G2 INTELLIGENCE
A DIVISION OF PLAIN LANGUAGE MEDIA

DIAGNOSTIC TESTING & Emerging Technologies

New Trends, Applications, and IVD Industry Analysis

January 2017

www.G2Intelligence.com

Upcoming Events

Lab Institute 2017
October 25-27.
www.labinstitute.com

Report Highlights Role Diagnostics Will Play in Food Allergy Safety

Despite the commonly held belief that the food allergy prevalence is rising, food allergies remain poorly studied and quantified, according a new report from the National Academies of Sciences, Engineering, and Medicine. The report says that most studies likely overestimate the proportion of the population with food allergies. The task force that developed the report entitled "Finding a Path to Safety in Food Allergy: Assessment of the Global Burden, Causes, Prevention, Management, and Public Policy," suggests that diagnostics will play an important role in promoting future food allergy safety. The Committee on Food Allergies proposes both improved education regarding the abilities and limitations of currently available tests, as well as areas of future research for improving food allergy-related diagnostics.

Continued on page 2

Sequencing Not Ready for First-Line, Newborn Screening

Scientists have been exploring the "hows" and "what ifs" of applying sequencing to newborn screening. However, two new National Institutes of Health-sponsored studies presented at the American Society of Human Genetics annual meeting (Vancouver, Oct. 18-22, 2016) are dashing hopes that every newborn will have their genome sequenced any time soon. The NBSeq project found that whole-exome sequencing (WES) does not have "acceptable" accuracy to replace traditional newborn screening, while, a second project, BabySeq, found that parents are not that interested in having their newborns sequenced.

Exome Sequencing Not Accurate Enough for Newborn Screening

The NBSeq project found that WES of newborn dried blood spots misses 25 percent of metabolic disorders found by traditional newborn screening with tandem mass spectrometry (MS/MS). The authors say these findings indicate limits to WES both in newborn screening and diagnostic testing.

Continued on page 8

Report Highlights Role Diagnostics Will Play in Food Allergy Safety, *from page 1*

Both the public and health care providers frequently misinterpret food allergies and their symptoms. The committee recommends health care providers use proper diagnostic methods and evidence-based health care for food allergy diagnosis.

Self-reported food allergies are known to be substantially higher rates than when allergies are confirmed with testing. This is often the result of the misconception that sensitization is the same as having a food allergy. However, self-reported medical history is necessary to "hone specific test selection," including differentiating food allergy from other non-immunologically mediated disorders associated with food (e.g., food intolerances). The committee recommends improved education regarding existing tests, as well as recognition of tests that are not currently recommended.

No simple diagnostic tests exist for food allergy and existing tests, the authors say, are imperfect and not well standardized. The authors acknowledge that additional standardization and validation would require "extensive study" in expanded populations, but recommend optimizing currently available diagnostic tests and validating methodology. Additionally, the authors suggest further study on the cost effectiveness of testing, as well as the utility of emerging technologies (e.g., genomics, epigenomics, and metabolomics).

Takeaway: The new report from the National Academies recognizes the important role diagnostics can play in improving the nation's understanding of the prevalence of food allergies and future food allergy safety. Yet, current diagnostics are plagued by a lack of standardization and misunderstanding of results.

Recommended Tests

- Skin prick tests can assist in diagnosing IgE-mediated food allergies, but positive results are not sufficient for diagnosis.
- Food-specific serum IgE tests are guided by clinical history, but positive results are not sufficient for diagnosis.
- Component resolved diagnostics (also known as molecular testing) can be used for diagnosis for select foods, although more evidence is needed from well-designed randomized controlled trials to assess their clinical utility. The authors call CRDs an "emerging testing methodology."
- An oral food challenge is considered the gold standard to confirm diagnosis of a food allergy. However, the test is expensive, must be administered under certain conditions and supervision, and remains underused. Proper identification of appropriate patients is necessary.

Non-Recommended Tests

Testing methodologies not recommended include atopy patch testing, total IgE, basophil activation tests, while "unproven" procedures include allergen-specific IgA, IgG, or IgG4; provocation neutralization, immune complexes, HLA screening, lymphocyte stimulation, facial thermography, gastric juice analysis, endoscopic allergen provocation, hair analysis, applied kinesiology, cytotoxic assays, electrodermal testing, mediator release assays, bioresonance, and iridology.

DTET

Kelly A. Hardy, JD,
Editorial Director

Glenn S. Demby,
Contributing Editor

Catherine Jones,
Contributing Editor and
Social Media Manager

Lori Solomon,
Contributing Writer

Barbara Manning Grimm,
Managing Editor

David van der Gulik,
Designer

Randy Cochran,
Corporate Licensing Manager

Myra Langsam,
Business Development

Michael Sherman,
Director of Marketing

Jim Pearmain,
General Manager

Pete Stowe,
Managing Partner

Mark T. Ziebarth,
Publisher

Diagnostic Testing and Emerging Technologies
(ISSN 2330-5177) is published by G2 Intelligence, Plain Language Media, LLLP, 15 Shaw Street, New London, CT, 06320.
Phone: 1-888-729-2315
Fax: 1-855-649-1623
Web site: www.G2Intelligence.com.

Sequencing Improves Prenatal Diagnosis Following Abnormal Ultrasound Findings

Nonsevere fetal malformations and structural abnormalities are relatively frequent findings of routine, prenatal ultrasounds. Yet, these findings provide a diagnostic challenge for clinicians, as they can vary by identifiable genetic cause and present with varying clinical significance. Often the lack of a precise diagnosis precludes accurate reproductive and fetal risk assessment. However, several small studies are showing the potential for sequencing-based testing to improve prenatal diagnosis.

Targeted-Exome Sequencing

The "Fetalis" targeted-exome sequencing strategy provided a definitive or highly likely diagnosis in 43 percent of cases of fetus with "troubling but non-extreme" abnormalities detected through prenatal ultrasound examination, according to a small study published in *PeerJ*. The targeted approach provided rapid, clinical diagnosis with few uncertain findings.

"Although this figure is obviously a very preliminary assessment from a limited number of cases, it nonetheless provides an initial proof-of-principle regarding the merits of the approach," write the authors led by Constantinos Pangalos, from InterGenetics in Greece, in the April 26 issue of *PeerJ*. "The volume of data … is an order of magnitude less than the corresponding whole-exome sequencing data and … affords a highly cost-effective, more simplified and timely diagnosis (even less than 1 week) during the course of pregnancy."

Typically, prenatal genetic diagnosis is limited to the investigation of possible chromosomal imbalances. Even array comparative genomic hybridization can only detect the underlying genetic cause in less than 15 percent of cases. While technically feasible, whole-exome or whole-genome sequencing (WES or WGS) yields complex results requiring time to analyze and are plagued with incidental findings and variants of unknown significance.

In the present study, the researchers used an expanded exome sequencing-based test, coupled to a bioinformatics-driven prioritization algorithm that targeted gene disorders (n=758 genes) presenting with abnormal prenatal ultrasound findings. DNA samples were extracted directly from uncultured amniotic fluid or chorionic villi sampling samples from 14 euploid fetuses (11 from on-going pregnancies and three products of abortion), all with various abnormalities or malformations detected on prenatal ultrasound examination.

The researchers made a definitive or highly likely diagnosis in six of 14 cases—in all three abortuses and in three out of 11 on-going pregnancies. In an additional on-going pregnancy case a ZIC1 variant of unknown clinical significance was detected, while in the seven remaining cases testing did not reveal any pathogenic variant(s). These eight on-going pregnancies were followed to birth. One neonate was found to harbor the PROKR2 mutation, presenting with isolated, minor structural cardiac abnormalities, while the remaining seven appeared as healthy neonates.

On average, a total of approximately 2,200 variants per case were detected following gene prioritization. Following variant filtering through the Fetalis

algorithm, approximately one to three potentially significant variants/mutations were left for manual inspection and final clinical evaluation.

Whole-Exome Sequencing

More recently, researchers found that WES can identify the cause of 20 percent of sonographic abnormalities, according to an abstract published in *Ultrasound in Obstetrics & Gynecology* in conjunction with the 26th World Congress on Ultrasound in Obstetrics and Gynecology (Italy; Sept. 24–28).

The researchers aimed to develop a strategy to use WES for trio analysis of multiple genes for rapid molecular diagnosis to inform pregnancy management. Amniotic fluid or CVS samples, along with germline DNA from both parents, was analyzed using microarray followed by next-generation sequencing for normal microarray samples. Variants were identified using a combination of published and in-house bioinformatics pipelines and potentially pathogenic mutations were confirmed by Sanger sequencing.

Of six cases analyzed, half had pathogenic mutations, all indicating recessive inheritance and high recurrence risks. Results were available within three weeks.

Takeaway: Sequencing-based testing holds promise to rapidly clarify diagnosis of abnormal prenatal ultrasound findings for pregnancy management.

G2 *INSIDER*

FDA Watch: New FDA Approvals & Applications in Diagnostics

A notable FDA Section 510(k) approval was granted before the close of 2016 for Foundation Medicine's FoundationFocus CDxBRCA, a next-generation sequencing-based companion diagnostic test. The FDA approved the test for use in identifying advanced ovarian cancer patients with BRCA mutations. Not coincidentally, the agency has or shortly will approve *pharmaceutical* products for treating ovarian cancer patients with the gene mutations detected by CDxBRCA, including Clovis Oncology's PARP inhibitor Rubraca.

At least three other diagnostics products received Section 510(k) clearance from the FDA in December, including:

Manufacturer(s)	Product(s)
Statlife	DenSeeMammo breast density assessment software based on BI-RADS guidelines that can be used in combination with Statlife's MammoRisk risk assessment tool
Animas Corporation (a subsidiary of Johnson & Johnson)	One Touch Vibe Plus insulin pump and continuous glucose monitoring system
Cepheid	Xpert MRSA NxG test for MRSA (methicillin-resistant Staphylococcus aureus) infection

Companies that submitted new 510(k) clearance applications during the month include:

- Biocartis for its Idylla molecular diagnostics platform
- Biocartis and Janssen Diagnostics for Janssen Idylla Respiratory IFV-RSV Panel for detecting influenza and respiratory syncytial virus using the Idylla platform
- GenMark Diagnostics for ePlex, a respiratory pathogen panel based on the company's eSensor electrochemical detection technology
- Great Basin Scientific for its molecular panel assay for stool pathogens.

INSIDE THE DIAGNOSTICS INDUSTRY

Medicare Coverage of Molecular Tests Continues to Evolve

Advanced diagnostic tests are emerging faster than the clinicians can document their clinical utility. All of this creates an interesting dilemma for payors as far as coverage is concerned. Normally the most cautious of payors, Medicare has demonstrated an increasing willingness to cover newfangled tests—at least in certain circumstances—with the expectation that they do work and that the studies will eventually catch up. The recent local coverage determinations (LCDs) issued by Palmetto, GBA, one of Medicare's most important contractors, is an excellent illustration of where things seem to be evolving with regard to Medicare coverage of new molecular diagnostic tests.

What's At Stake

First, a quick refresher on LCDs. Medicare covers only services that are "reasonable and necessary." Each Medicare contractor has discretion to decide which services meet those criteria. LCDs set out the particular contractor's coverage rules. So-called draft LCDs typically contain proposed revisions and updates to coverage rules and are open to comment for at least 45 days. Once the comment period ends, the contractor issues a final LCD.

Palmetto says there is conflicting evidence on Vectra DA's effectiveness, citing, among other things, a recent study suggesting that test scores yielded are unreliable and should not be used to guide treatment.

The lab test LCDs discussed in this article are draft LCDs that Palmetto issued on Dec. 23. The comment period runs between Feb. 6 and Mar. 23. So you should have plenty of time to respond if you want to weigh in.

Let's go through the 5 key coverage changes.

1. Eliminate Coverage of Vectra DA for Rheumatoid Arthritis (DL37024)

Test: Vectra DA generates a test score based on 12 biomarkers associated with rheumatoid arthritis inflammation that is used to track disease activity and a patient's response to treatment.

Proposed Change: The draft LCD proposes to end Medicare coverage of Vectra DA.

Explanation: Palmetto says there is conflicting evidence on Vectra DA's effectiveness, citing, among other things, a recent study suggesting that test scores yielded are unreliable and should not be used to guide treatment. Palmetto also notes that 2015 American College of Rheumatology treatment guidelines recommend "functional status assessment using a standardized, validated measure" and do not even mention biomarker testing.

Financial Impact: Vectra DA is manufactured by Myriad Genetics' subsidiary Crescendo Biosciences. Myriad "strongly disagrees" with the proposal and claims the cited study is flawed. There is a lot on the line. Ending Medicare coverage of Vectra DA could cut Myriad's revenues by $35 million to $40 million, according to one report (by a Piper Jaffray analyst cited in GenomeWeb).

INSIDE THE DIAGNOSTICS INDUSTRY

Palmetto ... says that prospective studies supporting the [Prolaris's] effectiveness for identifying low-risk patients who can then avoid unnecessary invasive procedures is enough to justify coverage.

2. Coverage of Prolaris for Intermediate-Risk Prostate Cancer Patients (DL37043)

Test: Prolaris measures the aggressiveness of prostate cancer by analyzing 31 cell cycle progression genes.

Proposed Change: The LCD proposes to cover the test for men who have favorable intermediate risk of prostate cancer under National Comprehensive Cancer Network (NCCN) guidelines.

Explanation: Palmetto acknowledges the current lack of evidence supporting Prolaris's clinical utility among men at intermediate risk of prostate cancer but says that prospective studies supporting the test's effectiveness for identifying low-risk patients who can then avoid unnecessary invasive procedures is enough to justify coverage. Last year, Palmetto and another Medicare contractor Noridian issued a final LCD covering Prolaris for patients meeting NCCN criteria for low- and very-low-risk prostate cancer.

Financial Impact: Like Vectra DA, Prolaris is manufactured by Myriad Genetics. If approved, the draft LCD proposal would expand coverage for about 15 percent of men or roughly 30,000 per year, according to an official company statement. Prolaris coverage in intermediate-risk patients is a $65 million market, according to the aforementioned Piper Jaffray analyst.

3. Limited Coverage of Xpresys for Lung Cancer Screening (DL37031)

Test: Xpresys is a molecular blood test in which expression levels of two proteins are assessed against five clinical risk factors to identify which lung nodules are likely benign and which patients are eligible for surveillance via noninvasive CT scans rather than invasive surgical procedures.

Proposed Change: Palmetto would cover Xpresys Lung version 2 (XL2) but only in limited circumstances. Under the LCD, XL2 would be covered only:

- To assess lung nodules of between 8 and 30 mm in diameter;
- For patients over age 40 who have a pre-test cancer risk of 50 percent or less.

Explanation: In February 2015, CMS announced that Medicare would cover lung cancer screening. But while it can save lives and minimize the need for costly treatment, low-dose computed tomography screens also detect intermediate lesions that cannot be defined as benign or malignant without costly and sometimes dangerous additional testing.

Financial Impact: So the capacity to detect benign tumors noninvasively makes biomarker tests like Xpresys, which is manufactured by Seattle-based Integrated Diagnostics and has been on the market only since 2014, potentially valuable. By the same token, only a few of these tests are commercially available; and they have yet to be adopted for routine clinical use. Accordingly, Medicare has been wary about covering them, as reflected in the LCD.

INSIDE THE DIAGNOSTICS INDUSTRY

4. Limited Coverage of DecisionDx-UM for Metastatic Cancer Risk (DL37033)

Test: DecisionDx-UM is a gene expression profile test assessing the expression levels of 15 messenger RNA transcripts to evaluate whether patients newly diagnosed with uveal melanoma (UM) are at risk for metastatic disease.

DecisionDx-UM was developed by an ocular oncologist and exclusively licensed to Castle Biosciences in 2009. The test is "now used as a standard of care by over 95 percent of ocular oncologists in the U.S.," according to the company website.

Proposed Change: Palmetto proposes limited coverage of DecisionDx-UM for patients diagnosed with UM when there is no evidence of distant metastatic disease at the time of diagnosis for purposes of determining whether the patient should be referred to a specialist for further surveillance. Physicians should not order the test unless they intend to act upon the results.

Explanation: Although there is enough clinical evidence to support clinical utility for now, the LCD stipulates that continued coverage will depend on publication and/or presentation of clinical utility evidence. This is in line with LCDs of other contractors, such as Noridian which began covering DecisionDx-UM last year.

Financial Impact: DecisionDx-UM was developed by an ocular oncologist and exclusively licensed to Castle Biosciences in 2009. The test is "now used as a standard of care by over 95 percent of ocular oncologists in the U.S.," according to the company website.

5. Coverage of Comprehensive Genomic Profiling (CGP) for Specific Cancers

Test: CGP cancer analysis is a single test that uses tissue from a tumor to detect genomic alterations and information that can guide diagnosis and individualized treatment.

Proposed Change: Palmetto issued LCDs covering CGP for patients with three different types of cancers: i. metastatic melanoma (DL37041); ii. metastatic colorectal cancer (DL37039); and iii. advanced primary peritoneal, fallopian tube and ovarian cancer (DL37045). All three of the LCDs include the same basic coverage conditions, including the requirement that:

- The patient be newly diagnosed with the cancer involved;
- The patient has not received CGP (or, in the case of metastatic melanoma, CGP or polymerase chain reaction (PCR)) testing for genomic alterations;
- The test is capable of detecting all four types of DNA alterations associated with cancer; and
- The test meets Palmetto's Analytical Performance Specifications for CGP (APS).

Explanation: The new CGP LCDs are significant for what they do not include, namely, the requirement that labs submit testing and patient data

INSIDE THE DIAGNOSTICS INDUSTRY

through registries, a burdensome obligation that has appeared in previous Palmetto CGP coverage policies.

Financial Impact: As in the brand-specific LCDs, Palmetto acknowledges the current lack of evidence supporting the clinical utility of CGP for metastatic melanoma but states its belief that the test works and will be validated by forthcoming studies.

Takeaway: Medicare is coming to accept molecular testing. Palmetto is only one Medicare contractor. But far from being a blip on the radar screen, the new Palmetto LCDs are a reflection of how CMS and its other contractors are coming around on newly developed molecular diagnostic testing—despite the current lack of evidence supporting their clinical effectiveness. In other words, the Medicare payor community is moving ahead with coverage in the expectation that the justifying scientific studies will eventually catch up and not the other way around.

Sequencing Not Ready for First-Line, Newborn Screening, *from page 1*

MS/MS detects many metabolic disorders with excellent sensitivity, but often does not identify the precise disorder, experts say. Given newborn screening is done at the population-level it must scale and have greater than 99 percent specificity. By contrast, sequencing performed on patients suspected of genetic diseases is cumbersome, requiring manual review from experts, and still has a diagnostic yield between 25 percent and 50 percent.

The NBSeq researchers used archived dried blood spots from all California newborns (July 2005 to December 2013) with disorders diagnosed by MS/MS plus a selection of false positives (n = 1,600 samples). To date, the group has sequenced 600 samples, and analyzed 184.

The researchers found that WES yields "vastly" more false negatives than MS/MS. In one quarter of newborns with metabolic disorders, WES did not identify rare alleles for genes responsible for their recessive Mendelian disorder. They systematically explored how different WES interpretation protocols impacted the prediction of metabolic disorders in newborns. While tuned analysis pipelines shifted the balance of false negatives versus false positives as part of exploration of how different interpretation protocols impacted identification of metabolic disorders, it did not yield acceptable specificity and sensitivity for newborn screening. While apparently unsuitable for first-line NBS, WES might yet improve NBS in NICU settings or help specify a diagnosis following positive MS/MS screens.

"The success of diagnostic WES is limited in part because patients' disorders may be genetically complex or not genetic," writes lead author Aashish Adhikari, a postdoc at University of California, Berkeley. "Our study suggests limits to identifying even monogenic disease as well; our work focused

on some of the best-characterized Mendelian disorders, yet recognized only three-quarters of the cases. This therefore suggests a ceiling to the potential of current diagnostic WES."

The authors add, though, that WES may be useful for diagnostic purposes in conjunction with positive MS/MS newborn screening findings.

Parents and physicians also agree that genetic sequencing will increase in importance in 10 years, with 82 percent of parents and 90 percent of physicians saying it will be more important in the future, compared to the 61 percent and 64 percent, respectively, that view genetic sequencing as important now.

Parents Not Very Interested in Sequencing

The BabySeq Project is a randomized controlled trial exploring the utility of sequencing for infants in both the neonatal intensive care unit (NICU) and well-baby nursery at Brigham and Women's Hospital in Boston. Half of infants are randomized to receive genetic sequencing. Families receive results during a session that involves review of state-mandated newborn screening results and family history. The families of infants randomized to sequencing also receive a report that includes pharmacogenomic variants and pathogenic and likely pathogenic variants in 1,800 genes associated with dominant and recessive monogenic conditions with childhood age of onset and high estimated penetrance, but without regard for actionability, the authors say.

To date, participation in the BabySeq project has been offered to the parents of 254 NICU infants and 1,193 healthy infants, of whom only 6 percent and 7 percent, respectively, have enrolled. Time from DNA extraction to issuance of a sequencing report has averaged 50 days.

Parents who declined before meeting with a study genetic counselor most often cited logistics of return visits as their primary reason for not participating. Parents who declined after meeting with a study genetic counselor cited the potential to receive unfavorable or uncertain results (38 percent), insurance discrimination (26 percent), and confidentiality/privacy concerns (22 percent) as their reasons for not participating.

A related BabySeq abstract surveyed participating parents and doctors about their perceptions of sequencing technology, compared to newborn screening.

The majority of parents (81 percent; n=159) and physicians (97 percent; n=67) agreed that there are health benefits associated with newborn screening. A smaller majority of parents (67 percent) and physicians (57 percent) agreed that there are health benefits associated with genomic sequencing. More physicians than parents agreed that there are risks associated with genomic screening (73 percent versus 35 percent, respectively). Both parents and physicians identified similar risks resulting from genomic sequencing, including psychological distress, genetic discrimination, impact on family, and the nature and potential uncertainty of genetic sequencing results. Parents and physicians also agree that genetic sequencing will increase in importance in 10 years, with 82 percent of parents and 90 percent of physicians saying it will be more important in the future, compared to the 61 percent and 64 percent, respectively, that view genetic sequencing as important now.

Takeaway: Despite much enthusiasm for the clinical application of WES, the technology is not yet ready for application to newborn screening.

2016 Year End Brought Closure to Many Diagnostic Deals

As 2016 came to a close, so too did a significant number of business deals involving diagnostic companies, tests and testing systems. Here's a summary of some of the recent transactions affecting diagnostics.

MERGERS & ACQUISITIONS		
Acquiring Company	**Target**	**Deal Summary**
Agilent Technologies	Multiplicom, Belgium-based molecular diagnostics firm spun off from Univ. of Antwerp in 2011	▪ Price: €68 million ($70.6 million) in cash ▪ AT to offer jobs to all 90 M employees ▪ Lure is M's BRCA Tumor MASTR Plus Dx test, first ovarian cancer companion test to get CE-IVD designation in Europe
Menarini-Silicon Biosystems	Janssen Diagnostics	▪ Price: Undisclosed ▪ MSB acquires JD's Cellsearch circulating tumor cell system for monitoring breast, prostate and colorectal cancers ▪ Cellsearch is only breast cancer monitoring system approved by China FDA
Abbott Laboratories	St. Jude Medical	▪ $25 billion merger ▪ European Commission OKs on antitrust grounds provided that: i. SJ divests Angio-Seal and Femoseal vascular closure assets; and ii. A divests Vado steerable sheath ▪ All latter assets already slated for sale to Japanese firm Terumo for $1 billion
Takara Bio USA Holdings	Rubicon Genomics	▪ Price: $75 million ▪ Helps T fortify position in pre-analytical genetic sample preparation and expand into in vitro fertilization
Grifols	Hologic, Inc.'s blood screening assets	▪ Price: $1.85 billion cash gross proceeds ▪ G and H were partners in blood screening business with H doing R&D and manufacturing and G concentrating on commercialization
Abbott Laboratories	Alere	▪ Abbott sues to get out of $5.8 billion acquisition deal inked in Feb. (See *LIR*, Dec. 2016)
DNA Diagnostics Center	Identigene, subsidiary of Sorenson Genomics	▪ Price: Undisclosed ▪ US/UK-based DDC acquires first company to sell in-home DNA paternity test collection kits in US mass retail stores including Rite Aid, CVS and Walmart
Boston Scientific	Neovasc	▪ 75 million in cash ▪ BS acquires 15% equity stake + N's advanced biological tissue business
Takara Bio USA Holdings (subsidiary of Takara Bio USA)	Wafergen Biosystems	▪ W shareholders approve merger announced in May ▪ Price: Aggregate cash price based on a multiple of W's 2016 calendar year revenues up—subject to $50 million cap ▪ T to make two separate $2.5 million deposits in Jan.
STRATEGIC ALLIANCES		
Partner 1	**Partner 2**	**Deal Summary**
Henry Ford Health System Pathology and Laboratory Medicine	Beckman Coulter Inc.	▪ Purpose 1: Fully automate HF Hospital lab ▪ Purpose 2: Modernize equipment at 12 other HF locations
Roche	Pacific Biosciences	▪ R ends 2013 $75 million agreement with PacBio to develop and commercialize diagnostic single-molecule sequencing system, effective Feb. 10, 2017
Agilent Genomics (the genomics arm of Agilent Technologies)	Transcriptic (Bay Area diagnostic software firm)	▪ Incorporates AG mutagenesis and cloning product lines to protocol library within T's robotic cloud laboratory ▪ Deal covers AG's QuikChange site-directed mutagenesis kits
Novogene	AITbiotech	▪ Form NovogeneAIT Genomics Singapore, a joint venture to establish a whole-genome sequencing and bioinformatics center in Singapore ▪ Joint venture will also collaborate with Genome Institute of Singapore in developing use of whole-genome sequencing for cancer diagnosis

STRATEGIC ALLIANCES, *Cont'd*		
Partner 1	**Partner 2**	**Deal Summary**
Royal Phillips	New York Medical College	▪ Expansion of current partnership to develop IntelliSpace Genomics, an application that provides analysis workflows for pathologists, oncologists and researchers by integrating raw data from multiple sources
Evogen	UCB	▪ Collaboration to develop EvoScore START, a diagnostic test that measures a panel of blood-based protein biomarkers to distinguish between epileptic seizures and other events
Courtagen Life Sciences	Certainty Health	▪ Gives Courtagen exclusive access to CH's mobile device-based data sharing platform for neurological diseases ▪ Allows Courtagen to import its own neurological disease data into the platform
SystemOne	Daktari Diagnostics	▪ Licensing partnership linking DD's point-of-care (POC) diagnostics technology platform to SO's Aspect connectivity platform to help implement POC connectivity in developing countries
Medtronic	University Hospitals (Cleveland)	▪ Partnership to improve workflow and identify operational efficiencies for catheterization and electrophysiology labs at UH Cleveland Medical Center
DISTRIBUTION AGREEMENTS		
Property Owner	**Distributor**	**Deal Summary**
MDxHealth	AceCGT Life Sciences Limited	▪ Product: Prostate Cancer test ▪ Territory: Hong Kong Macao ▪ Exclusive
Dovetail Genomics LLC	Tomy Digital Biology Co.	▪ Product: Genome assembly services for researchers ▪ Territory: Japan ▪ Exclusive
Illumina Netherlands	GenDx	▪ Product: Next-generation sequencing instruments and reagents used for HLA sequencing ▪ Territory: UK, Germany, Italy, Belgium, Netherlands, Luxembourg, Finland ▪ Non-exclusive reselling rights
NantHealth	Oncotest-Teva (subsidiary of Teva Pharmaceuticals)	▪ Product: GPS Cancer molecular test ▪ Territory: Israel ▪ Exclusive reselling rights
NantHealth	Lunatus	▪ Product: GPS Cancer molecular test ▪ Territory: Middle East, including UAE, Kuwait, Saudi Arabia, Oman, Bahrain, Qatar, Lebanon ▪ Exclusive reselling rights
Argos Technologies	Bibby Scientific	▪ Products: Molecular and cell biology research products, storage and cryo-storage equipment ▪ Territories: Europe, Middle East, Africa
Kapa Biosystems (owned by Roche)	Merck	▪ Products: Extends existing distribution alliance to include Kapa's polymerase chain reaction (PCR) and quantitative real-time PCR (qPCR) enzyme products ▪ Territory: All markets except US, Japan and Brazil ▪ Non-exclusive
Kapa Biosystems (owned by Roche)	MilliporeSigma	▪ Products: Extends existing distribution agreement to include Kapa's polymerase chain reaction (PCR) and quantitative real-time PCR (qPCR) enzyme products ▪ Territory: All markets except US, Japan and Brazil ▪ Non-exclusive
Senseonics	Roche	▪ Product: Eversense, S's long-term implantable continuous glucose monitor ▪ Territory: Extends current distributorship agreement covering Germany, Italy and the Netherlands to all of Europe (except Scandinavia), the Middle East (except Israel) and Africa ▪ Exclusive sale, promotion and marketing rights

LICENSES		
Licensor	**Licensee**	**Deal Summary**
Thermo Fisher Scientific	Singulex	■ Product: TF's BRAHMS PCT procalcitonin immunoassay ■ PCT used in US to assess critically ill patients' risks of severe sepsis and septic shock and mortality risks of patients diagnosed with sepsis ■ FDA recently approved use of PCT for critically ill patients before admission to the ICU (previously, the patient had to be in the ICU already) ■ Non-exclusive: Thermo has also licensed PCT to Roche and Biomérieux
Labcyte	Notable Labs	■ Product: L's Echo acoustic liquid handling technology for personalizing drug therapy ■ NL will use Echo in its own labs to functionally assess effects of FDA-approved drugs on live primary cancer cells from individual patients
Epicentre (a subsidiary of Illumina)	Lucigen	■ Products: Array of research products from E's AmpliScribe, CopyControl, MaxPlax and TranforMax product lines ■ L to take over manufacture and sale ■ Exclusive
SELLING & MARKETING AGREEMENTS		
Property Owner	**Seller**	**Deal Summary**
Good Start Genetics	Roche Diagnostics	■ Product: Gene Vu, GSG's screening test to identify carriers of genetic disorders ■ R to sell Gene Vu along with its own Harmony prenatal fetal aneuploidy test ■ Territory: US
Edico Genome	Amazon Web Services	■ Provides for E's Dragen bioinformatics platform to be sold on new Amazon cloud-based instances