assay steps, multiplexing, on-board controls, cost effectiveness and the delivery of results in minutes. The urology market has been the initial focus to validate the technology, while also serving as a bridge to the true platform nature of the technology encompassing infectious disease, women’s health, cardiology, companion diagnostics, and beyond, with applications in settings throughout the world.

June 26, 2010

Signature Diagnostics To Use Microarray Technology For Advanced Colorectal Cancer Tests

Affymetrix, Inc. and Signature Diagnostics AG today announced that they have signed a Powered by Affymetrix™ (PbA) agreement. Under the agreement, Signature Dx obtains a worldwide license to use Affymetrix® microarray technology to develop and commercialize diagnostic and prognostic colorectal cancer (CRC) tests.

Signature Dx plans to launch two microarray-based in vitro diagnostic (IVD) products by the fourth quarter of this year to enable earlier diagnosis and improved prognosis for CRC. Approximately 396,000 people are diagnosed with CRC annually in the five major European countries and the US, and millions more go undetected because of limitations in current diagnosis methods. Signature Dx will launch the tests in Europe and plans to seek US regulatory approval in the future.

Detector C is a validated, non-invasive, blood-based early detection test that has shown consistently high sensitivity of 90 percent for all four CRC stages (including early stages), and a specificity of 88 percent. Predictor C is a validated prognostic tissue test that predicts disease progression in stage II and III CRC patients and been shown to identify half of all stage II/III patients with a high risk of disease progression. "Colorectal cancer is one of the most common cancers worldwide and our innovative, multivariate IVD tests can significantly improve both the diagnosis and prognosis of the disease," said André Rosenthal, PhD, Chief Executive Officer of Signature Diagnostics. "Our novel Detector C blood screening product together with Affymetrix' gene expression array technology brings CRC screening to a new level of accuracy and sensitivity. This licensing agreement provides us with the underlying microarray technology for our diagnostic products in colorectal cancer."

"Signature Diagnostics' innovative colorectal cancer tests have the potential to vastly improve diagnosis and lead to better-informed treatment decisions for this disease," said Andrew Last, PhD, Executive Vice President and Chief Commercial Officer at Affymetrix. "This Powered by Affymetrix agreement demonstrates the importance of microarray technology in advancing healthcare and further reinforces Affymetrix' leadership position in the global shift towards personalized healthcare."

Signature Dx is a molecular diagnostics company based in Potsdam, Germany, focusing on the development and commercialization of novel in-vitro diagnostic (IVD) products for the prognosis and early detection (screening) of colorectal cancer. Using its state-of-the-art technologies in tissue and blood sample collection, molecular pathology, genome-wide tumor profiling technologies, data mining, and biostatistics, the company collaborates with many clinical and diagnostic partners. Signature Dx sponsors and conducts large prospective, multicenter clinical trials with more than 25 primary care hospitals and several dozen colonoscopy centers in Germany to discover and validate RNA biomarkers in colorectal cancer and colorectal cancer screening. The company's first products, Predictor C and Detector C, will be launched by the end of 2010 in its own ISO 15189 certified service lab.

The EU-5 and US screening population (aged 50 to 79) totals 170 million individuals. Approximately 5.1 million individuals (3 percent) have an undetected colorectal cancer (CRC). Only 396,000 CRC cases (7.8 percent) are presently diagnosed annually (EU-5: 220,000, USA: 176,000). Classical screening methods, including haemocult II (gFOBT) and colonoscopy, detect only 5 percent of these 396,000 CRC patients. In 4.7 million individuals affected with CRC, the asymptomatic cancer remains undetected. In Germany, 73,000 patients are diagnosed with CRC every year. Due to the risks and inconvenience associated with CRC colonoscopy screening (bleeding events, colon perforations), patient participation is low (3-5 percent p.a.). Therefore, CRC screening using colonoscopy results in the diagnosis of only 5,400 patients each year. Also, CRC screening, using gFOBT, is declining due to the test's inaccuracy and the difficulties associated with collecting stool samples. There is a great need for a non-invasive IVD that can detect early stage CRC and serve as a reliable screening tool.

CRC is the third most common cancer worldwide. In the five major European countries and the USA, approximately 396,000 individuals are diagnosed with CRC every year. Of these, 277,000 patients are diagnosed with stage II and stage III CRC. Approximately 30 percent of the patients with stage II and roughly 50 percent of those with stage III experience disease progression including distant metastasis of the liver and lung or local recurrence within three to five years after surgery. If the cancer spreads to distant organs, the five years survival rate is only 8 percent. Presently, there are no validated clinical parameters or biomarkers in use to identify patients with a high risk of disease progression. If this risk could be determined, a substantial number of patients with stage II/III disease would benefit from adjuvant chemotherapy in addition to surgery.

June 23, 2010

Epigenomics AG Successfully Validates Lung Cancer Test in Clinical Trial

Epigenomics AG a cancer molecular diagnostics company, successfully completed the pivotal performance evaluation study for its Epi proLung BL Reflex Assay, a lung cancer diagnostic test.

The test determines the DNA methylation status of the SHOX2 gene in bronchial lavage material routinely obtained during the clinical workup of patients with suspected lung cancer. Increased DNA methylation of the SHOX2 gene indicates the presence of malignant lung disease. The study has demonstrated that the analytical and clinical performance fulfills the requirements for its intended use as an aid in the diagnosis of lung cancer. This successful performance evaluation meets an important clinical trial milestone as a regulatory prerequisite to CE-marking of in vitro diagnostic products prior to market introduction. The completion of the study now paves the way for the European launch of the Epi *proLung* BL Reflex Assay which is expected within the next few weeks.

In clinical care today, lung cancer is typically confirmed by the analysis of tissue that is directly obtained from the tumor or by analyzing cellular material e.g. from rinsing the airways with saline solution during a bronchial lavage. However, in approximately half of the suspected cancer cases neither cytology nor histology provide conclusive results at the time of a patient's first bronchoscopy. This frequently leads to further time consuming and costly procedures bearing additional risks for patients. The Epi *proLung* BL Reflex Assay test addresses this clear medical need by helping pathologists to confirm the presence of malignant lung disease. "The Epi *proLung* BL Reflex Assay may provide critical additional information to pathologists when cytology

is not unequivocal. This represents the diagnostic value of the test", stated Prof. Manfred Dietel, Director of the Institute of Pathology of Charité – University Medicine Berlin at a recent Key Opinion Leader Meeting in Frankfurt am Main, Germany, at which Epigenomics has introduced the novel test to pathologists and oncologists.

The clinical performance of the test has been demonstrated in a case control study with individuals that have undergone diagnostic work-ups for suspected lung cancer within the University of Liverpool Cancer Research Centre, Roy Castle Lung Cancer Research Program UK, under Professor John K Field. Using the Epi proLung BL Reflex Assay, the DNA methylation status of the SHOX2 gene was determined in routinely obtained bronchial lavage of patients with confirmed bronchial carcinoma and patients with no evidence of malignant lung disease but other lung diseases at the time of bronchoscopy and a minimum lung cancer free survival of 18 months. In this critical patient group, the test correctly identified 81% of the lung cancer cases with only 5% false positive results translating into a specificity of 95%. This clinical performance evaluation study confirms previous research studies showing that methylated SHOX2 DNA is a highly specific biomarker for lung cancer in bronchial lavage. Furthermore, the performance evaluation study has demonstrated that the Epi *pro*Lung BL Reflex Assay is a technically robust and reliable diagnostic tool. Simple handling, short time to results and compatibility with standard molecular diagnostic laboratory equipment are expected to facilitate introduction of this test into clinical routine.

"We have shown in a number of clinical studies that the biomarker ^mSHOX2 has utility in supporting physicians in detecting lung cancer with certainty, thereby avoiding delays in establishing the final diagnosis. This allows them to initiate treatment sooner, thus improving the quality of life of the patient", stated Dr. Uwe Staub, Senior Vice President Product Development at Epigenomics. "Based on this successful pivotal clinical study showing impressive analytical and clinical performance we have met a key milestone for the launch of the Epi *pro*Lung BL Reflex Assay" added Dr. Staub.

With about 386,300 new cases in Europe in 2006 and about 219,000 new cases in the U.S. in 2009, lung cancer is the third (after Prostate and Breast Cancer) most common cancer in men and women, accounting for about 20 percent of all cancer deaths - more than any other cancer. Current guidelines do not recommend screening for lung cancer leading to a situation in which the majority of patients are diagnosed at advanced stages. The overall objective of the diagnostic work-up is to establish the definitive diagnosis with the least invasive methods to minimize the patient's risk. Individuals suspected to have lung carcinoma typically undergo chest X-ray, or CT scanning followed by more invasive procedures like bronchoscopy, i.e. the visual inspection of the bronchial airways with an endoscope and biopsy by needle or surgery. Until recently tumor markers have played only a minor role in this diagnostic process.

June 25, 2010

Association For Molecular Pathology Asks FDA To Address Barriers To Device Innovation

Yesterday, the Association for Molecular Pathology (AMP) gave public comments at the FDA's Center for Devices and Radiological Health (CDRH) Council meeting on Medical Device Innovation: Barriers to Market for Molecular Diagnostic Tests.

AMP commends the Federal departments and agencies that compose the Council on Medical Device Innovation for making efforts to identify and remove barriers to innovation and progress in transitioning basic and transitional research findings into routine clinical practice. In its remarks, AMP identified three barriers that impede the path to FDA clearance or approval for diagnostic tests and reduce the motivation to submit some medically useful tests for review.

Barrier 1. The paucity of standard reference materials for all areas of molecular diagnostics, i.e., genetic, oncology, and infectious disease testing, inhibits the production of appropriate control materials and methods. "AMP is eager to see more progress and investments in this area," said Dr. Mark Sobel, AMP's Executive Officer. "FDA can assist by providing a list of needed standard reference materials to relevant organizations such as the National Institute of Standards and Technology (NIST) and World Health Organization (WHO)."

Barrier 2. The difficulty of obtaining rare specimens for studies presents a barrier to submission of applications for the approval of new indications for currently approved tests. Herpes Simplex Virus (HSV) testing has been the standard of care for the diagnosis of central nervous system (CNS) disease (HSV encephalitis and meningitis) for over a decade, yet an FDA approved test does not yet exist. HSV CNS infections are relatively rare and any individual laboratory may receive only 1-2 HSV encephalitis positive specimens a year. Manufacturers who developed assays for the novel 2009 influenza H1N1 strain encountered similar difficulties in validating their assays using prospective clinical specimens after the peak of the pandemic had passed.

Dr. Sobel identified a potential solution to the shortage of specimens, "The FDA should work to establish a biorepository of clinically relevant infectious agents, including strain variants and subtypes, to facilitate the rapid development and validation of assays for infectious agents, particularly those with pandemic potential." Alternatively, AMP also asked the FDA to consider establishing alternative validation strategies that are independent of primary clinical specimens, but are, nonetheless, rigorously grounded in sound science and infectious disease medicine.

Barrier 3. Test manufacturers perceive that there is an inconsistent and unclear regulatory pathway for their submissions. Manufacturers have faced uncertainty and/or

inconsistency in the review of device submissions, in enforcement discretion, in device classification [510(k), 510(k) de novo, PMA, ASR, etc.], in requirements for acceptable analytical and clinical validations, and in requirements changing from the time of pre-IDE meetings through mid-trial. "IVD test manufacturers must then function within this uncertain regulatory environment, which makes it difficult to anticipate regulatory requirements and appropriately amend their business models," said Dr. Sobel.

To address the barriers identified above, AMP believes that the FDA can take several steps that would improve the regulatory process for molecular diagnostic tests without impinging upon an appropriate review to ensure that the public is protected.

FDA should ensure that policies and requirements are consistently applied, and that the scientific evidence and rationale for decisions are communicated effectively to diagnostic test manufacturers.

Communication from FDA to diagnostic test manufacturers should be as clear and as comprehensive as possible at the outset of the submission process. This will help manufacturers better plan their resources and time. It will also assuage undue angst that the regulatory bar will change during the process.

FDA should improve communication between government branches and agencies so that consistent requirements are developed and applied and demonstrations of clinical utility in one branch are recognized by the other branches.

FDA should involve the expert opinion of medical professional associations regarding clinical utility.

The Association for Molecular Pathology recognizes the difficulties that regulatory agencies face in the context of the rapidly changing landscape of diagnostic devices and technology and appreciates the transparent process FDA is undertaking to improve the review process for medical devices. AMP believes that a consistent, clear, and flexible regulatory process will result in improved public access to additional higher quality innovative tests; and could conceivably lower healthcare costs.

"AMP stands ready to assist the FDA through our expertise, creative problem solving, and unique perspective," added Dr. Sobel. "We would like to offer our input and interaction with the member departments and agencies to assist in developing a more consistent, evidence-based, and transparent process for regulating diagnostic devices."

June 24, 2010

Promise Seen for Detection of Alzheimer's

Dr. Daniel Skovronsky sat at a small round table in his corner office, laptop open, waiting for an e-mail message. His right leg jiggled nervously. A few minutes later, the message arrived — results that showed his tiny start-up company might have overcome one of the biggest obstacles in diagnosing Alzheimer's disease. It had found a dye and a brain scan that, he said, can show the hallmark plaque building up in the brains of people with the disease.

The findings, which will be presented at an international meeting of the Alzheimer's Association in Honolulu on July 11, must still be confirmed and approved by the Food and Drug Administration. But if they hold up, it will mean that for the first time doctors would have a reliable way to diagnose the presence of Alzheimer's in patients with memory problems.

And researchers would have a way to figure out whether drugs are slowing or halting the disease, a step that "will change everyone's thinking about Alzheimer's in a dramatic way," said Dr. Michael Weiner of the University of California, San Francisco, who is not part of the company's study and directs a federal project to study ways of diagnosing Alzheimer's.

Still, the long tale behind this finding shows just how difficult this disease is and why progress toward preventing or curing it has been so slow. Ever since Alzheimer's disease was described by a German doctor, Alois Alzheimer, in 1906, there was only one way to know for sure that a person had it. A pathologist, examining the brain after death, would see microscopic black freckles, plaque, sticking to brain slices like barnacles. Without plaque, a person with memory loss did not have the disease.

There is no treatment yet to stop or slow the progress of Alzheimer's. But every major drug company has new experimental drugs it hopes will work, particularly if they are started early. The questions though, are who should be getting the drugs and who really has Alzheimer's or is developing it?

Even at the best medical centers, doctors often are wrong. Twenty percent of people with dementia — a loss of memory and intellectual functions — who received a diagnosis of Alzheimer's, did not have it. There was no plaque when their brains were biopsied. Half with milder memory loss, thought to be on their way to Alzheimer's, do not get the disease. And with such a high rate of misdiagnosis, some who are mistakenly told that they have Alzheimer's are not treated for conditions, like depression or low levels of thyroid hormone or drug side effects and interactions, that are causing their memory problems.

Brain scans that showed plaque could help with some fundamental questions — who

has or is getting Alzheimer's, whether the disease ever stops or slows down on its own and even whether plaque is the main culprit causing brain cell death. Dr. Skovronsky thought he had a way to make scans work. He and his team had developed a dye that could get into the brain and stick to plaque. They labeled the dye with a commonly used radioactive tracer and used a PET scanner to directly see plaque in a living person's brain. But the technology and the dye itself were so new they had to be rigorously tested. And that is what brought Dr. Skovronsky, a thin and eager-looking 37-year-old, to his e-mail that recent day.

Five years ago, Dr. Skovronsky, who named his company Avid in part because that is what he is, had taken a big personal and professional gamble. He left academia and formed Avid Radiopharmaceuticals, based in Philadelphia, to develop his radioactive dye and designed a study with hospice patients to prove it worked.

Hospice patients were going to die soon and so, he reasoned, why not ask them to have scans and then brain autopsies afterward to see if the scans showed just what a pathologist would see. Some patients would be demented, others not. Some predicted his study would be impossible, if not unethical. But the F.D.A. said it wanted proof that the plaque on PET scans was the same as plaque in a brain autopsy.

The Avid study was designed to provide that proof. And the full results, contained in the e-mail message sent that day, May 14, were the moment of truth. When he saw them, Dr. Skovronsky said they were everything he had hoped for. "This is about as good as it gets," he said that day. He went into a rotunda that serves as Avid's lunchroom to tell the company's 50 employees. "This is a big day for us," he continued. "I thought about what I would say, but I have totally forgotten it." His employees applauded. Then they had champagne in blue plastic cups.

The type of scans used in this study, PET scans, are expensive and patients have to go to a scanning center, get injected with a radioactive dye, wait for the dye to reach their brain and then have a scan.

Other tests are being studied — ones that look for amyloid in cerebrospinal fluid that bathes the brain; MRI scans that look for shrinkage of the brain in areas needed for memory and reasoning; PET scans that look for uptake of glucose, a cellular fuel, to show areas where the brain was active and where it was not. The tests, though, were not necessarily specific for Alzheimer's and none had been studied to see if they accurately predicted plaque on autopsy.

Earlier this decade, two scientists at the University of Pittsburgh developed an amyloid dye that while not practical for widespread use, stunned scientists by showing it seemed possible to see amyloid in a living brain.

The researchers, Chester Mathis and William Klunk, began their work two decades ago, persevering even though they had no research money. In the first 10 years, they

tested more than 400 compounds. When they finally found one that seemed promising, they tested more than 300 variations. "On and on it went," Dr. Mathis said. Finally, in late 2001, they began working with collaborators in Sweden to test their dye in humans. On Valentine's Day 2002, the Swedish researchers injected the first Alzheimer's patient with the dye, known as Pittsburgh Compound B, and scanned the patient's brain.

It worked, the Swedish doctors told Dr. Mathis in an excited phone call.

A PET scan showed amyloid exactly where it would be expected. The Swedish doctors were convinced they were seeing actual plaque. They told Dr. Mathis it was time to celebrate. But Dr. Mathis worried. What if the same pattern occurred in people without Alzheimer's? Two weeks later, he got another call from Sweden. His colleagues had scanned a person without Alzheimer's. There was no sign of telltale plaques. His sweet reward came in July 2002, when the scans were shown to an audience of 5,000 scientists at an international conference on Alzheimer's.

"There was an audible gasp," Dr. Mathis said. "The field was taken aback." "The rest is history," he added. Yet there was a problem. Pittsburgh Compound B used carbon 11 as its radioactive tracer. And its half-life is 20 minutes. Researchers have to make it in a cyclotron in the basement of a medical center, quickly attach it to the dye, dash over to a patient lying in a scanner, and inject it.

And a critical question remained: Was a PET scan with the Pittsburgh dye really equivalent to a brain autopsy? Meanwhile, others, including Dr. Skovronsky, had another idea — use fluoride 18, with a half-life of about two hours. It could be made in the morning, and used that afternoon. And fluoride 18 is made routinely for two million cancer PET scans each year. Dr. Skovronsky, starting at the University of Pennsylvania and then at Avid, worked with a University of Pennsylvania chemist, Hank Kung, for nine years to find and develop the radioactive dye. The university had the patent; Avid licensed it. Finally, on June 8, 2007, a patient at Johns Hopkins had a scan with their compound. Plaque lit up.

Most of the time, the scans were as expected — those with Alzheimer's had lots of plaque, those with normal memories had little if any and those with mild memory impairment were in between. But about 20 percent of people over 60 with normal memories had plaque.

"Then we looked more carefully," Dr. Skovronsky said. "The 20 percent who had amyloid, though they were still statistically in the normal range, did worse on every memory test than the control group." What, Dr. Skovronsky asked, did that mean? Were they starting to develop Alzheimer's? If so, could dementia be stalled if there were drugs to stop amyloid from accumulating?

The definition of Alzheimer's is plaque plus memory loss and other symptoms of

mental decline. But what is not known because no one could follow the development of plaque before a person died, was whether people with plaque and normal memories were developing Alzheimer's.

"We've always assumed the pathology has been there, that the plaque has been there years before symptoms," said Dr. Steven T. DeKosky, an Alzheimer's researcher who is vice president and dean at the University of Virginia School of Medicine. "But we never had a way to detect plaque in living persons," he said. And so plaque in the brains of people with normal memories has been a puzzle. "Over the next couple of years, we will find out what it means."

On Oct. 23, 2008, Avid and two other companies, Bayer and General Electric, that are developing fluoride 18-based dyes for amyloid scans, got a pointed question from an advisory committee to the F.D.A.: How do you know that what you are seeing on scans is the same as the amyloid you see on autopsy?

It seemed impossible to answer. If researchers wait for their subjects to die before comparing scans with autopsies they can be waiting a long time.

But Avid had a plan, and the committee agreed in principle that it would work. Hospice patients would be study subjects, some with dementia, some without. All would have memory tests and brain scans. After death, their brains would be autopsied. Avid suggested that after the first 35 died, there should be enough data to know if the scans gave a true picture of the pathology. Then the F.D.A. could decide if the results were convincing enough to approve the dye for marketing.

Some doctors had misgivings, wondering how they could ask people who were sick and dying to be scanned just to help Alzheimer's research. But, they found, most patients and their families agreed and said they were grateful to have been asked. That was evident on May 19, when Dr. Skovronsky gave a lunch for patients' families in Sun City, Ariz., to thank them for participating. They thanked him.

"It really touched my heart to be in this," said Dorothy Wall, whose husband, Claude E. Wall, died of liver cancer in Sun City on March 3. "Something bad happens, and now something good happens."

Late last year, Avid saw the initial results of its hospice study — data from the first six patients. Then, as more patients were studied, the data from them were held by a company that would analyze it. Avid did not see the results until the study was completed. But those first six were encouraging.

A man diagnosed with Alzheimer's and cancer had a scan showing no plaque. His autopsy did not show it, either. The diagnosis was wrong. Another man with Parkinson's disease and dementia had been diagnosed as having dementia solely due to Parkinson's. His scan showed amyloid. So did the autopsy. He had Alzheimer's. A

woman with mild memory loss had a scan showing no amyloid. Her autopsy also found none. Three others had clinical diagnoses of Alzheimer's, confirmed by scans and autopsies.

Finally, on May 14, 35 patients had been scanned and autopsied. The Avid study was complete, and the full data will be presented at the meeting next month. Other companies, still doing their studies, did not yet have data to examine. And Dr. Skovronsky got that e-mail message. "This is going to have a big impact on Alzheimer's disease, guys," he told his staff that day.

June 17, 2010

Gen-Probe Makes \$50 Million Strategic Investment in Third Generation Sequencing Company Pacific Biosciences

Gen-Probe and Pacific Biosciences announced today that Gen-Probe has made a \$50 million strategic investment in Pacific Biosciences, a private sequencing company. In addition, the companies will work together to explore co-development of new integrated clinical diagnostics systems based on Pacific Biosciences' Single Molecule Real Time (SMRT(TM)) platform and Gen-Probe's expertise in diagnostics.

Gen-Probe and Pacific Biosciences will initially collaborate on an exclusive basis for up to 30 months, with the goal of developing a longer-term, preferred business relationship aimed toward improving the diagnosis of human diseases. The companies can also purchase certain of each others' products on preferential terms.

"We believe Pacific Biosciences' third-generation, single-molecule sequencing technology has the potential to play an important long-term role in strategically valuable, high-growth clinical diagnostics markets such as oncology, transplant diagnostics and pharmacogenomics due to its fast time to result, long read lengths, and ability to interrogate broad genomic regions in high resolution," said Carl Hull, Gen-Probe's president and chief executive officer. "We are excited to collaborate with Pacific Biosciences to develop an innovative sequencing system based on their best-in-class technologies."

Pacific Biosciences' SMRT DNA sequencing is expected to be a transformative technology that enables a new paradigm in genomic analysis. It enables, for the first time, the observation of natural DNA synthesis by a DNA polymerase as it occurs. The approach is based on eavesdropping on a single DNA polymerase molecule working in a continuous, processive manner.

"We see a significant opportunity for our SMRT platform in the molecular diagnostics market and are taking a proactive and strategic approach by collaborating with Gen-Probe, a proven leader in developing fully automated instrument systems for nucleic acid testing," said Hugh Martin, chairman and chief executive officer of Pacific Biosciences. "We believe Gen-Probe's expertise in instrument systems engineering and sample preparation, combined with their capabilities in clinical and regulatory affairs, will help us maximize the potential of our sequencing technology to benefit human health."

Pacific Biosciences' mission is to transform the way humankind acquires, processes and interprets data from living systems. The company has developed a disruptive technology platform for the real-time detection of biological events at single molecule resolution. Single Molecule Real Time (SMRT) Biology is designed to revolutionize life sciences by revealing the underlying networks that define living systems. The first application for the SMRT Biology platform is a paradigm changing approach to DNA sequencing. The SMRT Sequencing System should ultimately make it possible to sequence individual genomes as part of routine medical care. DNA sequencing is expected to be the first of many transformative SMRT Biology applications that will benefit society by driving radical advances in fields such as personalized medicine, agriculture, clean energy, and global health.

June 21, 2010

Exiqon Licenses Locked Nucleic Acids for Infectious Disease Diagnostics to BD

Exiqon A/S today announced that it has granted a non-exclusive license to BD (Becton, Dickinson and Company) to use Exiqon's proprietary locked nucleic acids (LNA™) technology in defined products for infectious disease diagnostics.

Exiqon will receive upfront and milestone payments, and royalty on global sales of the products covered by this agreement. Financial terms of the agreement were not disclosed. The U.S. DNA-based infectious diseases testing market is estimated by Frost and Sullivan to exceed \$2 billion in 2010. This agreement marks the first time LNA™ will be applied in the development of FDA-cleared diagnostic products.

"We are pleased to see BD has chosen to apply Exiqon's proprietary technology enabling these exciting new diagnostic products," said Lars Kongsbak, CEO & President of Exiqon. "We are excited that the LNA™ technology is now being applied to advanced diagnostic products."

Under the terms of this agreement, BD will market a number of defined LNA™-enhanced products to run on the new BD MAX™ System, BD's next-generation platform for molecular diagnostics based on real-time polymerase chain reaction.

LNA™ provides unique characteristics to molecular assays and offers many potential enhancements for developing advanced products. An inherent part of Exiqon's strategy to capitalize on its proprietary LNA™ technology is through license agreements within market segments that Exiqon does not plan to pursue itself.

June 21, 2010

Dako and Omnyx Sign Agreement Within Digital Pathology

Dako, a Danish based world leader in tissue-based cancer diagnostics, and Omnyx, a leader in digital pathology solutions, announced today that they have entered into a three-year agreement to develop clinical algorithms for digital pathology. The aim is to support pathologists in generating even more accurate, objective and reproducible diagnostic results.

Under the agreement, Dako will utilize its expertise in staining and image analysis to develop image analysis algorithms, which will be incorporated into the Omnyx digital pathology platform as part of Omnyx's overall strategy of providing pathologists with a comprehensive digital work environment. The algorithms developed under the agreement will be specifically optimized for Dako's breast cancer panel of immunohistochemical and in-situ hybridization tests.

"Digital pathology offers significant potential to improve the quality of cancer diagnosis by improving the consistency of test interpretation," says Dr. Michael Becich, University of Pittsburgh Medical Center in Pittsburgh, Pennsylvania. "The Omnyx/Dako partnership will help standardize the reagent-to-result process and enhance the ability of pathologists to interpret breast cancer tests".

Digital pathology is enabled by imaging systems and computer technology that allow for the digitization of glass slides and efficient management of the resulting image data. It enables pathologists to improve productivity by reviewing tissue sections without handling traditional glass slides and to interpret tissue based test results more objectively with the help of image analysis algorithms. Digital pathology also holds tremendous potential for standardizing test interpretation and for improving accuracy in cancer diagnostics.

“Dako is committed to improving patient care by finding ways to further enhance the standards and accuracy in cancer diagnostics. This agreement with Omnyx is another important step in the implementation of our strategy by joining forces with strong digital pathology partners. Digital pathology is important as it offers great potential to improve the quality of cancer diagnosis and care by helping standardize test interpretation to the benefit of pathologists and their patients,” says Lars Holmkvist, CEO of Dako.

“Omnyx sees a future where algorithms help pathologists make better clinical decisions. Our partnership with Dako will allow us to provide reliable, high-performance IHC algorithms to clinicians who use Dako tests. Enabling algorithms within the context of a complete digital workflow environment provides pathologists with a powerful set of tools to improve both confidence and efficiency,” comments Gene Cartwright, CEO of Omnyx.

Immunohistochemistry refers to the process of localizing antigens (e.g. proteins) in cells of a tissue section exploiting the principle of antibodies binding specifically to antigens in biological tissues. Immunohistochemistry and in-situ hybridization, which uses a DNA or RNA strand to identify abnormalities, are both widely used in the diagnosis of cancerous cells and also in the process of predicting a patient’s response to various treatments.

June 21, 2010

FDA Approves Test For Swift HIV Diagnosis

The FDA has approved an HIV diagnostic test that can detect the virus within days of infection. The ARCHITECT HIV Ag/Ab Combo assay, developed by Abbott detects both HIV antibodies and an antigen from the virus itself. It's the first such test licensed in the U.S., the agency said.

Because the viral antigen is present before antibodies develop, the test could detect HIV infections earlier than assays currently in use, a company spokesperson said. The test has been used in Europe since 2004 and should be available in the U.S. by the end of the year, according to Darcy Ross. The price of the test has not been set yet, she said.

Most diagnostic tests used today detect only HIV antibodies, the FDA said, and although the virus can be directly detected by nucleic acid testing, that method is not widely used in diagnostic settings. The Abbott test registers the presence of the HIV p24 antigen, as well as antibodies to HIV-1 groups M and O and HIV-2, which is less common and most often found in West Africa.

"Since individuals are most infectious to others shortly after infection, detecting HIV earlier is critical and life saving," said Peter Leone, MD, of the University of North Carolina Chapel Hill, in a statement issued by Abbott.

"Since individuals are most infectious to others shortly after infection, detecting HIV earlier is critical and life saving," said Peter Leone, M.D., medical director, North Carolina HIV/STD Prevention and Control Branch, University of North Carolina, Chapel Hill. "A significant percentage of new HIV infections are transmitted by someone with an undetected acute infection, so identifying more people earlier offers a significant opportunity for counseling, which can reduce high-risk behaviors and also initiate antiretroviral treatment for early-stage infection, if appropriate."

In the U.S., according to CDC estimates, about 56,000 people are newly infected with HIV every year -- which works out to about six new cases every hour. Worldwide, 2.7 million people acquire HIV each year, according to UNAIDS.

"The approval of this assay represents an advancement in our ability to better diagnose HIV infection in diagnostic settings where nucleic acid testing to detect the virus itself is not routinely used," according to Karen Midthun, MD, acting director of the FDA's Center for Biologics Evaluation and Research.

"It provides for more sensitive detection of recent HIV infections compared with antibody tests alone," she said in a statement.

The Abbott assay is not intended to be used for routine screening of blood donors, the FDA said, but it can be used to screen blood donors in urgent situations where licensed blood donor screening tests are unavailable or impractical.

Abbott's *ARCHITECT* HIV Ag/Ab Combo assay is the first test approved in the United States that can simultaneously detect both HIV antigen and antibodies. HIV antigen is a protein produced by the virus immediately after infection, whereas antibodies are developed days later as the body works to fight off the infection. Studies have demonstrated that Abbott's new test may detect HIV days earlier than antibody-only tests, which is important in controlling the spread of the virus.

Studies conducted by the Centers for Disease Control and Prevention (CDC) show that current antibody-only tests miss up to 10 percent of HIV infections in some high-risk populations because they do not detect antigens. However, Abbott's new assay detects the HIV p24 antigen, or the direct presence of HIV, allowing for diagnosis of early infections days before antibodies emerge.

"Abbott has long been a pioneer in HIV testing -- from the world's first test to detect HIV antibodies in 1985 -- to second and third generation immunoassay and molecular tests -- and now the development of the country's first antigen and antibody combination test," said Brian Blaser, senior vice president, Diagnostics, Abbott.

"Abbott is committed to fighting HIV and to bringing novel tests to physicians in order to help patients get the care they need as soon as possible."

This new test will run on Abbott's ARCHITECT family of diagnostic testing instruments. It is already approved for use outside the United States. In Europe, HIV antigen-antibody combination testing is routine in public health settings and HIV testing guidelines in the United Kingdom now direct clinicians to use the HIV combination test as the first-line test.

June 18, 2010

Leica Microsystems to Develop an Automated HER2 FISH Test

Leica Microsystems GmbH and Abbott have reached an agreement for Abbott to supply fluorescence in situ hybridization (FISH) probes that target the HER2 gene locus. The probes will be used to develop a fully automated FISH solution for HER2 testing on the Leica Microsystems' BOND™ an automated advanced staining platform.

Abbott's PathVysion FISH assay is the gold standard ISH (in situ hybridization) test for diagnosing the response of patients to Herceptin. Leica Microsystems will develop an automated version of this test to be performed on their BOND™ system using a standard protocol. Automation of the test on the Leica BOND™ system will enable Pathology laboratories to run this diagnostic test more efficiently. "With this new automated test we aim to provide a fast diagnostic result while maintaining the high standard associated with HER2 FISH testing, helping customers to provide time effective, individualized cancer therapy. We are pleased to be working together to advance patient cancer treatment," stated Arnd Kaldowski, President of Leica Biosystems.

The HER2 FISH test is designed to identify patients that are likely to respond to Herceptin, a drug which is used as a frontline therapy for treatment of breast cancer. Tumors, which over express HER2, are most suitable for treatment with Herceptin. HER2 over expression can be detected at the protein level using IHC (immunohistochemistry) or at the DNA level using ISH.

Intended Use

The PathVysion® HER-2 DNA Probe Kit (PathVysion Kit), which is FDA approved, is designed to detect amplification of the HER-2/neu gene via fluorescence in situ hybridization (FISH) in formalin-fixed, paraffin-embedded human breast cancer tissue specimens. Results from the PathVysion Kit are intended for use as an adjunct to

existing clinical and pathologic information currently used as prognostic factors in stage II, node-positive breast cancer patients. The PathVysion Kit is further indicated as an aid to predict disease-free and overall survival in patients with stage II, node positive breast cancer treated with adjuvant cyclophosphamide, doxorubicin, and 5-fluorouracil (CAF) chemotherapy.

The PathVysion Kit (see PathVysion package insert) is indicated as an aid in the assessment of patients for whom HERCEPTIN® (Trastuzumab) treatment is being

The PathVysion Kit is not intended for use to screen for or diagnose breast cancer. It is intended to be used as an adjunct to other prognostic factors currently used to predict disease-free and overall survival in stage II, node-positive breast cancer patients. In making decisions regarding adjuvant CAF treatment, all other available clinical information should also be taken into consideration, such as tumor size, number of involved lymph nodes, and hormone receptor status. No treatment decision for stage II, node-positive breast cancer patients should be based on HER-2/neu gene amplification status alone.

June 8, 2010

Celera Announces CE Mark for KIF6 Test -- Conformity Marking Allows Cardiovascular Pharmacogenomic Test To Be Marketed Throughout Europe

Celera today announced that it has signed a Declaration of Conformity and applied the CE mark to a real-time PCR (polymerase chain reaction) test for detection of a variant in the KIF6 gene, allowing the test to be marketed in the European Union and other geographic areas that recognize the CE Mark.

KIF6 encodes a kinesin, a member of a family of proteins involved in microtubule-mediated intracellular transport. Previous research has shown that a variant of the KIF6 gene is associated with up to a 55% increased risk of primary and recurrent coronary heart disease (CHD) events in the placebo arms of pravastatin clinical trials, and that this increased risk was significantly reduced with statin therapy.

"The application of the CE mark to our KIF6 test represents a significant milestone for Celera, allowing commercialization of the first in vitro diagnostic genetic product to predict risk for coronary heart disease and response to statin therapy. We also expect to submit a KIF6 test for pre-market approval to the Food and Drug Administration later this year as we continue to move our pipeline of proprietary genetic tests into routine clinical practice," said Kathy Ordonez, Chief Executive Officer of Celera.

The association between KIF6 and event reduction during pravastatin (Pravachol(R)) therapy has been demonstrated previously in three prospective, placebo-controlled randomized clinical trials on the prevention of CHD events: the secondary prevention Cholesterol and Recurrent Events (CARE) study; the primary prevention West of Scotland Coronary Prevention Study (WOSCOPS); and the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) study. Additionally, a genetic study of PROVE IT--TIMI 22 reported that in patients who experienced an acute coronary syndrome (ACS), high-dose atorvastatin (Lipitor(R)), compared with standard dose pravastatin, was significantly more effective at reducing CHD events in KIF6 carriers than in noncarriers. To date, the benefits of statin therapy for KIF6 carriers has only been demonstrated with atorvastatin and pravastatin therapy.

The KIF6 gene variant has also been reported to predict risk of CHD in prospective population genetic studies. This gene variant was associated with increased risk of CHD in Caucasian and African American participants of the Atherosclerosis Risk in Communities (ARIC) study (a study of 13,907 middle aged Americans), and with increased risk for myocardial infarction (MI) in both the Cardiovascular Health Study (a study of 4,522 Americans, aged 65 or older), and the Women's Health Study (a study of 25,283 women older than 45 years without a previous history of CHD). Thus, this KIF6 gene variant has been investigated in studies that included a total of approximately 55,000 people.

In a case-control analysis of subjects in the Ottawa Heart Study, no association was found between KIF6 and >50% coronary artery narrowing, which is a different clinical endpoint than the acute CHD event end point examined in the other KIF6 studies referenced above. Furthermore, 89% of the cases in the Ottawa Study were on statin therapy, which Celera believes may have suppressed the increased risk of KIF6 carriers.

The increased risk of CHD events observed in KIF6 carriers has been shown to be independent of other well-known CHD risk factors, including smoking, hypertension, cholesterol level, age, and sex, further supporting the conclusion that the KIF6 gene variant is an independent predictor of risk for CHD. Recently, the KIF6 protein was also shown to be expressed in atherosclerotic lesions in both mouse and human coronary arteries but not in normal arteries.

Celera is a healthcare business focusing on the integration of genetic testing into routine clinical care through a combination of products and services incorporating proprietary discoveries. Berkeley HeartLab, a subsidiary of Celera, offers services to predict cardiovascular disease risk and improve patient management. Celera also commercializes a wide range of molecular diagnostic products through Abbott and has licensed other relevant diagnostic technologies developed to provide personalized disease management in cancer.

June 9, 2010

QuantRx Submits 510(k) Application to FDA for Thyroid Point-of-Care Testing System Following Successful Completion of Studies Showing Quantitative Results

QuantRx Biomedical, a broad-based diagnostic company focused on the development and commercialization of innovative diagnostic products, today announced that it has completed clinical testing of the Q-Reader thyroid testing system. QuantRx Biomedical Corporation is pleased to be at this regulatory stage, which follows the completion of studies showing that the innovative Q-Reader thyroid testing system is capable of providing healthcare practitioners with laboratory level quantitative results within minutes, rather than waiting for results to be returned from a commercial laboratory.

"We are very excited about meeting this critical milestone," stated Walter Witoshkin, QuantRx Chief Executive Officer. "With the successful completion of our studies we believe we have made a significant step forward for the first of many planned diagnostic tests which are intended to provide rapid, low cost, quantitative results. The ability to introduce our proprietary technology, which will allow the healthcare professional to run in-clinic assays that had only been available from a commercial laboratory before, will be the basis of our market growth in both human and veterinary diagnostics."

The QN Diagnostics (QND) Q-Reader is a stand-alone instrument with a liquid crystal display (LCD) touch screen located on the top of the unit, and an integrated software analysis capability. Using QND's proprietary analysis software, the unit uses stored calibration data provided with each QND Assay Kit and an analyte concentration based upon the analyte-specific calibration curve to display a quantifiable reading to the healthcare practitioner on the LCD screen.

Proprietary QND Assays are housed within a plastic cassette, which contains a QND-lateral flow Assay Strip. The test system is intended for use at the point of care and to eliminate the need for samples to be taken from the patient and shipped with related documentation to an external laboratory, saving the time needed to return the test results to the health care practitioner.

According to Frost & Sullivan Senior Consultant, "The global in vitro diagnostics market has shown a consistent growth of 6.72 percent annually, a trend that is expected to continue until 2012. Point-of-Care (POC), the largest segment, is estimated to grow into an \$18 billion market by 2012."

At present, large commercial laboratories dominate this market, but that will change as more innovative technologies enter the arena. While the standard infrastructure clearly defines the limitations between the healthcare practitioner and the laboratory

personnel, rapid POC technology, such as the Q-Reader system, will soon blur these lines. POC rapid testing offering the potential for process simplification as well as the other factors, are poised to penetrate the diagnostics market aimed at the full spectrum of opportunities.

QuantRx Biomedical is focused on the development and commercialization of innovative products for advanced diagnosis of serious disease and health conditions. With synergistic expertise in the discovery of diagnostic platforms leveraging a vast portfolio of intellectual property, QuantRx's mission is to introduce products for use by medical professionals, institutions, and consumers that deliver more accurate, reliable, and faster diagnoses which result in improved patient care and a reduction in overall healthcare costs.

The QuantRx strategy targets significant market opportunities estimated to be in excess of \$5 billion worldwide. The Company's technology portfolio, with more than three dozen patents, patents pending and licensed patents, includes: (1) RapidSense(R) point-of-care testing products based on QuantRx core intellectual property related to lateral flow techniques for the consumer and healthcare professional markets (QN Diagnostics); (2) PAD technology for over-the-counter applications, and the diagnosis and treatment of women's health concerns and other medical needs, and (3) significant investments in: (a) genome-based diagnostic chips for the laboratory and healthcare professional markets; and (b) molecular imaging agents for positron emission tomography (PET) and fluorescence imaging, with initial application in cardiovascular disease, addressing significant unmet medical needs by providing clinicians with important tools for early discovery and assessment.

July 11, 2010

Continuous Improvement -- Factory Efficiency Comes to the Hospital

Dr. Howard Jeffries of Seattle Children's Hospital says one of his favorite improvements is a color-coded board for the cardiac intensive care unit, which provides an update on patients.

Two years ago, the supply system at Seattle Children's Hospital was so unreliable that Susanne Matthews, a nurse in the intensive care unit, would stockpile stuff — catheters in the closet, surgical dressings in patients' dresser drawers and clamps in the nurse's office. And she wasn't the only one.

"Nurses get very anxious when we can't get our hands on the tools we need for our patients," Ms. Matthews says, "so we grabbed them when we saw them, and stashed

them away." This, in turn, made the shortages more acute.

On a busy day last month in the I.C.U., it took Ms. Matthews just a few seconds to find the specialized tubing she needed to deliver medicine to an infant recovering from heart surgery. The tubing was nearby, in a fully stocked rack, thanks to a new supply system instituted by the hospital early last year following practices typically used in manufacturing or retailing, not health care.

There are two bins of each item; when one bin is empty, the second is pulled forward. Empty bins go to the central supply office and the bar codes are scanned to generate a new order. The hospital storeroom is now half its original size, and fewer supplies are discarded for exceeding their expiration dates.

The system is just one example of how Seattle Children's Hospital says it has improved patient care, and its bottom line, by using practices made famous by Toyota and others. The main goals of the approach, known as kaizen, are to reduce waste and to increase value for customers through continuous small improvements.

Manufacturers, particularly in the auto and aerospace industries, have been using these methods for many years. And while a sick child isn't a Camry, Seattle Children's Hospital has found that checklists, standardization and nonstop brainstorming with front-line staff and customers can pay off.

"It turns out the highest-quality care also is the most cost-effective because we make fewer mistakes and create better outcomes," says Patrick Hagan, the hospital's president. The program, called "continuous performance improvement," or C.P.I., examines every aspect of patients' stays at the hospital, from the time they arrive in the parking lot until they are discharged, to see what could work better for them and their families.

Last year, amid rising health care expenses nationally, C.P.I. helped cut Seattle Children's costs per patient by 3.7 percent, for a total savings of \$23 million, Mr. Hagan says. And as patient demand has grown in the last six years, he estimates that the hospital avoided spending \$180 million on capital projects by using its facilities more efficiently. It served 38,000 patients last year, up from 27,000 in 2004, without expansion or adding beds.

Similar methods are now in place at other hospitals and health systems, including Beth Israel Deaconess Medical Center in Boston, Park Nicollet Health Services in Minneapolis and Virginia Mason Medical Center, also in Seattle. So many others have called for advice that Seattle Children's put together a two-day workshop, presenting it to more than 200 medical workers and health care leaders from the United States and Europe.

"Some people think they have to choose between quality of care and saving money," said Dr. David Chand, who attended the training and now uses C.P.I. methods at Akron

Children's Hospital in Ohio. "C.P.I. improves both patient outcomes and the hospital's bottom line."

To increase the number of surgeries the hospital could perform, Dr. Chand's team spent about \$20,000 overhauling the process to sterilize instruments, avoiding a \$3.5 million expenditure to expand that department. More efficient scheduling in the M.R.I. department reduced the average waiting time for non-emergency M.R.I.'s from 25 days to 1 to 2.

All medical centers, especially larger ones, would have significant return on investment by using operations management techniques like C.P.I., says Eugene Litvak, president and chief executive of the Institute for Healthcare Optimization and an adjunct professor of operations management at the Harvard School of Public Health.

"The health care industry could be on the verge of an efficiency revolution, because it is currently so far behind in applying operations management methodologies," says Professor Litvak.

To be sure, not everyone believes that factory-floor methods belong in a hospital ward.

Nellie Munn, a registered nurse at the Minneapolis campus of Children's Hospitals and Clinics of Minnesota, thinks that many of the changes instituted by her hospital are inappropriate. She says that in an effort to reduce waste, consultants observed her and her colleagues and tried to determine the amount of time each of their tasks should take. But procedure times can't always be standardized, she says. For example, some children need to be calmed before IV's are inserted into their arms, or parents may need more information.

"The essence of nursing," she says, "is much more than a sum of the parts you can observe and write down on a wall full of sticky notes."

On June 10, Ms. Munn helped lead a one-day strike by the Minnesota Nurses Association against six local health care corporations, including her employer, partly in protest of lower staffing levels her union thinks have resulted from hospitals' "lean" methods. "We felt the cuts created an unsafe environment for patients," she said. The nurses' contract was settled on July 1, with no increase in staff levels.

Brian Lucas, a spokesman for Children's Hospitals and Clinics of Minnesota, says the lean efforts have been used to reduce unnecessary tasks and have not resulted in lower nurse-to-patient ratios. "To the contrary," he said, "they have allowed nurses to spend more time delivering care to patients."

Techniques like C.P.I. may indeed be hard for many hospitals to put into effect, says Mark Graban, a senior fellow at the Lean Enterprise Institute, a nonprofit research, education and publishing company. The process takes a large amount of time and requires a culture shift that many hospitals may not be able to accommodate or sustain. "If the leadership tries to force new ways of doing things, the staff may chafe under the successive changes," he says.

And George Lebovitz, a management professor at Boston University, says there are limits to performance-improvement methods in hospitals. "Human health is much more variable and complex than making a car," he said, "so even if you do everything 'right,' you can still have a bad outcome."

Physical layouts can also interfere with changes that hospitals want to make, like reducing the distance a chemotherapy patient has to walk. And the techniques can fall short of their potential if they are used in just one area of a hospital, because a patient typically moves through many different departments.

At Seattle Children's Hospital, Dr. John Waldhausen, the division chief of pediatric general and thoracic surgery, acknowledges that he and other doctors weren't initially very enthusiastic about C.P.I. because they thought it would take some decisions about patient care out of their hands.

Over time, he changed his mind, and he is now a vocal advocate of C.P.I. "When you look closely, C.P.I. is the same scientific method we learned in medical school, including hypotheses, data collection and analysis," he says. "It is not opinion and conjecture — it is data-driven."

TEN years ago, Seattle Children's set a goal to become the top hospital of its type in the country, and hired Joan Wellman & Associates, a process improvement consulting firm in Seattle, to help it get there. Ms. Wellman, who had worked with Boeing on its lean-manufacturing processes, suggested that the hospital apply similar principles.

Mr. Hagan says he became enthusiastic about lean manufacturing and C.P.I. after doing research and visiting local manufacturers. He directed the hospital staff to examine the "flow" of medicines, patients and information in the same way that plant managers study the flow of parts through a factory.

In a typical workshop at Seattle Children's, a group of doctors, nurses, administrators and representatives of patients' families set aside a 40-hour week to work through C.P.I. methods. They plot each "event" a patient might encounter — like filling out forms, interacting with certain staff members, having to walk various distances or having to wait for assistance — and brainstorm about how each could be improved, or even eliminated.

The hospital staff has been rolling out the program in stages over the last decade. "We have probably made over 1,000 small changes, and frankly it never ends," says Mr. Hagan.

In his C.P.I. training, Dr. Bryan H. King, director of the department of psychiatry and behavioral medicine, was one of the first Seattle Children's staff members to visit Japanese manufacturers. He learned that "waste" could be viewed as any action that didn't add value to the customer.

Turning to his psychiatric inpatient unit, he and his team worked to pinpoint the goal of each child's stay and to communicate daily with families. They also made other changes, like starting to arrange outpatient resources as soon as children enter the unit, rather than waiting until they are ready to leave. These kinds of changes increased satisfaction ratings from families and helped cut the average time in the hospital from 20 days to 10. The unit can now accommodate 650 children a year instead of 400.

Changes like these are celebrated by the hospital administration. "Their support fosters the idea that everyone can make positive changes to their departments," Dr. King said. Dr. Howard E. Jeffries, the hospital's medical director of C.P.I., is a fan of visual aids. One favorite is a white board at the entrance of the cardiac intensive care unit. A map of the rooms, labeled with patient names, provides a quick status report on how full the unit is and how ill the patients are. Stick-on stars indicate a patient who needs to be in isolation; a blue circle shows a patient on a ventilator.

"At a glance, staff coming in for their shift can get an idea of what's going on and what to be aware of," Dr. Jeffries says.

The same types of visual cues are used for inventory levels or inspection status in factories.

Another of his favorites is the "Days Without Infection" poster, like a construction site's "Days Without an Accident" sign. "It keeps our new safety protocols top of mind for people," he says.

Standardization is also a C.P.I. cornerstone. Last year, 10 surgeons at Seattle Children's performed appendectomies, and each doctor wanted the instrument cart set up differently. The surgeons and other medical staff members used C.P.I. to come up with a cart they all could use, reducing instrument preparation errors as well as inventory costs.

Dr. Lynn D. Martin, director of the anesthesiology and pain medicine department, says changes previously were instituted only when existing systems failed. Using C.P.I., teams can now make changes any time they think they can improve a process. When the operating room team saw that a tonsillectomy procedure involved filling out 21 separate forms, it sat down with the print vendor to remove duplications — and cut the number to 11.

The staff doesn't have to wait for the perfect solution, Dr. Martin says, just a better one, because they can "keep making improvements year after year."

Using C.P.I., the hospital has reduced the waiting time for many surgeries from three months to less than one. Recently, the bottleneck was not the surgeons' time, but a lack of available inpatient beds for recovery. Examining the hospital's census,

administrators saw that there were empty beds on weekends. They realized that by scheduling more surgeries on Fridays, patients could recover over the weekend, when more beds were free. The change also benefited parents and patients who would miss fewer work and school days.

Lack of space in the recovery room was another logjam, and the hospital planned a \$500,000 renovation to enlarge it. But a C.P.I. team saw that if a child's parents went to a common waiting room during surgery, instead of an individual recovery room, more surgeries could be scheduled. Parents were given beepers to alert them when their child would arrive in the recovery room — and maps and colored lines on the walls helped point the way. Plans for the expensive renovation have been scrapped.

IN the hospital's largest C.P.I. project yet, Lisa Brandenburg, the chief administrative officer, used the method to design a new \$70 million clinic and surgical facility in Bellevue, Wash., just east of Seattle.

Medical buildings often have standard benchmarks — basing the number of examination rooms, for example, on the expected volume of patients. Ms. Brandenburg and her team instead used C.P.I. to map out common paths that patients, staff members, supplies and information would flow through. They worked in an empty office building, using cardboard mock-ups of surgical sites, recovery rooms, anesthesia areas and waiting rooms. Fifty staff members then play-acted various scenarios to test the design's effectiveness.

The final design reduces walking distances and waiting times for patients by grouping related facilities together and creating rooms that can be used for more than one purpose. The hospital was able to shave 30,000 square feet and \$20 million off of the new building, which is to open July 20.

"We can't wait to see it in use," says Ms. Brandenburg.
