Important Developments in Clinical Testing/IVD Devices

The 69th American Association for Clinical Chemistry (AACC) Annual Scientific Meeting and Clinical Lab Expo took place this year in San Diego from July 30th to August 3rd, 2007. This meeting makes a good place to start when one wishes to discuss the latest trends in in vitro diagnostics, those devices used to detect disease.

The meeting had record breaking attendance with over 21,300 attendees, a record breaking attendance. The Clinical Lab Expo also broke records with 789 exhibitors covering 246,000 net square feet. Kalorama Information attended and has summarized those developments.

During this meeting and Expo, new technologies and products were discussed:

- **CRISPR** - a revolutionary technology
- **Automation**, and the introduction of new, large, automated platforms
- **Rapid point-of-care** testing with single pathogen infectious disease tests
- **Syndromic testing** for infectious disease identification and antibiotic resistance
- **Next generation sequencing** – moving into in vitro diagnostics with the FDA approval of a sequencing based companion diagnostic test.
- **Targeting Disease** – Opioid Abuse, Alzheimer’s Disease testing, HAIs, Sepsis, Acute Kidney disease among the threats targeted by IVD vendor offerings.
- **Connectivity** – Vendors showcased solutions that keep test products connected to provider EHRs.
Gene Editing – Moving Towards the Clinical Laboratory

CRISPR is a gene-editing technology that is changing life science research and has the potential to dramatically change medicine. CRISPR gene editing technology was a highlight of the first day of the meeting when Jennifer Doudna, PhD (University of California, Berkeley) delivered the Wallace H. Coulter Lectorship Award plenary with her talk, “CRISPR Biology, Technology & Ethics: The Future of Genome Engineering.” During this presentation, Dr. Doudna discussed her laboratory’s findings, which she calls a “molecular scalpel for genomes.”

CRISPR (clustered regularly interspaced short palindromic repeats) are DNA sequences that have a key role in a bacterial defense system, functioning as an immune system that protects bacteria and other microorganisms against viruses. Multiple CRISPR-Cas (CRISPR associated) systems have identified, each with unique Cas proteins.

This is early stage technology that is not yet being utilized in diagnostic testing, although several clinical trials are listed in ClinicalTrials.gov. These trials are (or will) evaluate the role of CRISPR in potential new treatments for certain disease. Several of these studies have not yet started recruiting.

Meanwhile, CRISPR technology is a promising technology with the potential to transform diagnostic testing. CRISPR already here and is progressing rapidly. Clinical laboratory leaders have started the discussions about the role and ethical use of CRISPR, and CRISPR was part of the discussion at a session on “Ethics in Laboratory Medicine” that took place on Wednesday of the annual meeting.
Automation – Introduction of New Large, Automated Platforms

Automation, and large high-throughput automated analyzers, have been an import segment of the clinical laboratory market for many years. This year, several new or recently introduced instrument platforms for the central core laboratory were showcased at the annual AACC meeting. These newer automated platforms include:

- **Abbott Alinity**: Abbott has been developing a line of harmonized next-generation diagnostic systems called Alinity. Abbott first unveiled this product platform in August 2016, although the systems were not CE-marked or FDA cleared at the time. For the core lab, this new family of systems will include: Alinity c (clinical chemistry system), Alinity I (immunoassay system), Alinity ci-series (clinical chemistry and immunoassay systems), Alinity hq (hematology analyzer), and Alinity PRO (software applications). The i-STAT Alinity for point-of-care testing is currently available.

- **Avioq** showcased the VioOne Chemiluminescent Immunoassay System (VioOne Chemiluminescent Immunoassays and Analyzers). This new platform has a test menu that includes over 70 different assays. Avioq reports that throughput on this analyzer ranges from 60 to 280 samples in one hour, and that the first result is delivered in 15 minutes.

- **Siemens Healthineers** showcased the company’s recently FDA cleared Atellica Solution, which consists of flexible, scalable, automation-ready immunoassay and chemistry analyzers that can create over 300 customizable configurations. Siemens also showcased the Atellica PM 1.0 Software, a process-management tool, and the Atellica MDX 160 Sample Prep instrument.

- **Roche** showcased the cobas® 6800 system and cobas® 8800 systems, which are large automated, moderate complexity platforms for molecular diagnostic assays. Roche also showcased the cobas® 8000 modular analyzer series. This large platform has a throughput of 2.5 million to 15 million tests per year.

- **The Sarstedt BL 1200 ID** is a modular accessioning and sorting instrument that can be used in conjunction with any analytical platform. The unit features a Bulk Loader that eliminates manual sorting and pre-racking. Multiple tube sizes and types are accepted,
and capped tubes are simply poured into the loader for walk-away processing. Tubes are automatically singularized and the tube type and barcode are identified. Sort and distribution rules are customized to targeted racks and centrifuge adapters or to bulk bins. Up to 1,200 tubes can be processed per hour, and an optional Pick and Place module allows the BL 1200 ID to be connected to a track system.

The above products are selected examples of new platforms that are being developed or have recently been introduced. Other instrument platforms as well as older platforms from these and other companies were also shown at AACC. New this year was also cobas® e 801 immunoassay module.

**Rapid Point-of-care Testing – Single Pathogen Infectious Disease Tests**

Wednesday’s plenary session at the AACC meeting focused on antimicrobial resistance, as Victoria Fraser, MD (Washington University School of Medicine) gave a presentation entitled “Antibiotic Resistance: A Public Health Crisis.” It was reported that in 2013, antibiotic resistance was responsible for 2 million infections and more than 20,000 deaths in the U.S. There is critical need to reduce unnecessary use of antibiotics. Rapid diagnosis can identify patients with viral infections to prevent treatment of these patients with antibiotics.

This need for rapid infectious disease tests has been recognized for several years, and a number of companies have developed molecular tests to meet this need. Two examples that were shown at this year’s AACC meeting are:

- Alere showcased the Alere i, a rapid instrument system based on an isothermal amplification system that can perform assays in 15 minutes or less. Available tests include Alere i Influenza A&B, Alere i Strep A, and (most recently) Alere i RSV. The Alere i Influenza A&B test was the CLIA waived rapid influenza test. All three tests are now CLIA waived.

- Roche’s cobas® Liat® PCR System is a real-time PCR-based system that currently has three tests available: Influenza A/B, Influenza A/B & RSV, and Strep A. These tests are also CLIA waived, and results are available in 15 to 20 minutes.

Other companies also offer rapid molecular infectious disease tests. For example, Cepheid has developed the GeneXpert system for on demand molecular diagnostic testing. Tests are available to detect MRSA, *C. difficile*, carbapenem resistance, vancomycin resistant
enterococcus (VRE) and others. Some of these tests detect antibiotic resistance genes, providing additional information. However, they are not as rapid as the Alere and Roche tests. Also, performing these tests requires more time than the Alere i and Liat platforms.

More recently, Cepheid introduced the Xpert®Xpress Flu/RSV and Xpert®Xpress Flu tests, which can provide results more rapidly. Another company, Quidel, offers rapid infectious disease tests, based on both molecular and on immunoassay platforms.

Luminex has developed the ARIES System, which is a real-time PCR System. Several individual infectious disease tests are available.

These are just some examples of rapid infectious disease tests.

**Syndromic Testing for Infectious Disease Identification and Antibiotic Resistance**

All of the rapid infectious disease tests discussed so far detect a single pathogen an (maybe) also an antibiotic resistance gene. However, if a patient presents with general symptoms of a respiratory infection, or with symptoms of a gastrointestinal infection or some other type of infection, there are several different pathogens that may have caused the infection. This has led to the development of syndromic panels that include a panel of pathogens and often also resistance genes commonly found with the targeted type of syndromic infection.

Some of these companies were exhibitors at the AACC Annual Meeting. Examples include:

- BioFire Diagnostics (a bioMérieux company) has commercialized the FilmArray platform. Four syndromic panels are currently available: Respiratory Panel, Meningitis/Encephilitis (ME) Panel, Gastrointestinal (GI)Panel, and Blood Culture Identification (BCID) panel. BioFire Diagnostics also offers the FilmArray® Respiratory Panel EZ on the FilmArray® EZ Configuration platform. This is a CLIA waived test designed for point-of-care settings.

- Curetis currently has developed the Unyvero Platform. Unyvero cartridges are available for three applications: (1) Unyvero HPN Pneumonia Cartridge - 19 resistance markers and 20 pathogens, (2) Unyvero i60 ITI Cartridge - For implant and tissue infections; For detection of up to 102 analytes, and (3) Unyvero BCU Cartridge - For blood culture; For detection of up to 103 analytes. In addition, an intra-abdominal infection application is in
development. In the United States, Curetis has conducted clinical trials and submitted to the FDA, seeking clearance of the Unyvero Platform and Lower Respiratory Tract Infection (LRT) Application Cartridge

- GenMark Diagnostics has developed the ePlex® System. A respiratory panel is currently available.
- In addition to the single disease tests, Luminex is developing tests on the company’s VERIGENE platform. Luminex showcased the VERIGENE Respiratory Pathogen’s Flex Test at the AACC Annual Meeting. Luminex has also developed two gastrointestinal infection tests. The VERIGENE Enteric Pathogens (EP) Test detects nine bacterial and viral targets in patients with community-acquired diarrhea. In addition, Luminex offers a single pathogen gastrointestinal test – the VERIGENE *C. difficile* Test (CDF).

**Heavy Interest in Next Generation Sequencing Exhibits and Sessions as NGS Continues to Move into In Vitro Diagnostics**

Next generation sequencing has historically been a research tool, and more recently a technology that is widely used by clinical laboratories offering laboratory developed tests (LDTs) for oncology and selected other applications. This year’s AACC meeting saw the introduction of an *in vitro* diagnostic (IVD) next generation sequencing based kit.

Thermo Fisher Scientific showcased the company’s new Ion Torrent Oncomine Dx Target Test, which had been approved by the FDA in June of this year. Clinical laboratories can now order a kit from Thermo Fisher Scientific, and then perform the test using Thermo Fisher’s Ion PGM Dx System, which was FDA cleared in parallel for use on formalin-fixed, paraffin-embedded (FFPE) tissue samples.

The Oncomine Dx Target Test is a companion diagnostic test that is the first next-generation sequencing based test that simultaneously screens tumor samples for biomarkers associated with three FDA-approved therapies for non-small cell lung cancer. This test evaluates 23 genes associated with non-small cell lung cancer. Results from the analysis of three of these genes (BRAF, ROS1, and EGFR) can be used to identify patients who are eligible for three FDA-approved therapies [TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib), XALKORI® (crizotinib), and IRESSA® (gefitinib)].
Meanwhile, at the same meeting where laboratorians were introduced to the first FDA approved IVD test for use as a companion diagnostic test for lung cancer therapies, Jay Shendure (University of Washington spoke at a plenary session on the topic “Beyond Sequencing: New Frontiers in Genomics.”

**Other Developments: Opioid Abuse, POCT, Connectivity, Sepsis**

A wide range of sessions at this year’s AACC case studies in clinical toxicology, marijuana metabolites and pharmacokinetics, how people try to beat drug testing and defend positive results. With marijuana use permitted in some form in so many states, test providers, pathologists and researches have struggled for an effective way to test for its abuse. An afternoon symposium on Cannabis Impaired Driving: Biological Markers and Behavioral Indicators of Recent Cannabis Intake examined the latest research on the disposition of cannabinoids in blood and oral fluid in occasional and chronic frequent cannabis users after controlled cannabis administration. A Thursday morning symposium "At the Juncture of Pain Management and Addiction" was expected to tackle the lab pathologists role in being the physician's "consultant" in clinical decisions regarding opioid use and the IVD tests available to help them with that role.

IVD Vendors also had offerings in DUA - Medica Corporation of Redford, MA, today announced the expanded capability of its EasyRA® clinical chemistry analyzer to now provide drugs of abuse urine screening (DAU). The company's EasyRA will offer a panel of drugs of abuse with simply interpreted positive or negative results, to eliminate the need for subjective interpretation in the moderately-complex setting. The reagents to enable the new assays are immediately available from Medica’s distribution partners.

The seriousness which the health care system is taking sepsis, a killer of 30 million Americans annual, was on display at the event with an increased focus on PCT testing. PCT or procalcitonin test may be used, along with other tests and examinations, to help detect or rule out sepsis in a seriously ill person. It has primarily been used in people who seek care at emergency departments or who are admitted to intensive care units (ICUs) with signs and symptoms that may be due to sepsis. Beckman Coulter announced PCT Results for their AU480/680/5800 chemistry analyzers. The company said the PCT assay offers laboratories the ability to provide sepsis testing through a simple chemistry menu addition. Roche Diagnostics showcased its Elects BRAHMS PCT Assay which the company said was the only fully automated and integrated PCT solution in the United States.
Sepsis was not the only disease tackled by vendors. Clostridium difficile (C. diff), a health care associated infection, was the target of IVD products from Luminex and Dia Sorin in different assay formats.

Vendor Ortho Clinical Diagnostics touted the establishment of its NephroCheck® test, on OCD's VITROS system, which the vendor said was the first fully automated risk assessment tool for predicting Acute Kidney Injury (AKI). The test has received CE Mark clearance, signifying conformance to all EU regulations, and is now available for purchase and use on Ortho’s VITROS® Systems in Europe.

AKI, the sudden loss of kidney function, can develop without warning and potentially lead to kidney failure and death. The disease causes as many as two million deaths annually worldwide3. AKI is caused by renal stress contributed to by major surgery, drugs, toxins, serious infection, or chronic illness and trauma. Up to 50 percent of patients in intensive care develop some stage of AKI. bioMerieux and BioPorto are among companies offering testing products in this area. "AKI is where sepsis was 15 years ago," said Fernando Chaves, Ortho Clinical Diagnostics' global head of Clinical and Scientific Affairs, in an interview with Kalorama. Chavez suggested most tests treat kidney disease too late, and that the testing for heart disease should be a model for AKI.

Kalorama Information noted the following developments of note at the AACC meeting this year:

- The Spartan Cube, the world’s smallest DNA-testing device, is the fastest way to identify potential individuals for research studies based on their genetics. One-in-four people carry APOE genetic mutations that increase the risk of developing Alzheimer’s.(1) These genetic carriers can be ideal candidates for research, and the Cube can accelerate the identification of these individuals. For example, the Spartan Cube enables testing in doctors’ offices, walk-in clinics or even nursing homes.

- New YFV Protein: Aalto Bio Reagents announced their first-to-market recombinant Yellow Fever Virus (YFV) protein at AACC in San Diego from 1st - 3rd August. Yellow Fever virus is a potentially fatal mosquito-borne flavivirus which is prevalent in tropical and subtropical locations in South America and Africa. It is the next flavivirus threatening the population of Brazil, with local health officials reporting a sharp rise in cases this year. The company, founded in 1978, Aalto Bio Reagents is a developer and
provider of raw materials to the in-vitro diagnostics industry and to research laboratories globally. Infectious disease is one of the most important markets for IVD, and Kalorama covers this extensively in its market study on this area.

- Order-to-Report Multiplex PCR: Segene Inc. announced a Random Access System. The company says the system can provide order-to-report on the same day by simultaneously performing high multiplex real-time PCR testing on a single platform, regardless of specimen type or assays. Rapid, accurate diagnosis and prompt treatment are especially critical for a successful treatment of infectious diseases such as tuberculosis, acute diarrhea, sepsis or meningitis. The company said most existing MDx systems are unable to perform same-day reporting for same day treatment, because clinical laboratories typically perform testing after a sufficient number of specimens are collected.

- Simplified LDT for Leukemia and Lymphoma: Beckman Coulter presented its ClearLLab reagents at the meeting, these products deliver the first preformulated, IVD antibody cocktails for leukemia and lymphoma immunophenotyping in the clinical lab. Previously, labs would have had to make and validate their own antibody cocktails. ClearLLab simplifies and standardizes the process. The products are cleared via the FDA De Novo Process for in vitro diagnostic use in the US. For clinical laboratories it means they no longer have to develop their own laboratory developed test (LDT), a technically demanding, manual, time-consuming, and potentially error-prone process.

- Focus on Middle East IVD: Long a target for IVD companies seeking emerging market growth, the Middle East will now have a laboratory association with global pull. AACC announced on Monday that it will launch a new laboratory medicine conference and expedition next spring – AACC Middle East. AACC Middle East will showcase AACC’s globally-renowned education and scientific programs paired with a dynamic exposition in Abu Dhabi, United Arab Emirates (UAE), March 22-24, 2018. The scientific program will feature experts from the U.S. and the Middle East, sharing knowledge and innovation. Attendees will meet and network with experts in the field, and engage with their peers during the scientific program highlighting recent advances in laboratory medicine. Kalorama’s report on the Middle East IVD market can be found at https://www.kaloramainformation.com/IVD-Middle-East-10336235/

- Connected Lab, “Data Lakes”: Roche’s booth at AACC 2017 features a virtual reality tour that will demonstrate the company’s concept of connected lab. “The idea of a connected lab begins with an integrated core lab with connected automation.” said Jack Phillips, president and CEO of Roche Diagnostics Corporation in a press release. “But it also involves linking instruments to data lakes, laboratories to physicians, and high-medical-value tests to clinical insights to help improve the way physicians manage their patients.” A data lake is a storage repository that holds a vast amount of raw data in its native format and doesn't structure it and define how it will be structured, until the data is
needed. The company is the largest IVD company, according to Kalorama Information and competes in nearly every IVD sub market; while it is also demonstrating a new cobas e 801 high-volume immunoassay platform that Roche says provides nearly twice the throughput on the same footprint as its predecessor.

- Three Instruments, One Tube Loader: Sebia’s automated portfolio, the CAPILLARYS 3 TERA, CAPILLARYS 2 Flex Piercing, and MINICAP Flex Piercing systems, provide what the company says is full walkaway capability. The test menu includes serum & urine* protein and immunotyping, hemoglobinopathy*, CDT, and HbA1c. CAPILLARYS 3 MC2, the first automated capillary separation system with work cell capabilities. Their CAPILLARYS 3 MC2, combines two CAPILLARYS 3 instruments with a tube loader, capacity of 712 samples, for maximum walk away time. The system can a dedicated or multi-assay system with up to three CAPILLARYS 3 instruments connected to one tube loader. The addition of the tube loader with the CAPILLARYS 3 MC, allows for added capacity and work cell productivity.

- 9 Minute Cardiac Markers: Elecsys® TnT Gen 5 assay is intended to aid in the diagnosis of myocardial infarction (MI). As the only high-sensitive Troponin assay in the U.S. and designed to offer excellent precision, the assay delivers accurate results in only 9 minutes, enabling clinicians to accurately diagnose patients with a suspected heart attack.

- Same Day Multiplex For TB, Sepsis, Meningitis, Others: Seegene Inc. announced a Random Access System. The company says the system can provide order-to-report on the same day by simultaneously performing high multiplex real-time PCR testing on a single platform, regardless of specimen type or assays. Rapid, accurate diagnosis and prompt treatment are especially critical for a successful treatment of infectious diseases such as tuberculosis, acute diarrhea, sepsis or meningitis. The company said most existing MDx systems are unable to perform same-day reporting for same day treatment, because clinical laboratories typically perform testing after a sufficient number of specimens are collected.

- Simplified LDT for Leukemia and Lymphoma: Beckman Coulter presented its ClearLLab reagents at the meeting, these products deliver the first preformulated, IVD antibody cocktails for leukemia and lymphoma** immunophenotyping in the clinical lab. Previously, labs would have had to make and validate their own antibody cocktails. ClearLLab simplifies and standardizes the process. The products are cleared via the FDA De Novo Process for in vitro diagnostic use in the US. For clinical laboratories it means they no longer have to develop their own laboratory developed test (LDT), a technically demanding, manual, time-consuming, and potentially error-prone process.

- Trinity Biotech promoted its Syphilis Health Check. The company claims the product is the only CLIA waived rapid screening product for the disease. This product can be used as an initial screening test or in conjunction with a non-treponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection.
- Siemens Healthineers' launched its Xprecia Stride Coagulation Analyzer. The handheld testing fingerprick device has a large, intuitive touchscreen on the handle. PT/INR testing is used for the monitoring of oral anticoagulation therapy (OAT) with warfarin. The company says the unit provides lab accuracy and integrates with EHR though Siemens-owned UniPOC Software.

- Sarstedt showcased its S-Monovette POC Collect Kit. The system is an innovative, point of care collection system for venous sampling, designed to be easy to use but yet precise enough to avoid risking blood exposure.

- Roche Diagnostics CoaguCheck XS Plus System delivered CLIA-waived testing with enhanced connectivity. Also on display was the company's cobas Liat, an automated multiplex real-time RT-PCR assay for the rapid in vitro qualitative detection and discrimination of Influenza A virus and Influenza B virus RNA in nasopharyngeal swab specimens. The test is intended for use as an aid in the differential diagnosis of Influenza A, Influenza B, and RSV and is aimed at POLs and small clinics.

- Orchard Software launched its Orchard Trellis, a POC testing information system that the company says simplifies the integration, administration, and management of point-of-care testing (POCT). POCT results are integrated into the EHR, promoting fast access and making results available for population health management. Status of POCT sites (instruments, user certifications, QC, patient result statuses) can be quickly analyzed via an information dashboard, and result evaluation rules functionality, Levey-Jennings QC graphs, and linearity reports are offered.

- The epoc Blood Analysis system delivers blood gas and electrolyte results in about 30 seconds, according to the manufacturer. Currently part of Alere, Siemens Healthineers recently announced its intention to buy the unit that owns epoc due to Alere's merger with Abbott. Abbott's iStat blood gas POC system was also on display at the meeting.

- A palm sized dock and disposable assay specific test cassettes were a feature of Mesa Biotech's Accula System. The San Diego-based company says its MDX-POC system will allow healthcare professionals to access actionable, laboratory-quality results at the POC in 30 minutes or less with greater sensitivity and specificity than many current infectious disease rapid immunodiagnostic tests.
Access our entire library of market data and analysis—all instantly available and fully searchable—saving you time and money.

Powered by world-class technology, the Kalorama Information Knowledge Center offers convenient access to Kalorama's pharmaceutical, diagnostic, biotech, medical device and health care research.

Authoritative content from a trusted name.
Get comprehensive, quality research from a premier global publisher specializing in health care. Kalorama's research is used by top industry decision makers and frequently cited by leading news organizations.

Smarter and faster searching.
Find what you need in seconds. A search on our Knowledge Center allows you to view or filter by report, figures, or tables—giving you a shortcut to the content you want to view. You can also preview the search results, allowing you to quickly determine whether that piece of content is relevant.

With the Knowledge Center functionality at your disposal, you can:

- Clip relevant sections from multiple sources and drop them into presentations and reports.
- Add a chart to a PowerPoint presentation.
- Download tables into Excel.
- Share notes on the research with clients.
The Kalorama Advantage
Tapping 20 years worth of expertise, the Kalorama Information Knowledge Center makes it easy for you to confidently obtain the research you need to stay ahead of your competition.*

• Primary research based on industry interviews
• Expert overviews & analysis of world markets
• Market size & segmentation
• Historical data & projections
• Analysis of current & emerging market trends
• Reviews of current products & pipelines
• Competitor insights & profiles of key industry players
• Growth opportunities
• Numerous graphs & tables

About Us
• We only write health care reports and have published reports for more than two decades.
• We utilize established expert industry analysts.
• Our industry analysts don’t just recite data, they provide key insights and conclusions.
• Our customers include top drug, diagnostic and device companies.

The Knowledge Center is now available to government agencies through our partnership with Carahsoft.

Get a Free Demo of the Knowledge Center

Topics Covered
• In Vitro Diagnostic (IVD) Tests
• Electrostimulation
• Next-Generation Sequencing
• Health care IT
• Vaccine Markets
• Home Care Products
• Physician Office Laboratory (POL) Testing Markets
• Infusion Pump Markets
• Diabetes Treatments
• Cancer Treatments
• Medical Device Regulation
• Market for Respiratory Equipment and Disposables
• Vaccines: Adult and Pediatric
• Billing Software
• Imaging Markets
• World Pharmaceutical and Biopharmaceutical Markets
• Long Term Care
• Outsourcing in Drug Discovery
• Wound Care Markets
• Remote & Wireless Patient Monitoring Markets
• OTC Drug Market
• ISH and Other Cancer Diagnostics
• Prescription Dermatological Drugs
• Global Market for Medical Devices
• Lab Automation
• Clinical Laboratory Services
• EMR