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HIGHLIGHTS

FDA Watch: Discussion Paper Signals New Approach (Not Retreat) to LDT Regulation

After nearly two years of inactivity, things are suddenly heating up on FDA regulation of laboratory developed tests (LDTs). As promised, the agency took action on LDTs by the end of 2016—but not in the way everybody expected. Instead of finalizing the controversial rule it proposed in October 2014, the agency announced that it was putting LDT regulation on ice pending discussions with the new Congress and administration.

Some may have interpreted the November announcement as signalling the FDA's intention to withdraw from LDT regulation altogether. But on Jan. 13, the agency dashed those hopes by issuing a discussion paper that reaffirms its intention to regulate LDTs. The silver lining is that the agency seems to have softened its approach.

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Diagnostic Deals: A Roundup of January's Mergers, Acquisitions, Alliances, Licenses and Other Major Transactions

January 2017 has already seen an unusually high volume of diagnostic deal making. Here is a quick overview of the key deals and what they portend.

M&A

While Abbott Laboratories made the biggest deal by completing its $25 billion purchase of St. Jude Medical (see story on page 8), Bio-Rad Laboratories may have been the month's most active company. On Jan. 9, Bio-Rad unveiled the new next-generation sequencing (NGS) tool it developed in collaboration with Illumina. A first of its kind, the Illumina Bio-Rad Single-Cell Sequencing Solution enables researchers to study how single cells affect tissue function, disease and therapeutic response.

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Diagnostic Deals, *from page 1*

Less than a week later, Bio-Rad announced that it had reached agreement to acquire droplet-based PCR systems manufacturer RainDance Technologies for an undisclosed amount. The purchase, which is expected to close in the first quarter, dramatically expands Bio-Rad's capacity to research liquid biopsy via absorption of RainDance's systems for partitioning samples into one million droplets. The solutions "will extend our reach into next-generation sequencing applications and strengthen our position in the area of Droplet Digital PCR," noted Bio-Rad CEO Norman Schwartz in a statement. But Bio-Rad's busy month took an unwelcome turn a few days later when the US Patent and Trademark Office's Patent Trial and Appeal Board handed down a ruling in RainDance's ongoing patent dispute with 10x Genomics that invalidates a number of the former's droplet size manipulation systems patent claims. It is unclear how the ruling will affect Bio-Rad's acquisition of RainDance.

LabCorp, PerkinElmer and QIAGEN were among the major diagnostics companies to announce new acquisition deals during the month. Meanwhile, M&A deals to close during the month included Invitae's purchase of patient-provider data connectivity platform AltaVoice, and Bruker's acquisitions of two companies in Germany, including—SCiLS, an informatics firm known for its MALDI imaging products, and InVivo, a biotech firm specializing in antibody and immunoassay development.

Strategic Alliances

It was also a very busy month for Illumina, which, in addition to launching the Illumina Bio-Rad Single-Cell Sequencing Solution product described above, unveiled a pair of important new strategic deals on Jan. 9: a partnership to integrate its BaseSpace® Sequence Hub with IBM's Watson for Genomics; and a collaboration to integrate its genetic variation analysis sequencing systems with Royal Phillips's IntelliSpace Genomics informatics platform.

In fact, pooling of data integration and analysis technology was the principle theme behind many of the month's key strategic alliances, including deals combining:

- 10x Genomics Chromium system with PerkinElmer's automated technologies to create jointly offered NGS solutions;
- Edico Genome's Dragen bioinformatics processor with Dell EMC's IU Dell 4130 server for genome analysis to develop bundled NGS computing and storage solutions; and
- LifeNome's bioinformatics platform with testing products developed by Imagene Labs to expand the existing partnership's range of "wellness genomics" products.

Meanwhile, less than a month after acquiring Belgian genomics firm Multiplicom, Agilent Technologies teamed with Centre for Human Genetics of the University of Leuven and University Hospital of Leuven for joint research of reimplantation genetic testing with an eye to developing systems enabling labs to use single sequencing workflow for preimplantation genetic analysis for single gene disorders and translocation carriers. Here is a run down on recent deals of note:

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MERGERS & ACQUISITIONS		
Acquiring Company	**Target**	**Deal Summary**

Abbott Laboratories	St. Jude Medical	▪ Closing of $25 billion merger expands Abbott access to $30 billion cardiovascular device market
		▪ Combined $9.8 billion in CV and neuromodulation platform sales
		▪ To gain antitrust approval:
		  ▪ Abbott had to sell off Vado steerable sheath for percutaneous procedures
		  ▪ SJ had to sell off Angio-Seal and Femoseal vascular closure assets
		▪ Terumo acquires divested assets for $1 billion

Bio-Rad Laboratories	RainDance Technologies	▪ Price: undisclosed ▪ Expected closing date: 1Q 2017 ▪ RD specializes in droplet-based genomic tools used to research liquid biopsy ▪ RD assets acquired, including RainDrop Digital PCR, ThunderStorm and ThunderBolts systems reportedly 500 x greater than Bio-Rad's internal capacity to partition samples into droplets
Laboratory Corp. of America	Mount Sinai Health System outpatient lab centers	▪ Price: Undisclosed ▪ Expected closing date: Undisclosed ▪ LabCorp to acquire 7 Mt. Sinai outreach labs in NYC area—adding to its existing network of 120 lab centers in the region ▪ LabCorp will provide clinical pathology, cytology and cytology-related molecular testing
PerkinElmer	Tulip Diagnostics Private	▪ Price: Undisclosed ▪ Expected closing date: 1Q 2017 ▪ Tulip, which is based in India, produces in vitro diagnostic reagents, kits and instruments ▪ Products include screening tests for malaria, HIV, hepatitis and other infectious diseases ▪ Latest instance of PE's strategy of expanding in developing markets
QIAGEN	OmicSoft Corp.	▪ Price: Undisclosed ▪ Expected closing date: Undisclosed ▪ Adding Q's genomics software expands Q's bioinformatics capacity and portfolio
Invitae Corp.	AltaVoice (formerly PatientCrossroads)	▪ Price: Undisclosed ▪ Status: Closed ▪ Privately-held AV is a data company with a platform for connecting patients with clinicians ▪ Companies will integrate efforts to develop networks combining genetic and clinical data for medical treatment and research
Bruker	SCiLS	▪ Price: Undisclosed ▪ Status: Closed ▪ Germany-based SCiLS is an informatics firm specializing in products for matrix-assisted laser desorption/ionization (MALDI) imaging ▪ SCiLS assets complement B's own MALDI systems
Bruker	InVivo Biotech Services	▪ Price: $276 million ▪ Status: Closed ▪ Germany-based InVivo is a biotech firm specializing in antibody and immunoassay development ▪ InVivo had $5 million in 2016 sales revenue
CareDx Pty (CareDx subsidiary)	Illumina subsidiary Conexio Genomics	▪ CareDx Pty acquires Conexio's sequencing-based HLA typing assets ▪ Price: Up to $735,000 in total (including up to $232,792 for finished goods, $156,159 for unfinished inventory and quarterly payments equal to 20 percent of the gross revenue from sale of products using assets purchased) ▪ Illumina to provide CareDx Pty with access to the services of one of its employees for 12 months to help with transfer of manufacturing operations and expertise associated with assets purchased
Hospital Corporation of America	Genospace	▪ Price: Undisclosed ▪ Expected Closing Date: 1Q 2017 ▪ Genospace, which develops software for personalized medicine, to merge with HCA's Sarah Cannon Cancer institute as a wholly-owned subsidiary
Takara Bio USA Holdings	Rubicon Genomics	▪ Price: $75 million ▪ Status: Closed ▪ Takara fortifies position in pre-analytical genetic sample preparation and expands into in vitro fertilization
Digipath, Inc.	Two family-owned independent labs in New Jersey (one of which also serves the Pennsylvania market)	▪ Price: Undisclosed ▪ Status: Non-binding Letter of Intent with undetermined/undisclosed closing date ▪ Digipath is an independent cannabis lab testing and media firm ▪ D's diagnostic branch, Digipath Labs, aspires to be the market leader known for establishing best practices for cannabis testing

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STRATEGIC ALLIANCES, PARTNERSHIPS & COLLABORATIONS		
Partner 1	**Partner 2**	**Deal Summary**
Illumina	IBM Watson Health	▪ Partnership integrating Watson for Genomics with Illumina's BaseSpace® Sequence Hub ▪ Objective: Standardize and simplify interpretation of genomic data ▪ Dynamic: Watson to interpret data generated by Illumina's TruSight® Tumor 170 solid tumor profile—so named because it detects variants for cancers across 170 genes
Illumina	Royal Phillips	▪ Partnership integrating Illumina's sequencing systems for genetic variation analysis with RP's IntelliSpace Genomics clinical informatics platform ▪ Deal also provides for coordinated sales/marketing of the resulting solutions ▪ Partners will also participate with US health system doing clinical research to develop precision medicine oncology programs ▪ Dynamic: Watson to interpret data generated by Illumina's TruSight® Tumor 170 solid tumor profile—so named because it detects variants for cancers across 170 genes
PerkinElmer	10x Genomics	▪ Combine 10x's Chromium system with PE's automated technologies to create jointly offered automated next generation sequencing solution
Agilent Technologies	Centre for Human Genetics of the University of Leuven and University Hospital of Leuven (Belgium)	▪ Joint research of reimplantation genetic testing ▪ Objective: Allow labs to use single sequencing workflow for preimplantation genetic analysis for single gene disorders and translocation carriers ▪ Follows Agilent's acquisition of Belgian genomics firm Multiplicom last month
Northwell Health	Individumed (Germany-based personalized cancer services provider)	▪ Objective: Create cancer research biobank to support precision medicine and drug development ▪ 3-year agreement ▪ Dynamic: NH to collect lung, breast, pancreatic and other cancer tissue at 3 of its hospitals ▪ Individumed to focus on tissue tracking, handling, recovery and storage
Northwell Health	Avizia (telehealth systems vendor)	▪ NH to use A's technology to align its telehealth infrastructure encompassing network of hospitals, labs, MD offices and other outpatient providers across the NY metro area ▪ A technology will also be used to improve communication among network providers
Teladoc, Inc.	Analyte Health, Inc.	▪ Partnership to use T's telehealth platform to connect patients, telehealth providers and labs ▪ Objective: Quick, easy and efficient test ordering, specimen collection and lab results reporting
Ohio University Hospitals Seidman Cancer Center	Tempus (genomic analysis firm)	▪ Objective: Provide genomic data analysis and decision making support to Seidman Cancer Center oncologists ▪ Since Oct., Tempus has made similar deals with Mayo Clinic, Rush Univ. Med. Center and Univ. of Pennsylvania's Abramson Cancer Center
German National Center for Tumor Disease (NCT) Heidelberg	Protagen	▪ NCT to use Protagen's SeroTag platform to identify biomarkers for predicting response of melanoma patients to immunotherapy
Lantern Pharma	Cancer Genetics	▪ Collaboration to develop biomarker panels for grouping cancer patients based on their responses to treatment for use in drug development ▪ Will also develop liquid-biopsy tests for patient selection and monitoring
Pfizer	The Scripps Research Institute	▪ Pfizer to pay undisclosed fee to gain access to TSRI's chemical synthesis technology ▪ Objective: Develop technology for creating next-generation DNA-encoded libraries for use in drug development
KeyGene	Genalice	▪ 3-year extension of existing partnership for development of plant DNA analysis software ▪ KeyGene also announced a pair of new licensing deals this month (see below)
SpeeDx (Australian diagnostics firm)	UgenTec (Belgian software developer)	▪ UT to use its software to interpret results of SD's diagnostic tests for sexually-transmitted and other infectious diseases
Helomics	MDNA	▪ Collaborate to develop new liquid biopsy tests using MDNA's Mitomic Technology platform ▪ H to promote MDNA's Prostate Core Mitomic Test and liquid biopsy Prostate Mitomic Test in select US markets
Good Start Genetics	Genome Medical	▪ GM to provide genetic counseling support for GSG's recently launched VeriYou, a saliva test that uses next-generation sequencing to screen for gene mutations associated with cystic fibrosis and spinal muscular atrophy
Amgen	Adaptive Biotechnologies	▪ Collaboration to develop and commercialize ClonoSeq, Adaptive's next generation sequencing-based immune profiling assay to assess minimal residual disease in patients with acute lymphoblastic leukemia ▪ Adaptive to seek FDA approval for ClonoSeq

STRATEGIC ALLIANCES, PARTNERSHIPS & COLLABORATIONS, *Cont'd.*		
Partner 1	**Partner 2**	**Deal Summary**
Biodesix	Bioyong Technology (Chinese life sciences company)	▪ Objective: Develop Biodesix's Veristrat test for China and develop new MALDI mass spec tests for oncology ▪ Potential to extend to other Asia-Pacific countries
Parkinson's Institute and Clinical Center	Centogene	▪ Partnership to provide panel-based genetic screening for genetic variants associated with Parkinson's disease ▪ Screening provided for a US patient cohort ▪ Centogene to perform genetic characterization at its CLIA-certified labs in Germany
University of California, San Francisco	Two Pore Guys	▪ UCSF oncologists to use TPG's handheld nanopore circulating tumor DNA detection platform to develop liquid biopsy assay
Bristol-Myers Squibb	GeneCentric Diagnostics	▪ Collaboration to use GCD's Cancer Subtype Platform to identify translational biomarkers for BMS's cancer immunotherapy Opdivo (nivolumab)
Guardant Health	Separate deals with: ▪ AstraZeneca ▪ Merck ▪ Merck KGaA ▪ Pfizer	▪ Objective: Develop 500-plus-gene liquid biopsy panel that drug companies can use to speed up clinical trials and development of targeted cancer drugs and immunotherapies
Metabolon	InnVentis (Israeli precision medicine firm)	▪ Partnership to study metabolomics in individuals with arthritis and other chronic inflammatory diseases for diagnostic and treatment purposes
Edico Genome	Dell EMC	▪ Objective: Develop a bundled compute and storage solution for rapid and effective analysis of next generation sequencing data ▪ Amazon recently began selling EG's Dragen bioinformatics platform on new cloud-based instances
Imagene Labs (Singapore)	LifeNome	▪ Expansion of existing "wellness genomics" partnership in Southeast Asia to include China & Hong Kong ▪ Partnership under which Imagene incorporates LN's bioinformatics platform into Imagene's consumer genomics testing products
DISTRIBUTION AGREEMENTS		
Property Owner	**Distributor**	**Deal Summary**
Interpace Diagnostics	Best Med Opinion	▪ Products: Interpace's cancer molecular diagnostics ▪ Territories: Israel ▪ Exclusive
Trovagene	Alliance Global	▪ Product: Trovagene's Trovera liquid biopsy test ▪ Territories: Middle East, Africa, Central and South Asia ▪ Provides for early access to research-only liquid biopsy kits Trovagene is co-developing with Boreal Genomics
Trovagene	Instituto Diagnostico and Sorgente Genetica Varelli	▪ Product: Trovagene's Trovera liquid biopsy test ▪ Territory: Italy ▪ Provides for early access to research-only liquid biopsy kits Trovagene is co-developing with Boreal Genomics
Trovagene	Progenetics	▪ Product: Trovagene's Trovera liquid biopsy test ▪ Territory: Israel ▪ Provides for early access to research-only liquid biopsy kits Trovagene is co-developing with Boreal Genomics
Trovagene	Amplitech	▪ Product: Trovagene's Trovera liquid biopsy test ▪ Territories: France, Belgium and Switzerland ▪ Provides for early access to research-only liquid biopsy kits Trovagene is co-developing with Boreal Genomics
Trovagene	NM Genomix	▪ Product: Trovagene's Trovera liquid biopsy test ▪ Territories: Bulgaria and Eastern Europe ▪ Provides for early access to research-only liquid biopsy kits Trovagene is co-developing with Boreal Genomics
Trovagene	Diagnostica Longwood	▪ Product: Trovagene's Trovera liquid biopsy test ▪ Territories: Spain and Portugal ▪ Provides for early access to research-only liquid biopsy kits Trovagene is co-developing with Boreal Genomics
Mobidiag (Finnish IV diagnostics firm)	Wallac Oy (subsidiary of PerkinElmer)	▪ Products: Amplidiag real-time, PCR-based IVD gastro-intestinal tests including Amplidiag H.pylori+ClariR, Stool Parasites, CarbaR+VRE, C.difficile+027, Bacterial GE and Amplidiag Easy System ▪ Territory: South Africa

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DISTRIBUTION AGREEMENTS, *Cont'd.*		
Property Owner	**Distributor**	**Deal Summary**
Sera Prognostics	Laboratory Corp. of America	▪ Product: Sera's PreTRM test for preterm birth ▪ Territory: US ▪ Exclusive ▪ LabCorp also to lead a $40 million Series C funding round to finance Sera's collection of clinical data to support reimbursement of PreTRM
FactBio	Filgren	▪ Products: Knowledge Sharing Platform (Kusp) and other FactBio products ▪ Territory: Japan ▪ Term: 2 years ▪ Exclusive
Contextual Genomics	Sonic Healthcare	▪ Products: Contextual's Find-It next generation sequencing solid tumor test ▪ Territories: Across Sonic's (which is Australian-based) international labs network
Natera	Bio-Reference Laboratories	▪ Natera ends 2013 distribution agreement with Bio-References ▪ Products: Panorama (noninvasive prenatal test) and Horizon (carrier screening test)—Natera will now market these tests itself ▪ Natera also sues Bio-Reference for breach of contract claiming that Bio-Reference used technology it licensed from Natera to develop and launch a competing prenatal assay called ClariTest
LICENSES		
Licensor	**Licensee**	**Deal Summary**
Transgenomic	LifeLabs	▪ Property: Transgenomics's ICE-COLD-PCR technology for LifeLabs's use in its mutation enrichment platform for cancer testing ▪ Term: 3 years with option to renew ▪ Non-exclusive ▪ In August, Transgenomic granted non-exclusive distribution rights for ICE-COLD-PCR to VWR International
KeyGene	University of Minnesota	▪ Property: KeyGene's Sequence-Based Genotyping technology ▪ UMN gets right to incorporate technology into its own genotyping platforms that it offers for use by academic community and industry
CareDx Pty (subsidiary of CareDx)	Illumina subsidiary Conexio Genomics	▪ Properties: Sequencing-based HLA typing software, technology and trademarks owned by Conexio ▪ Side deal to CareDx Pty's acquisition of Conexio's HLA assets (listed above in ACQUISITIONS)
NEW PRODUCTS		
Company(ies)		**Product(s)**
Quest Diagnostics		▪ Test service for physicians to evaluate response of patients with hepatitis B virus to drug therapies
Bio-Rad Laboratories + Illumina		▪ Illumina Bio-Rad Single-Cell Sequencing Solution for studying impact of single cells on tissue function, disease and therapeutic response
Abbott Laboratories		▪ EnSite Precision cardiac mapping system ▪ Advisor FL circular mapping catheter
CloudHealth Genomics		▪ HealthySeq NGS based liquid biopsy test for detecting genetic alterations in healthy individuals
Celmatix		▪ Fertilome genetic screen for evaluating impact of a female's DNA on her reproductive health
Bioline (subsidiary of Meridian Biosciences)		▪ Range of EPIK miRNA Select assays to complement existing assays
QIAGEN		▪ New gene panels for oncology to enhance existing GeneReader NGS System
Baylor Genetics		▪ PreSeek, a non-invasive prenatal multi-gene sequencing screen

Takeaway: The turn of the calendar year has brought a significant number of diagnostic deals.

Diagnostics Earnings Report: Abbott, Quest, Genomics Labs Pace Fourth Quarter Growth

Fourth quarter earnings reports are starting to trickle in. Here is a big picture roundup of some of the key results so far.

Gainers

Companies with strong 4Q diagnostics revenues include:

- **Abbott Laboratories:** Year-over-year (YOY) growth of 3 percent driven by 4 percent increase in infectious disease testing and Core Laboratory sales (from $969 million to $1 billion)—offsetting 1 percent foreign exchange loss and 8 percent decline in molecular diagnostics due to wind-down of genetics business;
- **Quest Diagnostics:** Quarterly revenues of $1.86 billion on 0.7 percent growth (on a reported basis) and full year revenues of $7.52 billion on 0.3 percent growth;
- **Luminex:** Expected YOY growth of 20 percent for 4Q and 14 percent for year with revenues of, respectively, $72 million and $271 million, easily beating Wall Street estimates of $70.3 million and $268.9 million; and
- **Invitae Corporation:** Among best performing of genetic information companies with expected 33 percent revenue growth (as compared to Q3) driven by 200 percent YOY increase in billable test volume with approximately 59,000 tests for the year.

The genomic testing sector was strong with robust quarterly YOY growth reported by:

- **T2 Biosystems** (+50 percent) (preliminary);
- **NanoString Technologies** (+15 percent) (preliminary); and
- **GenMark Diagnostics** (+13 percent).

Decliners

Although gainers generally outnumbered decliners, companies with weaker than expected diagnostics revenues included:

- **Meridian Bioscience:** Decline of 1 percent for 3 months ended Dec. 31, 2016 (which is actually the company's first quarter) to $46.8 million, well below Wall Street estimate of $51.2 million, due to 4 percent decline in core diagnostics business which more than offset 3 percent growth in molecular diagnostics;
- **Quidel:** Expected 4Q revenue of $52 to $53 million, as opposed to Wall Street estimate of $63.1 million, which the company attributes to weak sales of influenza kits caused by late start to flu season; and
- **Fluidigm:** YOY decline of 19 percent (roughly $25 million v. $30.7 million in 4Q 2015) and expected 9 percent decline in full year revenues.

Takeaway: 2017 has started with more positive than negative earnings reports.

Deal of the Month: $25 Billion Acquisition of St. Jude Med Cements Abbott as Leader in Cardiovascular Device Market

In a month with an unusually heavy volume of diagnostic deal making (see DIAGNOSTICS DEALS on page 1), the headline story was Abbott Laboratories' $25 billion purchase of fellow device-making giant St. Jude Medical, which finally closed on Jan. 4.

Already a leader in stents and mitral valve repair (via its MitraClip device), acquisition of St. Jude's heart failure and vascular disease products portfolio makes Abbott arguably the strongest player in just about all aspects of the $30 billion cardiovascular (CV) device market, not to mention one of the biggest overall medical device manufacturers in the world. "The addition of St. Jude Medical creates one of the broadest medical device portfolios in the world and provides a steady stream of technologies and therapies for many years to come," according to a statement from Abbott CEO Miles White.

Despite advances in the management of heart disease, CV disease remains the leading cause of death.

Almost Too Big to Happen

In fact, the sheer magnitude of the deal almost led to its undoing on antitrust grounds. Combined, the two companies had reported CV device revenues of $9.8 billion in 2016 and would have controlled over 70% of the market for vascular closure devices. Adding to the effect is what the U.S. Federal Trade Commission (FTC) characterized as St. Jude's "near monopoly" in steerable sheaths sales.

Accordingly, both companies had to agree to divest substantial assets to gain FTC and European antitrust approval:

- Abbott had to sell off its Vado™ Steerable Sheath products; and
- St. Jude's had to shed Angio-Seal™ and FermoSeal™ vascular closure products.

Tokyo-based Terumo Corporation has agreed to purchase all of the divested assets for a reported $1.12 billion in all-cash deal.

Latest Developments in the Abbott-Alere Merger

There were also new developments affecting Abbott's other strategic acquisition—the Alere merger. On Jan. 25, Alere announced that the deal has been cleared by the European Commission and expressed confidence that the "merger will close according to the terms of the agreement." But Abbott remained tight-lipped and barely even mentioned the deal in its fourth quarter earnings call.

Context & Big Picture

Despite advances in the management of heart disease, CV disease remains the leading cause of death. Laboratory testing continues to play a pivotal role in risk assessment and management of CV disease. Accordingly, while many of the lab giants have staked out a presence in device, the driver of CV deals by labs has been the development of new diagnostic tests, including screening tests using genetic and other personalized biomarkers to identify individuals at risk of particular CV conditions.

Because these deals tend to be small in dollar volume and involve lesser known start-ups in the genomics space, they fly under the radar. But they are taking place and at a growing frequency. A typical recent example is the $8.2 million seed financing completed by San Diego genomics firm Molecular Stethoscope on Jan. 5 to fund development of new RNA-based liquid biopsy tests for cardiometabolic diseases including via a two-year research collaboration with Pfizer. (For more on CV biomarker test development activity by labs, see "Special Focus: Cardiovascular Biomarkers: Interest Seen in Biomarkers for Cardiovascular Disease Risk, But Adoption, Evidence of Clinical Utility Lags," *Diagnostic Testing & Emerging Technologies*, May 2013, p. 8).

INDUSTRY BUZZ

Arizona Fraud Suit Opens New Front in the Legal War against Theranos

The Arizona Attorney General's Office (AGO) recently issued a request for proposal signaling a new legal battle for Theranos: state consumer fraud lawsuits. The AGO indicated in its request that it was initiating a law suit against Theranos and its subsidiaries alleging violations of the Arizona Consumer Fraud Act for representations related to its blood testing equipment and its Wellness Centers.

This is the latest litigation threat to the company previously hyped for its technology that promised to disrupt the diagnostic blood testing industry. In July 2016, the Center for Medicare and Medicaid Services imposed sanctions against Theranos and excluded its CEO, Elizabeth Holmes, from operating a blood testing lab for two years. Thereafter, the company shifted its focus to developing technology—namely the miniLab (a compact 2.5 cubic feet device containing a mini-robot processing single use cartridges, "Our ultimate goal is to commercialize miniaturized, automated laboratories capable of small-volume sample testing, with an emphasis on vulnerable patient populations, including oncology, pediatrics, and intensive care," the company's Oct. 5 statement explained.

The legal troubles continued beyond CMS's regulatory enforcement actions, with civil lawsuits, including a class action fraud suit by investors and a breach of contract claim by Walgreens. (See "Walgreens Terminates Contract with Theranos," *LIR*, July 7, 2016.) But the Arizona consumer fraud case is the first by a state government. And it could spawn more consumer fraud suits from other states, including California where Theranos is based. (For more on the Theranos saga, see "Theranos Shifts Focus from Labs to Technology," *Diagnostic Testing & Emerging Technologies*, Oct. 26, 2016.)

The company, however, continues to put on a brave face with releases in January noting that a reengineering of its operations and streamlining of staff with a "core team of 220 professionals" to pursue its business plan including commercialization of the miniLab. It explained this "restructuring follows a period of significant change at the company that has included the building out of its executive team with substantial additional regulatory, compliance and operational expertise." As late as January 17, 2017, the company also announced formation of an eight-member Technology Advisory Board that will "work alongside Theranos' leadership and internal research and development teams in various areas, including advising the company on peer-reviewed publication submissions and on presentations at scientific meetings."

Industry Buzz: First HIPAA Breach Notification Settlement Totals $475,000

Patient health information breaches—whether from hacking, glitches or just plain old carelessness—remain an all too common occurrence in labs and other health care institutions. A new HIPAA rule took effect in 2013 requiring providers to furnish timely notification of such breaches. And on January 3, 2017, a large Illinois health system named Presence Health became the first provider to settle allegations it violated those notification requirements.

The Rule

Under the HIPAA rule, providers must furnish notification of breaches to three sets of recipients:

1. The HHS Office of Civil Rights (OCR);
2. The individuals affected by the breach; and
3. The media (if the breach affects 500 or more individuals).

The deadline for notification: within 60 days of discovering the breach.

What Happened

On October 22, 2013, Presence discovered that paper-based OR schedules for one of its surgery centers had been removed from the files. The missing records listed personal health information of 836 individuals, including names, birth dates, medical record numbers, dates and types of procedures received and anesthesia administered.

It was a breach requiring notification under the HIPAA rule. The good news is that Presence did send out all of the required notices. The bad news is that it did so only well after the 60-day deadline had expired:

Notice Recipient	Notice Due Date	Actual Notice Date	Days Late
OCR	Dec. 22, 2013	Jan. 31, 2014	41
836 individual patients	Dec. 22, 2013	Feb. 3, 2014	44
Media outlets	Dec. 22, 2013	Feb. 5, 2014	46

The Case

The OCR charged Presence with a separate HIPAA violation for each one of the notices that was late (as well as additional violations committed later on that were discovered during the investigation). Faced with potential liability in the millions, Presence decided to settle the claims. The price tag: $475,000 and the promise to adopt a Corrective Action Plan implementing measures to prevent future violations.

Takeaway: Based on the settlement agreement, it appears that Presence understood and made earnest efforts to comply with its breach notification obligations. Unfortunately, it took too long to do so. Although it is not clear why the notices were late, what can be said with confidence is that implementing clear and specific rules and timetables for responding to and reporting data breaches is crucial to ensure compliance with HIPAA breach notification requirements.

Discussion Paper Signals New Approach (Not Retreat) to LDT Regulation, *from page 1*

The FDA's New Thinking on LDTs

The discussion paper summarizes the feedback it received on the 2014 proposed rule. But its real significance is the discussion of how the FDA's own thinking on LDT regulation has evolved since 2014. Over the two years of "engagement," "positions of many groups, including the FDA, have evolved," the paper notes. It then alludes to an alternative model and outlines the key features it may incorporate, including:

- Phased in oversight program over four years rather than the originally proposed nine years;
- Grandfathering for many LDTs already on the market;
- Broader definition of LDTs for unmet needs;
- Collaboration between FDA and third parties to use existing review standards and certification programs—such as the National Glycohemoglobin Standardization Program or the Cholesterol Reference Method Laboratory Network—for evidence standards;
- Potential leveraging of existing review programs for third-party review such as New York State's Clinical Laboratory Evaluation Program and independent CLIA accreditation programs;
- Clinical collaboration with stakeholders and health care professional organizations on standards for analytical and clinical validity;
- Public availability of evidence of analytical and clinical validity;
- Reliance on CLIA certification requirements plus three FDA quality systems requirements regarding test development processes—design controls, acceptance activities, and procedures for corrective and preventive action (CAPA); and
- Postmarket surveillance requiring labs to report serious adverse events for texts except for traditional LDTs, LDTs for public health surveillance, specific transplantation related LDTs, and forensic-use LDTs.

New FDA Approvals

In other FDA news, at least four diagnostics products received clearance from the FDA in January so far, including:

Manufacturer(s)	Product(s)
Arterys	Arterys Cardio DL software providing automated ventricle segmentation from conventional heart MRI scans (which also received CE clearance in December)
Luminex	Aries Group B Streptococcus (GBS) assay for antepartum detection of GBS colonization in pregnant women from Lim broth enriched vaginal-rectal swab specimens
Hologic	Pre-market approval of Aptima HIV-1 Quant test for HIV viral load monitoring in the US (also CE-IVD approved for both monitoring and diagnosis outside the US)
IncellDx	IVD Class I status approval of IncellPrep single-cell preparation kit for solid tissues (which also received CE-IVD approval in Europe)

New FDA Applications

Companies that submitted new FDA applications during the month include:

- **QIAGEN** for pre-market approval of QuantiFERON®-TB Gold Plus, the fourth generation of its tuberculosis infection blood test;
- **HTG Molecular Diagnostics** for pre-market approval of HTG EdgeSeq ALK Plus Assay used as a companion diagnostic for crizotinib;
- **Curetis** for its Unyvero system and Unyvero lower respiratory tract panel molecular test platform and cartridge, respectively;
- **Great Basin Scientific** for its molecular panel assay for stool pathogens.

New CE Marks

Hologic's Aptima HIV-1 Quant test for HIV viral load monitoring that received FDA pre-market approval for monitoring in the US also received CE-IVD marking for both monitoring and diagnosis in Europe this month. Other products to receive CE marking for Europe in January:

Manufacturer(s)	Product(s)
GenePOC	Revogene instrument and tests for GBS and Clostridium difficile
Sophia Genetics	CE-IVD certification of Hereditary Cancer Solution for examining 27 genes associated with hereditary breast, ovarian and gastrointestinal cancers
Volition Rx	NuQ Colorectal Cancer Screening Triage Test (blood-based test)
IncellDx	IVD Class I status approval of IncellPrep single-cell preparation kit for solid tissues (which also received FDA IVD Class I status approval)