Innovation in the IVD Industry – A Look Back Over the Last Decade

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An overview of key innovations in the IVD field from 2010-2019

As we enter a new decade, it is interesting to look back at the IVD innovations in the past 10 years – of which there have been many – to identify those that have had a significant impact on diagnostic medicine. The examples included in this article reflect many of the ways that the IVD industry has continued to produce new and improved tests and products in some of the areas of greatest need, such as cancer, companion diagnostics, infectious diseases, sepsis, and others. Our examples are not intended to be an exhaustive list of every innovation that has come to light, but they represent some of those that have impacted (or have the potential to impact) clinical decision making or are an improvement to an existing "gold standard" test. Let's take a look:

Cancer Tests

New tests for cancer, mostly molecular-based tests, continually emerged over the last 10 years, offering improved screening, diagnosis, prognosis, or monitoring of treatment response. EAC expects this area to continue to be a major segment for innovation in the coming decade.

- ***Cologuard Colon Cancer Screen***
  After many years of clinical trials, Exact Sciences obtained FDA approval in 2014 for its Cologuard stool DNA test for colorectal cancer. This screening test has now achieved widespread reimbursement from Medicare and private payers. In 2019, according to Exact Sciences, the company performed close to 1.7 million Cologuard screening tests in its CLIA laboratory facility, nearly double its 2018 test volume. The test is far superior to traditional fecal occult blood tests (FOBT) in terms of sensitivity and specificity, which, in turn, translates to fewer false negative and false positive test results.

- ***Sequence-Based Lung and Thyroid Cancer Tests***
  Veracyte introduced two gene expression cancer tests using RNA whole transcriptome sequencing. The first, called Percepta, helps to classify suspicious looking lung nodules as cancerous or non-cancerous, thus avoiding many invasive procedures and surgeries. The second test, Afirma, is for thyroid cancer and indicates whether a needle biopsy specimen taken from the thyroid is cancerous or not. Biopsies using traditional pathology yield many equivocal results which, in turn, leads to many unnecessary surgeries to remove the thyroid gland. Both tests are performed in Veracyte's CLIA certified laboratory.

- ***Prostate Cancer Gene Expression Test***
  In 2013, Genomic Health (now part of Exact Sciences) introduced its Oncotype DX prostate cancer test, which measures gene expression levels of 17 relevant genes to help predict the aggressiveness of a patient's prostate cancer. This helps inform physician decisions regarding "watchful waiting" or pursuing treatment immediately. This test follows on the heels of Genomic Health's highly successful Oncotype DX breast cancer test which determines which early stage breast cancer patients will not benefit from chemotherapy.

- ***Pan-cancer Next Generation Sequencing (NGS) Panels***
  Next Generation Sequencing (NGS) "pan-cancer" panels are emerging as the new standard of care in working up cancer patients to determine personalized treatment regimens. Many IVD vendors and CLIA laboratories now offer pan-cancer gene mutation panels using NGS technology, a capability not available 10 years ago. These panels detect dozens, even hundreds, of mutations associated with a wide range of solid tumors, enabling clinicians to optimize treatment strategies or even recommend the patient for specific clinical trials. Some of the pan-cancer panels now offered include Thermo Fisher's 52 gene Oncomine Dx panel for tissue samples and Illumina's TruSight Oncology 500 that detects 523 mutations in tissue samples (Research Use Only). In addition, Foundation Medicine and Guardant Health offer pan-cancer panels for both tissue and plasma samples through their certified CLIA laboratories.

Companion Diagnostics (CDx)

Although Companion Diagnostics (CDx) first came to the forefront with the introduction of the Her2 test for breast cancer more than 20 years ago, there has been ongoing and continual development, illustrating the growing trend in personalized medicine, particularly when it comes to cancer treatments. Below are examples of some of the CDx assays that have emerged in the past 10 years.

- ***PD-L1 Marker***
  In 2015, Agilent's Dako division introduced the new tissue pathology CDx test for PD-L1, an immunohistochemistry marker that can assess suitability for the immunotherapy drug, Keytruda, in non-small cell lung cancer (NSCLC) patients. Since then, the approval has been expanded to several other cancers. Similarly, Roche Diagnostic's Ventana unit obtained FDA approval for its PD-L1 assay as a companion diagnostic for patients with urothelial and triple-negative breast cancer (defined as Her2, ER & PR negative) in order to determine the suitability for its drug, Tecentriq.

- ***BRAF, KRAS, EGFR and PIK3CA PCR Mutation Assays and the Beginning of the Liquid Biopsy Era***
  In 2011, Roche received FDA approval for a PCR based tissue assay for the BRAF gene mutation for use with its melanoma drug, Zelboraf. This was followed in 2015 with FDA approval for a KRAS mutation assay that is associated with use of anti-EGFR therapies in colon cancer. Later, in 2017, Roche received FDA approval for the first so-called "liquid biopsy" CDx assay, which detects cell free DNA (cfDNA) in plasma samples for the EGFR mutation associated with NSCLC and treatment with the Roche drug, Tarceva, thus beginning the era of the liquid biopsy.

More recently, Qiagen, which also offers several CDx test kits, obtained FDA approval for its PIK3CA PCR kit for use in breast cancer and linked it with the new drug therapy called Piqray. It is also approved for both tissue and plasma samples.

- ***NGS Cancer Panel CDx Assays***

  In 2017, Thermo Fisher received FDA approval for the first NGS-based CDx assay for NSCLC. The assay, called Oncomine Dx, detects 23 gene mutations associated with NSCLS; among these 23 genes are several different mutations specifically tied to FDA-approved NSCLS therapies. Similarly, Foundation Medicine, now a division of Roche, introduced in 2017 the FoundationOne CDx NGS panel that examines 324 genes associated with several different solid tumors and targeted drug therapies. This test is performed in the Foundation Medicine CLIA certified laboratory.

Infectious Disease and Sepsis

Innovations in this area range from rapid molecular assays to full automation, both for high and low throughput needs. Moreover, test turnaround time has been reduced dramatically for many types of tests. EAC also wanted to highlight tests in the sepsis area that have the potential to improve antimicrobial stewardship as well as the potential to reduce patient morbidity or hospital length of stay.

- ***Use of Molecular Platforms at the Point of Care***

  Twenty years ago, the idea of a 15 minute point-of-care molecular test would have been a fantasy to most laboratorians and clinicians, but during this past decade, we have seen the emergence and adoption of rapid, CLIA-waived molecular tests for use at the point-of-care. Now clinicians can get higher quality results for tests such as influenza, RSV and Strep A in 10-20 minutes using “sample-to-answer” instruments that are smaller than a toaster. More tests are being developed (e.g., STIs) and some may already be available outside the US.

- ***Zika Virus Testing (the Impact of New Outbreaks)***

  The 2015 Zika virus outbreak, which started in Brazil and quickly spread to other countries in South, Central and North America, drove the development of new rapid Zika virus tests that had not previously existed. IVD manufacturers quickly produced rapid immuno-based and molecular-based assays to test at risk patients and those with suspected infections. Both Roche and Grifols now offer FDA approved Zika molecular assays for screening blood donations along with numerous other companies that offer other immunoassay and molecular tests.

- ***Multiplex Syndromic Panels***

  The use of large, multiplex syndromic infectious disease panels skyrocketed over the past decade, spurred by companies such as bioMérieux with the BioFire FilmArray, GenMark’s ePlex system and Luminex’s Verigene to name a few. Large, multiplex panels with the ability to identify 20 or more pathogens are available for respiratory infections, gastrointestinal infections and meningitis as well as rapid identification of positive blood cultures.

These syndromic panels eliminate the need to perform several different types of cultures or numerous separate molecular tests and enable faster treatment decisions by the clinician. EAC estimates that annual revenues from the sale of these syndromic panels are now in the vicinity of $800 million.

- ***Host Response Bacterial versus Viral Assay***

  MeMed, an Israeli based diagnostic company, has introduced the first immunoassay biomarker panel designed to differentiate bacterial from viral infections. The MeMed BV is a CE Mark ELISA assay that combines measurement of 3 biomarkers from blood with machine learning to distinguish bacterial from viral infection. The 3 biomarkers measured are C-Reactive Protein (CRP), IP-10 and TRAIL. As an example, the MeMed test can be used in upper and lower respiratory infections where widespread overuse of antibiotics is common. The goal is to improve antibiotic stewardship and reduce the vast number of unnecessary antibiotic prescriptions. A rapid point-of-care version of the test is under development.

- ***Host Response Sepsis Assay***

  Immunexpress received FDA clearance in 2017 for its SeptiCyte assay, which is the first FDA cleared host response assay that examines RNA gene expression of specific immune system genes along with an algorithm to form a genetic signature for diagnosing sepsis. A laboratory version of the test is currently available and the company has partnered with Belgium based Biocartis to develop a 90 minute sample-to-answer version of the test on its Idylla molecular platform. This may allow a clinician to rule out sepsis and avoid starting expensive antibiotics or confirm a suspicion of sepsis and begin treatment immediately.

- ***Direct from Blood Sepsis Pathogen Test***

  In 2018, T2 Biosystems received FDA clearance for its T2Bacteria Panel, a direct from whole blood sepsis test for the most common pathogens causing bacteremia. This was followed in 2019 with CE Mark for the T2Resistance Panel that detects 13 antibiotic resistance genes commonly found in sepsis. T2 also has a fungemia panel for detection of various Candida species in blood. Test results are generally available in 3-4 hours once the sample is loaded into the instrument. T2 uses a patented magnetic resonance technology for detection of the pathogens.

- ***Blood Culture ID and Antibiotic Susceptibility***

  In February 2017, the FDA granted the *de novo* request from Accelerate Diagnostics to market its Pheno system instrument and PhenoTest for rapid identification and antibiotic susceptibility testing of positive blood cultures. Now laboratories can obtain a pathogen identification from a positive blood culture in approximately 1.5 hours and an antibiotic susceptibility profile in about 7 hours, a day or two faster than using traditional microbiology.

Other Areas of Innovation

Below are examples of other unique tests that EAC views as transformational in that they are "game-changing" to the patient or the practice of medicine.

- ***Direct-to-Consumer (DTC) Genetic Testing***

  During the past decade, we witnessed the emergence of DTC genomic testing where consumers can mail in a saliva sample and receive a genetic report on ancestral origins and/or genetic information related to inheritance and risk of certain types of health conditions (e.g., Alzheimer's, Parkinson's disease, colon cancer), all at a cost of $100-$300. Companies such as 23andMe have tapped into this emerging consumer market performing more than 1 million tests to date. In turn, consumers can be better informed about their health risks.

- ***Non-Invasive Prenatal Testing (NIPT)***

  Since 2011, NIPT testing has been used to screen pregnant women for fetal chromosomal trisomy disorders like Down syndrome. These tests use NGS or DNA microarrays to detect minute quantities of fetal DNA that are shed from the placenta into the maternal bloodstream. Over the past decade, NIPT was rapidly adopted to screen pregnant women considered at high risk for giving birth to an infant with trisomy disorders, and increasingly, insurance companies are covering the cost of the test, even for lower risk pregnancies. EAC believes that NIPT will likely become the standard of care worldwide over the coming decade. Moreover, the test vendors continue to expand the spectrum of chromosomal disorders that the assays can detect in a maternal sample. Most of the NIPT testing in the US is performed by a handful of CLIA certified laboratories such Natera, Roche/Ariosa Diagnostics and Illumina.

- ***Continuous Glucose Monitoring (CGM)***

  Continuous glucose monitors utilize glucose sensors that are inserted under the skin or are worn on the skin using an adhesive patch, usually on the upper arm or abdomen. Frequent glucose measurements are automatically taken and sent to a receiver device, such as an iPhone, that contains a CGM app. Although CGM first appeared on the market prior to 2010, the new generation of CGM products offered by Dexcom, Abbott and Medtronic are simpler and more convenient to use and eliminates or greatly reduces the need for finger stick glucose tests. This has transformed the diabetes testing market and sent CGM sales soaring past the $3 billion mark. It is noteworthy that much of the market opportunity still remains untapped. Ultimately, CGM leads to better blood glucose control for diabetics compared to traditional finger stick glucose methods, thereby improving patient outcomes.

Lastly, EAC closes by noting that with the news of the recent and serious coronavirus outbreak in China, IVD manufacturers have rushed to develop assays to detect this new 2019-nCoV strain. As an example, Chinese based diagnostic leader BGI has already received emergency authorization by China's FDA to sell an NGS based assay as well as a real-time PCR assay. This illustrates the ability of IVD vendors to rapidly respond to public health emergencies.

About Enterprise Analysis Corporation (EAC)

EAC offers strategic consulting and market research services for diagnostics companies, providing the information needed to improve market understanding and make better business decisions. With our deep expertise in IVD, we act as a bridge between Diagnostic Science (suppliers) and Clinical Medicine (end-users, labs, and physicians) delivering voice of the customer and market insights across all phases of a product or company life cycle.

EAC Facts:

- Based in Stamford, CT
- 30+ years in operation
- More than 100 years of combined IVD experience
- Over 1,400 projects completed for more than 160 client companies
- Global operations: US, Europe, Asia, and Latin America
- Conducts independent and customized proprietary research

In addition to strategic consulting in areas such as market opportunity assessment and portfolio analysis, we conduct primary research using proven methodologies including conjoint analysis, outcome research, pricing and workflow studies, user satisfaction assessments, and others.

About The Author
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Mark Hughes joined EAC in 1997 and has more than 35 years of experience in the clinical diagnostics industry. His projects have included technology assessment, market analysis, business strategy and due diligence for major diagnostic, pharmaceutical and start-up biotechnology companies, as well as investment banks and venture capital firms. Mark is often quoted in many industry publications for his insights into the IVD industry.

Mark began his career in clinical research at the Harvard School of Public Health and progressed into immunoassay research and development for the former Dade Behring's Clinical Assay division. He has held management positions in market research and business planning at the Ares-Serono Group and Gene-Trak Systems. Mark received his B.S. from the University of Massachusetts at Amherst and his M.B.A. from Duke University.

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