

Strategic Information for the Analytical & Life Science Instrument Industry

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Volume 27, Issue 9 August 15, 2018

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The 2018 IBO Design Awards

Each year, in our August 15th issue, *IBO* recognizes outstanding industrial design of analytical instrumentation with the winners of the *IBO* Design Awards. Each Award winner stands out for how its industrial design not only creates a better looking instrument but is key to enhancing the user experience and instrument functionality. Criteria for the Awards include innovation, utility and approachability.

Simplicity is a theme of this year's Awards as each winner integrates its key design features into a seemingly simple



appearance, even though the instruments themselves reinvent the presentation of its technology to meet users' needs in a new way. In doing so, the design is non-intrusive, harmonious with users' needs and requirements, and highlights the system's advantages and defining features.

Nominees are selected from instruments that *IBO* staff view at trade show, online and in print. To be eligible for a 2018 Award, the system must have begun commercial shipments between August 2017 and July 2018.

Gold Award

This year's winner of the Gold Award, Agilent Technologies' Ultivo triple quadrupole MS system, is a major leap forward in instrument size reduction and, consequently, utility. The instrument is 70% smaller in size compared to other triple quad MS systems. In fact, it does not even resemble an MS triple quadrupole system, making its visual appearance completely unique and benefiting users in way ways. And blending form and function, the system maintains the performance capabilities of a standard triple quadrupole MS system.



Agilent Technologies Ultivo MS as part of LC stack

The Ultivo measures 15.6 in $(39.5 \text{ cm}) \times 34.6 \text{ in } (88 \text{ cm}) \times 12.6 \text{ in } (32 \text{ cm})$. It weighs 130 lbs (50 kg). The system was completely designed in house by Agilent.

As Shane Tichy, PhD, R&D manager at Agilent, told *IBO*, "Ultivo was designed from the ground up to provide superior LC/MS triple quad performance in a significantly smaller size, so labs can improve productivity without requiring increased lab space,". The dramatic reduction in size enables new options for triple quad users, such as placing a greater number of systems in one lab, thus running a greater number of samples each day, or integrating the system into a LC stack. "It was designed to be harmonized with the look of the LC stack," said Dr. Tichy. "So, as well as aesthetics, the instrument chassis had to be able to hold a certain amount of weight. The configuration was designed so that the entire LC stack could rest on top of the mass spectrometer."

Accessibility for service is also a result of the industrial design. "There were functional design aspects as well," stated Monty Benefiel, vice president and general manager of Agilent's Mass Spectrometry Division. "Instruments



stacked on top of the mass spec reduces the footprint, but we also needed to make sure that access was optimized for serviceability and maintenance," he explained. This design feature meets end-user needs. "You can service and maintain Ultivo without having to remove the LC from the top of the mass spec as everything is accessible from the side, the back or the front."

To make Ultivo so compact, extensive engineering was required, and a new approach to the core technology. "We set out to make it relatively the same size as our multi-sampler module within the LC stack. We held our ground on that, and kept engineering until we got it to fit in that form factor," said Dr. Shane. "The actual engineering was the greatest challenge because we were pushing new levels of performance in significantly smaller ion optics, thus causing us to rethink years of innovation in our current product line," he noted. Mr. Benefiel told *IBO*, "Reducing the size by 70% while being able to deliver the same or better analytical performance was a challenge—it required innovation. The intellectual property that we were able to generate as a result of doing this is pretty significant."

As Dr. Tichy explained, the innovations were extensive. "From a technical standpoint, customers told us that they needed to be able to perform more analyses, more efficiently, with less operator intervention at lower limits of quantitation," he told IBO. "Some of the Ultivo innovations are the patented Cyclone Ion Guide that ensures greater ion transfer emission efficiency, leading to optimized sensitivity and reproducible results; the state-of-the-art Vortex Collision Cell that provides consistent mass fragmentation while efficiently transmitting fragment ions at the fastest current rates; a novel virtual pre-filter at the entrance and exit of the resolving quadrupoles that delivers maximum ion transmission while allowing for quicker positive/negative and faster MRMs; the new VacShield that allows ventless ion injector exchange capabilities that increase customer uptime; and an easy-change door assembly that allows the customer to replace the electron multiplier quickly without de-stacking the instruments." Each new feature had to be engineered for a reduction in size. The quadruople design made use of a new shape to make it shorter. Also made shorter than traditional systems are the ion cyclone guide and collision cell. The pre and post filters are thinner, also saving space.

In designing the system to be so compact, manufacturing innovation was also required. "Critical in our ability to shrink the size of the instrument, was manufacturing capabilities that are unique to Agilent," noted Mr. Benefiel. "When you start to reduce the size, you need also to consider the complexity of miniaturization, as well as tolerances to ensuring reproducibility. We invested significantly to ensure we were able to address those aspects."

Silver Award

Shimadzu's benchtop linear MALDI-8020 MS system is this year's winner of the Silver Award. Like the Ultivo, the MALDI-8020 reinvents the user experience through a significantly reduced footprint for its technology. It also employs a unique shape that incorporates the traditional flight tube in such a way to enhance the users' perception of the compact size. Clean lines and the front vertical black stripe serve to provide a user friendly appearance and guide user interaction.





Shimadzu MALDI-8020

The MALDI-8020 measures 3.5 ft (1,055 mm) x 1.5 ft (450 mm) x 2.4 in (745 mm) and weighs 190 lb (86 kg).

The MALDI-8020's industrial design was aimed at improving the user experience. "The smaller footprint allows use in more laboratories and the easier operational aspects allow more people, from students to experienced researchers, to operate the system comfortably," explained Takeshi Fujita, manager at Shimadzu. The design also had to address a wide range of users and labs. "Together with these software packages, the system offers a walk-up solution for automated MALDI analysis which can be operated by non-expert users, making MALDI-TOF amenable to virtually any laboratory," he said. The system's target markets include clinical labs and academia.

Besides size, the MALDI-8020's design increases utilization by providing the user with installation options. "Laboratories often have to contend with space limitations, which necessitate the need for smaller but still powerful instruments," explained Dr. Fujita. The design also improves usability through its shape. "It can be installed at any orientation, diagonally or vertically, according to the customer's laboratory, enabling more installation flexibility," he said.

Other space saving features are integral to the design, allowing the system to be pushed against a wall. "[T]he backpanel position for the power cable or communication cable is recessed from the actual back position of the instrument by approximately 70 mm [2.75 in]," noted Dr. Fujita. "This recession keeps enough space for cable connector height and cable bending, or fan intake. The warmed air inside is ventilated efficiently from the outlet fan located in the chimney."

Besides the functionality embedded in the physical design, the visual attributes can contribute to an overall perception of the MALDI-8020 as small but also high quality. "From an aesthetic standpoint, the actual machined aluminium door was used to appeal to users for luxury and real texture," noted Dr. Fujita. This design feature was integrated to create unified appearance. "For the flight tube cover/chimney cover, the aluminium extrusion was used."

In addition, the MALDI-8020's external features enhance ease of operation and ergonomics. "Beyond the space issue, another goal was to make the system easier to use," said Dr. Fujita. "With this in mind, the MALDI-8020 incorporates a LED indicator that shows the instrument's status. This indicator is located at the same height point as a user's eyes when sitting for optimum visibility." The position of the sample "door" is optimized for a user who is either sitting or standing.

Interacting with the instrument is also made simpler and more intuitive by the door. "Additionally, a load-lock



chamber for sample plate exchange can be implemented quickly. The door for this sample exchange is designed to be opened or closed softly," explained Dr. Fujita. "The vacuum seal O-ring on the door can be compressed by the springs and magnets perfectly, not by user's force."

The benchtop system is a new addition to Shimadzu's MALDI line and thus its appearance can be used as a defining factor. "The return to a benchtop model, offered in addition to a range of floor standing models, has been an important point in our marketing efforts," explained Dr. Fujita. "[As well as] expanding our system offerings, it appeals to customers looking for a smaller system with a sleek exterior design, but one that also delivers reliable performance in a robust, easy-to-maintain platform."

Bronze Award

IBO's 2018 Bronze Award for instrument industrial design goes to Dolomite Bio's Nadia single-cell profiling system. The system's novel shape and modern design features, such as the flowing curves and smooth edges, distinguish it from traditional lab instrumentation, creating the perception of accessibility and emphasizing its advanced microfluidics technology. Most notably, the system is not a box, as it is seemingly "open" to the user, inviting interaction.



Nadia Single-Cell Profiling System

Dolomite Bio did not respond to IBO's request for an interview. System measurements were unavailable.

The Nadia's angled orientation, color placement and recessed plate holder intuitively communicate user touch points. Design features that enhance usability include a compact footprint, sample loading guide lights that flash different colors for each separate pipetting step and touchscreen interface. Application-specific cartridges are automatically recognized.

The compact design encases features for optimized functionality such as 4 stirrer drivers, 3 pressure pumps and temperature control. In addition, the design accommodates use with Dolomite Bio's Nadia Innovate for protocol development as the instrument's design enables easy connection of the Nadia Innovate to the Nadia Innovate cartridge.



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Clinical Lab Disruptors

Heading into the fall of 2018, the clinical lab industry continues to encounter and adjust to a number of foundational disruptions affecting reimbursement, technological changes and industry dynamics. IMV, a sister company of *IBO*'s publisher Strategic Directions International, commissioned a survey of over 100 clinical laboratory leaders to assess the impact of various disruptors. This article was prepared based on the survey and 10 interviews conducted on behalf of *IBO*.

The IMV survey highlights the impact of new molecular/genetic tests in centralized laboratories and Medicare Part B cuts as the most important disruptions to the clinical lab industry. Additional disruptions viewed as less impactful include (in descending order of importance from the IMV survey): point-of-care testing, industry consolidation including healthcare mega mergers, recent FDA laboratory test approvals, and Center for Medicare and Medicaid (CMS) National Coverage Decisions (NCDs) for next generation DNA and RNA sequencing (NGS).

From a volume perspective, there were 8.7 billion clinical lab tests completed in 2017.

According to the report "U.S. Clinical Laboratory Industry Forecast and Trends, 2018–2020" and the CMS CLIA Database, in 2017, the clinical laboratory industry in aggregate generated \$97 billion in revenue. Clinical labs are a mature industry growing at approximately 3% per annum. Within that top-line number, drug testing and molecular/genetic testing is growing at low double-digit rates, while anatomic pathology and Pap/HPV testing is exhibiting a modest decline.

From a volume perspective, there were 8.7 billion clinical lab tests completed in 2017. The largest segment remains hospital laboratories as just under half of the market. Independent laboratories, including LabCorp and Quest, constitute just over 30% of the volume.



Genetic and Molecular Testing

Molecular and genetic centralized testing labs historically focused on discrete clinical questions. For example, Genomic Health developed the OncoType Dx assay, which produces a Breast Recurrence Score (RS) for informing adjuvant chemotherapy decisions in node-negative, estrogen receptor (ER)+, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer assessed to be at intermediate risk of recurrence.

Increasingly, these laboratories are developing more complex tests that move beyond the technical capacities of many clinical laboratories. More importantly, they are increasingly relying on proprietary databases—manifested in reference populations—to inform treatment decisions in a wide range of diseases areas and therapeutics. Therefore, the centralized laboratories are the only providers that can deploy their proprietary reference populations, driving volume more than access to the technology, cost or other factors.

The IMV survey of clinical laboratories indicates that less than half of clinical labs are sending out to centralized laboratories today.

Cancer treatment decision support is an example of volume migrating to centralized laboratories. Some of the earliest approved cancer immunotherapies—the hottest area in cancer therapeutics today—were supported by an IHC screen that could be performed in the majority of clinical laboratories.

As immunotherapy expands and providers look for better predictors of therapeutic response, the diagnostic techniques are migrating to more complex assays, such as tumor mutational burden (TMB), microsatellite instability (MSI) and RNA gene expression. These assays are typically beyond the capacity of most laboratories, leading to more send-outs to centralized labs such as Foundation Medicine (Roche), Caris Life Sciences, OmniSeq and Tempus.

The IMV survey of clinical laboratories indicated that less than half of clinical labs are sending out to centralized laboratories today. Of the respondents that indicated they are currently sending out to centralized labs, over half of those respondents expect the volume they send out to increase over the next two years. Taken together, it appears there are opportunities for centralized laboratories to increase their volume within existing accounts and add new accounts over the next two years.

Medicare Part B

The second most important disruption as selected by the IMV survey is Medicare Part B cuts for laboratory testing. According to Lale White, CEO of Xifin, Medicare Part B cuts will be the most disruptive financial event in three decades for the clinical laboratory testing market.

The most likely canary in the coal mine for these cuts are likely to be nursing home laboratories. Medicare Part B lab tests make up 40%–80% of total revenue for most nursing home laboratories. Most nursing home labs or skilled nursing facilities operate with net profit margins of 2%– 4%, and the implied Medicare Part B cuts are likely to take some percentage of these labs into financial loss. According to David Nichols, president and founder of the Nichols Management Group, "CMS could create a real hole where labs cannot operate."

The IMV survey asked clinical laboratory leaders what they intended to do to adjust to Medicare Part B cuts. Only 15% of respondents indicated they plan no changes. Sixty-four percent of respondents indicated that they plan to explore new technologies that will help them reduce costs. Forty-eight percent indicated that they plan to renegotiate supplier agreements for instruments and reagents. Many labs will be executing on multiple tactics to adjust to the new reimbursement reality.

For further information, including accompanying slides, please visit <u>Clinical Disruptors</u>.



HPLC 2018: PAT, Pot, Performance and Potential

The 47th International Symposium on High Performance Liquid Phase Separations and Related Techniques was held at the Marriott Wardman Park in Washington, DC, from July 29th to August 2nd. The conference hosted 870 attendees from 34 countries and 203 talks.

New Products

While the scientific program formed the heart of the meeting, there was also activity at the booths of the exhibition hall. Several new products—including instruments, columns and consumables—were introduced. The most prominent new products in the exhibition were from Shimadzu and Activated Research Company (ARC). Shimadzu introduced the Nexera Bio, a UHPLC system designed specifically for biomolecule analysis. In the past, traditional HPLC has been unsuitable for protein analysis, due to adsorption onto stainless steel surfaces and the high salt condition in the mobile phase that causes corrosion. Nexera Bio tackles that problem by utilizing metal-free components for its wetted surface, joining other similar products on the market for these challenging samples. The new system features a carbon-coated pump head to prevent solvent contamination due to surface activity. It also has a ceramic injection needle to minimize sample carryover. Shimadzu launched Nexera Bio a week before HPLC 2018, and it is now ready to be shipped in the US.

ARC introduced a new detector for HPLC, the new Solvere Carbon Selective Detector, which utilizes flame ionization technology. Usually associated with GC detectors, ARC has modified the technology for use in HPLC. With its proprietary ActiveDiffusion technology, the detector system removes the solvent from the column effluent, and the remaining carbon analytes are then transferred into the FID for detection. The Solvere Carbon Selective Detector will be ready for shipment by October.

Technical Sessions

In addition to new products introduced in the exhibit hall, there were numerous technical sessions during the four-day conference. The sessions covered breakthrough technologies, applications and improvements of HPLC and related analytical techniques. Common trends observed among the sessions include HPLC applications in biomolecule analysis, online HPLC for pharmaceutical Process Analytical Technology (PAT) applications, multiple-dimension HPLC, chiral molecule analysis, performance-improvement techniques, and cannabis and drug testing applications.

One well-attended session relating to PAT, presented by Eli Lilly and Company, showcased the company's in-house developed solution for automated process sampling, sample preparation and online chromatography. They indicated that by utilizing a mobile dilution cart with two valves between the sample preparation and process lines, PAT data management produced live chromatographic data on pharmaceutical production processes, facilitating real-time processing decisions. Other sessions presented online chromatography applications in continuous manufacturing of pharmaceuticals.

Several sessions covered many aspects of multi-dimensional HPLC. Building upon two-dimensional HPLC technology, which was was initially employed to characterize unknown peaks and identify peak purity, 4D LC/MS is now possible, as presented by Robert Kopf, PhD, from Roche. His experiment on monoclonal antibody analysis using 4D LC/MS showed improvements through online reduction and digestion of fractionated peaks, which resulted in an efficiency gain of more than 80%. Despite its powerful analyzing power, method development for multiple dimensional analysis remains costly and time consuming, due to the intricate setup and difficulty in optimizing running conditions. Bob W.J. Pirok, PhD, from the University of Amsterdam suggested the employment of artificial intelligence software to provide faster 2D HPLC method development based on data from past chromatographic data and retention patterns.

A presentation from Genentech illustrated the advantages of using size exclusion chromatography as the first chromatographic method, as it provides a useful separation with minimal chemical effects on the analytes of interest, which can then be followed by a second technique. This strategy was discussed in the context of new



therapeutic modalities that are beginning to cross the boundaries of small molecule and large molecule, which require new tools and collaborative hybrid teams in order to properly characterize. While 2D separation techniques were clearly a strong focus of development, Sebastiaan Eeltink, PhD, of the Vrije Universiteit Brussel showed the current state of his lab's ongoing research into developing microfluidic devices for 3D separations.

Enantiomeric separation of chiral molecules was another big topic at HPLC 2018, as several presenters covered the subject in the technical sessions. Erik L. Regalado, PhD, from Merck presented on the general trend towards a universal chromatographic method in the pharmaceutical industry. Ultrafast chiral chromatography is one of the most heavily researched areas in the industry, as more than half of available drugs are chiral with multiple chiral centers. Genentech has also tapped into this field with their rapid chiral compound separations with multiple heart-cutting 2D HPLC. The first dimension analyzes achiral compounds with six columns in parallel, while the second dimension further separates the chiral compounds found in the first dimension.

HPLC performance improvements were also a popular topic at the show, covering various aspects from throughput to stationary phase architecture. Fabrice Gritti, PhD, from Waters discussed the dispersion effect caused by column frits in high-throughput gradient LC and suggested a redesign of packed column frits to improve peak capacity.

Adam Socia, PhD, from Merck presented on techniques for consistent retention time in drug manufacturing. Interactions between the stationary phase and SDS (sodium dodecyl sulfate) or other excipients usually cause a shift in retention times. A suggested solution to this problem is to increase the pH of the mobile phase to minimize such interactions. Another session by Roche studied the improvement of monoclonal antibody separation using large pore superficially porous particles and ultra-high-performance hydrophobic interaction chromatography.

Last but not least, the use of HPLC in cannabis testing was covered in several sessions, as this particular application has been growing rapidly in recent years. There was a specific short course dedicated to cannabis analysis at the conference. In one of the sessions, Avinash Dalmia, PhD, from PerkinElmer presented a study of pesticide residue analysis in cannabis as regulated by California and Oregon. Among the largest cannabis markets in the US, these two states have been providing the most rigorous standards and detection limits. Analyzing pesticide residue at 100nppb to fulfill California's state limit is possible using LC/MS coupled with an APCI source. Analysis of nicotine and illegal drugs were also covered in other sessions by utilizing chiral separations and multiple injection methods.

In 2019, two HPLC conferences are scheduled by the organizers: Milan, Italy, in June and Kyoto, Japan, in December. The following year, HPLC 2020 will be held in San Diego, California.

AACC 2018: Clinical and Diagnostic Companies Stress Integration and Partnerships

The American Association of Clinical Chemistry (AACC) hosted its 70th Annual Scientific Meeting & Clinical Lab Expo in Chicago, Illinois, from July 29 to August 2. According to preliminary figures provided by conference organizers, attendance declined 6.5% from last year's event held in San Diego, California, but increased 2.6% from the 2014 conference, the last time the even was held in Chicago. The conference marked the largest number of attendees at the annual meeting when it has been held outside of California. The total number of exhibitors increased year over year by 3.8% to 819. The 71st Annual AACC Annual Scientific Meeting and Laboratory Expo will be held August 4–9, 2019 in Anaheim, California.

The exhibit hall was a sight to see as clinical lab professionals from around the world came together to discover the latest advances in clinical diagnostics and gain insight into the future of lab medicine and translational research. New products were introduced by many companies, including Fujirebio and Roche. Roche introduced several additions to its cobas product line, which featured the 6800/8800 systems and m 511 Hematology Analyzer, both of which showcase fully integrated and automated solutions in core labs and hematology, respectively. Fujirebio launched the LUMIPULSE G1200, a mid-sized, fully automated immunoassay instrument using chemiluminescent enzyme immunoassay technology, that is described as user friendly and designed to simplify lab workflows.

As a way to continue to pave the way for MS in clinical settings, SCIEX Diagnostics unveiled its Topaz Prep Station,



an automated workstation for labs regularly processing a high volume of samples. The new sample preparation workstation works with the Topaz LC-MS/MS System, which designed to be easy enough to operate for those new to MS. Michael Jarvis, technical marketing manager, Clinical, at SCIEX, discussed the importance of keeping the clinical lab community abreast with the benefits of MS in the clinical setting. "It's our job to educate and train the [clinical lab] community on new advancements in technology," he said. Mr. Jarvis further detailed SCIEX's commitment to engage the clinical diagnostics community through the SCIEX University, SCIEX's education portal that offers support, training and continuing education on LC/MS and LC/MS/MS.

On the other side of the exhibit hall, Sysmex celebrated 50 years serving labs with products and solutions in hematology, urinalysis and flow cytometry. Sysmex showcased its ability to providing personalized, convenient lab education through the VIRT (Virtual Instructor-Led Training) training, which is offered as a free and unlimited educational resource. Designed for labs, students are trained by Sysmex's technical professionals through streaming HD instructional videos on lab technology and workflows. Stephanie Post, senior director of Marketing Communications, Commercial Operations, Training & Development Program Management, for Sysmex America informed *IBO* of the latest developments in customer engagement. She cited the company's BeyondCare Quality Monitor (BCQM), designed to proactively detect any issues and alert customers when potential problems with their hematology analyzers. The BCQM can also place a service call on the customer's behalf if issues are detected.

In an interview with Porex, a supplier of porous polymers used across a variety of areas in clinical sciences, including sample prep for IVD, molecular and clinical diagnostics, liquid handling and microfluidic applications, *IBO* learned more about their newly unveiled *Collection to Detection* solutions. Maria DeCapua, vice president of Marketing and BioMedical Sciences, detailed the importance of sample integrity and knowing if a sample is contaminated on the front end, before analysis. Precision is especially crucial when the result of the test could mean the difference between the diagnosis of a terminal or benign illness. Ms. DeCapua explained that, in labs, when a sample is found contaminated after it is tested, it can damage a lab's operation, and if enough contaminated samples are discovered, a lab's credibility. On July 31, Porex revealed results from an independent study that demonstrated Porex's diagnostics materials hold clinical compatibility for up to seven days. She emphasized that in the face of challenges such as decreasing sample sizes, clean samples void of contaminants are integral to reaching accurate conclusions or diagnoses.

Mission Acquisition: Collaboration and Comprehensive Portfolios

IBO also had the opportunity to interview several clinical diagnostics executives on the subject of integration and the latest business developments and acquisitions.

In an interview with PerkinElmer and EUROIMMUN, which PerkinElmer acquired in 2017 (see **IBO** 6/30/17), Dennis Flannelly, PerkinElmer's vice president of Diagnostics, along with EUROIMMUN's CEO Hamid Erfanian and Wolfgang Schlumberger, PhD, vice chairman of EUROIMMUN Medizinische Labordiagnostika, discussed the company's enriched diagnostics portfolio as a result of the integration of EUROIMMUN as well as the purchase of Vanadis Diagnostics in 2016 (see **IBO** 4/15/16).

EUROIMMUN specializes in diagnostic products for autoimmune diagnostics, infectious serology, allergy diagnostics, antigen detection, molecular genetic diagnostics and automation. The company offers tests to diagnose a vast array of diseases, infections, bacteria, viruses and parasites, along with emerging viruses (i.e., Zika) using its ELISA products and systems, such as the EUROLab Workstation, which provides a fully automated processing of ELISA.

According to PerkinElmer, EUROIMMUN's portfolio EUROIMMUN is designed to provide its customers with what they need on a custom basis, with menus of tests based entirely on the needs and demands of a given laboratory. As Mr. Erfanian stated, "Laboratories are looking to have partners who understand what they need. We look to provide the customer with a personalized service."

Vanadis Diagnostics, a provider of non-invasive prenatal testing (NIPT) products, endeavors to make accurate NIPT solutions accessible for all women and simplify NIPT through the use of its proprietary enzymatic sample preparation tools. This sample preparation technique creates and quantifies fluorescent DNA, eliminating the steps involving complex DNA sequencing or microarrays. Vanadis' NIPT platform also offers a complete solution and processes the entire test (sample to result) without the need for extensive technician supervision.



In an interview with *IBO*, Gus Salem, group president of the Scientific Fluidics & Optics Group at IDEX Health & Sciences, discussed the company's latest business developments, including the acquisition of Finger Lakes Instrumentation (FLI), announced on July 25, just days before AACC. FLI provides low-noise, cooled CCD and high-speed, high-sensitivity, cooled CMOS cameras for scientific and astronomical imaging, complementing the existing IDEX portfolio of solutions for the life sciences and analytical instrumentation markets. As Mr. Salem told *IBO*, "FLI is a great strategic fit in terms of our [IDEX's] product portfolio." In another acquisition to complement an existing product line, last year, IDEX acquired microfluidics company thinXXS Microtechnology, a microfluidic consumables business serving the life sciences, point-of-care and veterinary markets.

Discussing these acquisitions, Mr. Salem noted that the range of industry applications that exist for technological innovations in the IDEX product portfolio uncover additional possibilities in fluidics and microfluidics, and FLI opens doors as a supplier of solutions used in furthering research in astronomy. As the clinical diagnostics and instrumentation market dynamic shifts to servicing industry partners in an advisory or consultative capacity, an increased focus on partnering and collaboration is what will ultimately drive IDEX, he explained and its extensive network of solutions, products, brands and industry partners forward.

In the press conference hosted by Roche Diagnostics, Roche Diagnostics CEO Ron Diggelmann, Jack Phillips, the president and CEO of Roche Diagnostics North America, and Justin Bruek of NorthShore University Health System spoke in depth about health care information management. Throughout the briefing, Roche cited several acquisitions and partnerships, conveying that collaboration is an integral part of their strategy for the future. The acquisitions and partnerships were depicted as part of a continuum involving multiple variables: research, laboratory, clinical settings and payers.

The company's recent acquisitions of Foundation Medicine, Flatiron Health, Viewics and Navify, as well as its partnership with GE Healthcare were noteworthy mentions throughout the meeting. One commonality among the acquired entities is that they generate and house a tremendous amount of patient health information and data that can be used to overcome challenges in the gray area of reimbursement to solving for unmet needs in cancer diagnostics and personalized medicine. With these acquisitions and partnerships comes the challenge of managing data, and leveraging that information to make better clinical decisions and yield improved patient outcomes. The partnership with GE conveys the commitment to this effort by developing a clinical decision support platform that will integrate in-vivo data from medical imaging provided by GE and Roche's in-vitro data from their biomarkers, genomics and sequencing and tissue pathology products. As Mr. Phillips stated in the session, "Our intent is to provide tools and solutions to make sense of all of this [data]."

Lab Efficiencies at AACC that Cannot Be Seen or Heard

Many of the companies at the AACC Clinical Lab Expo held in Chicago were showcasing new tests added to workflows and production lines, but few were thinking about launching new advancements that make instruments better for the environment or better for the life of the laboratory.

Thermo Fisher Scientific is certainly in the hunt to move from research to routine, but also has been working on a top-to-bottom business review of how to make products that are more efficient and sustainable. "There is a lot of noise in a lab environment and we have been working to reduce that noise to levels that are barely noticeable," said William "Bill" McMahon, president of Laboratory Equipment while demonstrating a TSX Series under the counter 35 decibel lab refrigeration unit at AACC.

Besides noise reduction—to the level its next generation of products. The target energy reduction footprint is between 35%–50%, which will not only be better for the environment but also a lower cost to operate for the lab.Specifications for the <u>US EPA ENERGY STAR program for laboratory refrigerator and freezers</u> was presented starting in December 2016 and published this May.



Micromeritics Buys Microreactor Company

Norcross, GA 8/1/18—Micromeritics Instruments, which provides scientific instrumentation for materials characterization, has purchased Process Integral Development (PID Eng & Tech) for an undisclosed amount. Based in Spain, PID Eng & Tech develops and sells modular lab microreactors for measuring catalytic activity and studying chemical reaction yield and kinetics. It also supplies pilot plant reactors and other lab equipment. "We have been distribution partners for PID Eng & Tech for several years," commented Micromeritics President Preston Hendrix. "This deepens our portfolio of products and services for the characterization of catalysts, where we are already active and have a large global base of customers. Additionally, PID Eng & Tech adds breadth to our organization by addressing adjacent workplaces within the markets we serve with their pilot plant, custom equipment and services offering."

This is Micromeritics' second acquisition this year (see IBO 6/30/18). Last year, the company completed a refinancing agreement of its credit facilities providing it with new financial flexibility, according to TM Capital. Micromeritics' chemisorption (chemical adsorption) and physical adsorption instruments are used to test catalytic materials. PID Eng & Tech's installed base includes over 400 units of its Microactivity Effi system, according to the company's website.

Cell Suppliers Merge

Memphis, TN and Bothel, WA 8/7/18—Key Biologics, a supplier of human immune cells as raw materials, has merged with Astarte Biologics, a provider of characterized immune cells and reagents. Financial details were not disclosed. Ampersand Capital Partners has made an investment in the new company. "Our partnership with Key represents a highly complementary union of cell collection with downstream processing, characterization, and model and assay development capabilities," stated Astarte Biologics founder and CEO Dr. Anne Lodge.

Both companies provide cell and blood products. In addition, Astarte Biologics provides research antigens, reagent kits and services for immunology and inflammation applications. The combination creates a supplier of raw materials and downstream products for research, scale-up and therapeutic applications, The combined company plans to open a new facility in Boston, Massachusetts, in 2019.

LEWA Divests Chromatography Systems Business

Kyoto, Japan and Holliston, MA 8/10/18—YMC, which provides lab and process chromatography solutions to the pharmaceutical market, has entered into an agreement to acquire LEWA-Nikkiso America's pharmaceutical systems business from LEWA, a division of Nikkiso. LEWA-Nikkiso America provides production-scale chromatography systems, including the EcoPrime LPLC, HPLC, simulated moving bed (SMB) and continuous chromatography systems. Financial details were not disclosed. "Through this acquisition, we will create the first Americas-based manufacturing for YMC," stated YMC CEO Ryuji Yamamura. "In addition, we believe acquiring LEWA's extensive experience in precision purification systems and automation for GMP-scale equipment can unlock YMC's mostly untapped growth potential for systems outside of Asia." LEWA will continue to supply pumps for the systems. The deal is expected to close in the fourth quarter.

The purchase adds process-scale chromatography to YMC's current chromatography product line, which includes columns as well as HPLC and preparative LC systems. The deal includes LEWA-Nikkiso America's agreements with ChromaCon and Bayer Technology Services, related to the companies' SMB technologies. YMC stated that the management team and staff of the acquired business will remain in place. YMC also stated that LEWA was exiting the business due its view that the business needed to add complementary products, such as columns, in order to succeed. The acquired business is based in Devens, Massachusetts.



Second Quarter Results: Illumina, PerkinElmer, Thermo Fisher Scientific, Waters

Illumina Consumables Revenue Exceeds Expectations

Illumina Q2 FY18					
	Rev. (\$M)	Chg.	% of Rev.		
Consumables	\$540	34.3%	65%		
Instrument	\$127	-6.6%	15%		
Other Products	\$6	20.0%	1%		
Service & Other	\$157	31.9%	15%		

Click to enlarge

Illumina second quarter revenues grew 25.4%, including two percentage points growth from currency effects. (See \underline{IBO} 7/31/18.) Illumina's strong second quarter revenues were led by faster-than-expected sales growth for sequencing consumables.

Illumina Q2 FY18 Rev. Chg.					
	Sequencing	Microarrays			
Consumables	34.6%	32.8%			
Instrument	-5.4%	-33.3%			
Other Products	20.0%	0.0%			
Service & Other	37.7%	21.4%			

Click to enlarge

Sales of sequencing consumables grew 34.6% and were up 31% excluding early stocking by Chinese customers in response to tariffs. Sales of consumables for high-throughput sequencers (NovaSeq, HiSeq) grew over 35%, while sales for mid-throughput sequencers (NextSeq) consumables rose over 50%. Sales of low-throughput sequencers (MiniSeq, MiSeq, iSeq) consumables also increased, totaling over 10% of sequencing consumables revenue. In addition, impacting consumables sales, library preparation revenue rose 25% to make up close to 15% of the sequencing consumables business.

Illumina Adjusted Operating Results Q2 2018					
Adj. Op. Profit (\$M) Chg. Adj. Op. Margin Chg. (pps)					
\$236	60.5%	28.4%	6.2%		

Click to enlarge

Although sequencer revenue declined year over year, sales were up 8% sequentially. More than 200 separate labs now have NovaSeqs installed. The company expects to ship 330–350 NovaSeqs in 2018. Half of low-throughput sequencer sales were to new-to-sequencing customers. As for sequencing services revenue, it was approximately evenly divided between maintenance contracts and sequencing services.



	Illumina Q2 201	8
	% of Rev.	Chg.
US	54%	19.0%
Europe	25%	35.2%
Greater China	14%	37.2%
Asia Pacific	7%	19.6%
Other	3%	42.1%

Click to enlarge

The company raised its revenue growth rate guidance for the year from 15%-16% to 20%, in part due to demand for NovaSeq consumables. Second quarter revenues are expected to be flat or up modestly.

PerkinElmer Reports Strong Organic Growth

PerkinElmer Q2 2018						
	Rev. (\$M)	% of Rev.	Chg.	Currency	Acq./ Div.	Org. Growth
Total Company	\$703.4		28.6%	2%	16%	11%
Discovery & Analytical Solutions	\$430.6	61%	12.4%	2%	0%	10%
Diagnostics	\$272.7	39%	66.5%	3%	53%	11%

Click to enlarge

PerkinElmer's second quarter sales grew double-digit organically for the company as a whole company and each of its two divisions (see <u>Bottom Line</u>). Product and Service revenues rose 39.6% and 8.2% to make up 70% and 30% of sales, respectively. All figures below are given on an organic basis.

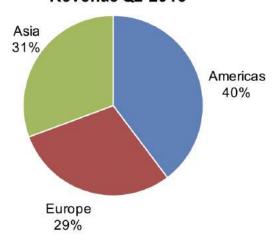
PerkinElmer Adjusted Operating Results Q2 2018							
	Adj. Op. Profit (\$M)	Chg.	Adj. Op. Margin	Chg. (pps)			
Total Company	\$138.3	41.4%	11.0%	178			
Discovery & Analytical Solutions	\$76.4	20.1%	17.7%	114			
Diagnostics	\$77.2	60.5%	28.3%	-104			

Click to enlarge

Geographically, Asian and European sales each grew double digits. American sales rose high single digits. China and India both recorded double-digit sales growth.



PerkinElmer Discovery & Analytical Solutions Revenue Q2 2918

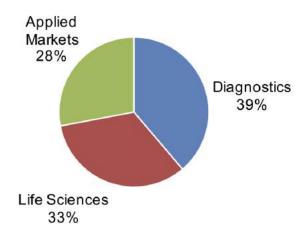


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Discovery & Analytical Solutions sales were led by imaging, high-content screening, analytical instruments, informatics and service sales. Sales to the life science end-market were up double digit, while sales to applied end-market rose high single digits. Sales to applied markets were driven by the industrial and Asian food testing end-markets, with sales for each up high in the single digits.

In the Diagnostic segment, reproductive health sales grew high single digits. Sales for genomics and immunodiagnostics each grew double digits. The genomics business is expected to post \$50 million in revenues by 2020. Sales for Tulip Diagnostics rose in high teens.

PerkinElmer Q2 2018 Rev. by End-market



Click to enlarge

The company raised its full-year organic revenues growth guidance from 5% to 6%, including 7% growth for core Diagnostic sales. EUROIMMUN is expected to add 1% to annual growth. Second quarter sales are anticipated to rise 10% organically, or 29% including 16% growth from acquisitions.

Broad-based Growth for Thermo Fisher Scientific



Thermo Fisher Scientific Q2 2018						
	Rev. (\$M)	Chg.	% of Total Rev.	% Organic Chg.		
Total Company	\$6,078	21.8%		8%		
Life Sciences Solutions	\$1,569	11.7%	25%	9%		
Analytical Instruments	\$1,311	12.4%	21%	9%		
Specialty Diagnostics	\$932	8.1%	15%	5%		
Laboratory Products & Services	\$2,550	42.3%	40%	9%		

Click to enlarge

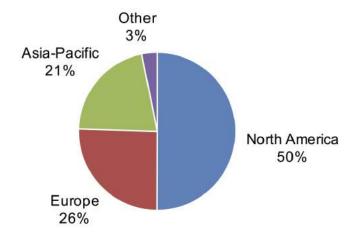
Reported double-digit second quarter revenue growth for Thermo Fisher Scientific included 12% acquisitions net of divestitures and a 2% benefit from currency. (See <u>IBO 7/31/18</u>.) The company reported broad-based growth, including strength in its chromatography, MS, clinical trial services and the bioprocess businesses.

	Adj. Op. Profit (\$M)	Chg.	Adj. Op. Margin	Chg. (bps)
Total Company	\$1,403	21.1%	23.1%	-14
Life Sciences Solutions	\$522	16.5%	33.3%	138
Analytical Instruments	\$291	25.4%	22.2%	230
Specialty Diagnostics	\$253	8.1%	27.1%	0
Laboratory Products & Services	\$337	37.6%	13.2%	-46

Click to enlarge

Asia-Pacific and Rest of World led regional growth, with sales for each increasing in the low teens. Within Asia-Pacific sales, Chinese sales rose more than 26% to \$648 million. European sales rose high-single digits, while North American revenue climbed mid-single digits. Within North America, US sales grew 17.3% to \$2.9 billion.

Thermo Fisher Scientific Rev. Q2 2018

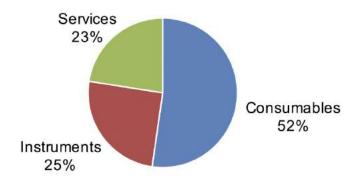


Click to enlarge

Sales to the biotech and pharmaceutical end-markets increased in the mid-teens, while academic and government revenue rose high single digits. Sales to the industrial and applied end-market as well as diagnostics and healthcare both grew mid-single digits.



Thermo Fisher Scientific Revenue Type Q1 FY18



Click to enlarge

The company narrowed its full-year revenue guidance to 13%-14% growth, including 6% organic growth. The company attributed the increase to higher organic growth, Patheon's strong performance and greater negative impact from currency.

Service Revenue Up Double Digits for Waters

Waters Q2 FY18						
	Rev. (\$M)	Chg.	% of Total Rev.			
Waters	\$596.2	6.8%				
Waters Div.	\$527.3	5.9%	88%			
Instrument Systems	\$239.9	0.6%	40%			
Chemistry	\$99.1	9.1%	17%			
Service	\$188.2	11.8%	32%			
TA	\$68.9	14.0%	12%			
Instrument Systems	\$49.8	14.6%	8%			
Service	\$19.1	12.3%	3%			

Click to enlarge

Waters second quarter revenues grew 5% in constant currency, as constant currency sales for the Waters Division and TA Instruments increased 4% and 12%, respectively. (See **IBO** 7/31/18.) All figures below are in constant currency. Service sales led growth, rising 9% in the second quarter, followed by chemistry sales, with a 6% increase and a 2% increase in instrument sales.

Waters Q2 2018					
Adj. Op. Profit (\$M) Chg. Adj. Op. Margin Chg. (bps					
\$182.0	8.8%	30.5%	56		

Click to enlarge

Pharmaceutical end-market growth was led by China's double-digit sales growth. However, sales in developed markets declined moderately due to slower demand from large pharma. After a weak first quarter, pharmaceutical sales in India rose sequentially. TA Instrument and Waters Division chemicals sector sales were the standouts among industrial markets. Academic and government sales were strong, with the exception of the biomedical



research sector.

Waters Q2 FY18							
	Rev. (\$M)	Chg.	Constant Curr. Chg.	% of Rev.			
Pharmaceutical	\$338.4	5.9%	4%	57%			
Industrial	\$183.7	5.2%	3%	31%			
Govt. & Academic	\$74.2	15.8%	13%	12%			

Click to enlarge

On a geographic basis, Chinese demand rose 16.6% to make up 18% of total Waters sales. Although total company sales for India were flat, the company noted a sequential increase in pharmaceutical sales in the country. US sales declined 1.8%, due to slower sales of biomedical LC/MS systems to pharmaceutical and industrial markets.

Waters Q2 FY18							
	Rev. (\$M)	Chg.	Constant Curr. Chg.	% of Rev.			
Asia	\$236.9	9.8%	8%	40%			
Americas	\$198.1	0.8%	1%	33%			
Europe	\$161.2	10.4%	5%	27%			

Click to enlarge

By product line, MS sales were led by tandem quadrupole systems, while demand for high-resolution systems, which make up about 25% of MS sales, were softer. Stand-alone chromatography revenue was also healthy

Waters forecast third quarter organic sales to increase 4%-6%, with currency subtracting 1%-2% growth. The company maintained its annual sales guidance of 4%-6% growth excluding currency effects.

Fast Protein Liquid Chromatography

Fast protein LC (FPLC) is a specialized form of HPLC that is designed for biomolecule purification and separation. The essential difference between HPLC and FPLC lies in the operating conditions. Protein structure cannot survive harsh conditions such as high pressure, high temperature, extreme pH or solvents typically used for HPLC.

As FPLC is designed to separate proteins, it utilizes lower pressure compared to regular HPLC and facilitates low-temperature operation. In place of solvents, FPLC uses buffers as its mobile phase in order to provide the optimum environment for protein separation.

Compared with HPLC and UHPLC, where pressures can usually go as high as 150 MPa, FPLC operates at lower pressures of 3–5 MPa. The lower pressure prevents the disintegration of protein structure while the sample is flowing through the column. Along with the low pressure, FPLC employs a higher flow rate of up to 100 mL/min to facilitate a larger sample volume.

In addition, proteins prefer low temperature to maintain their structure; the working temperature for proteins is usually around 4°C. Hence, FPLC instruments are often placed in a cold room with high humidity, and the components for FPLC need to have the durability to withstand this working environment.

Furthermore, the usage of buffers with high salt concentration to maintain protein structure would cause corrosion to stainless steel chromatography systems, and the metal ions from the stainless steel can interact with the protein



and disturb its structure. In order to prevent these issues, FPLC is usually built with biocompatible materials, such as polyether ether ketone (PEEK) ceramic, titanium or carbon coating.

In terms of columns, FPLC has different size and packing materials compared to regular HPLC. HPLC columns are typically packed with silica beads, which have small particle sizes for high-pressure applications, while FPLC columns employ polymers/resins with larger particle sizes. Resins for FPLC are not as pressure resistant as silica beads and tend to be more sensitive to air bubbles. As pressure resistance is not an issue for FPLC, FPLC columns are usually made from transparent and biocompatible glass. With transparent columns, users can visually check the columns for air bubbles and monitor the stationary-phase condition during separations. Typical column chemistries utilized in an FPLC system include size exclusion, ion exchange, affinity and hydrophobic interaction chromatography.

FPLC was initially used only for protein separations; however, the wide variety of buffer and resins available for this technique has broadened its applications. In recent years, FPLC has found uses in life science academic research, especially proteome research. Biotechnology and pharmaceutical companies also utilize FPLC to purify monoclonal antibodies for antibody drug conjugates and other biotherapeutic applications.

The global FPLC market was estimated to be over \$100 million in 2017, with a mid-single digit growth rate anticipated in 2018. The US and Europe led regional demand due to advanced life science research and a strong biotech and pharma sector in these regions. The Chinese government's heavy investments in building its biotech industry has also created a high potential for FPLC demand in the country.

Currently, only a handful of vendors offer FPLC systems. GE Healthcare has upgraded its AKTA FPLC into AKTA Pure, equipped with a flexible and automated protein purification system. Bio-Rad Laboratories offers several models of its NGC and BioLogic systems. Knauer also competes in the FPLC market with its extensive Azura product line. ChromaCon, a smaller vendor, offers an FPLC system with its Contichrom product line. Large manufacturers such as Agilent Technologies, Shimadzu and Waters provide at least one bio-inert option in their HPLC product lines.

Leading Vendors:

- GE Healthcare
- Bio-Rad Laboratories
- Knauer

Largest Market:

- Academia
- Biotechnology
- Pharmaceuticals

Instrument Cost:

• \$20,000-\$50,000

Government

At the end of last month, the US military's Defense Advanced Research Projects Agency (DARPA) stated it would make dozens of grants available, worth \$75 million in total, to scientists in the academic and industry sector as part of the new Electronics Resurgence Initiative. The Initiative's goal is to develop novel chip designs and materials, such as carbon nanotubes, to drive innovation in the silicon chip industry. Within the next few years, funding for the DARPA Initiative will reach \$300 million, totaling \$1.5 billion over five years.

The speed of chips is stagnant and new generations of chips are only 30% better in terms of energy efficiency. Over the past few decades, the limits of silicon as a chip material have been pushed, leaving fabricators nearing the



physical confines of how silicon can be utilized. A major issue with silicon chips is the lack of space, as electrons are restricted to parts of silicon that are only one hundred atoms wide, which requires complicated designs to ensure that the electrons do not leak.

Additionally, costs for the fabrication plants in which silicon chips are made are in the billions, making it difficult for more than a handful of companies to set up manufacturing facilities, which is also curbing innovation and competition in the field. Because of this, some companies are designing specialized chips that can only be used in specific applications, which has diminished their incentive to spend on pre-competitive basic R&D.

The DARPA Initiative hopes to address these issues and foster innovation, through studying different materials, methods and designs to create a new generation of chips.

Source: Science

Chemicals

The chemical industry had a robust 2017, with the global top 50 companies in the sector bringing in combined sales of \$851.0 billion, a 12.2% jump. This is a welcome reprieve from 2015 and 2016, in which the global top 50 companies reported declines in sales. The sales growth in 2017 is largely attributed to increasing oil prices as well as a healthy economy.

Not one company in the global top 50 lost money in 2017, and only 13 companies reported decreases in profit. Generally, combined profitability for the top 50 companies rose 14.4%, reaching \$108.6 billion. While the chemical industry is poised for another successful year, the threat of US-China tariffs could negatively affect the industry, specifically US petrochemical product manufacturers.

BASF topped the list of the global top 50 chemical companies, bringing in sales of \$69.2 billion in 2017, an 11.8% rise. DowDuPonte and Sinopec reported sales of \$62.5 billion and \$55.3 billion, respectively, while SABIC and Ineos had respective sales of \$37.6 billion and \$34.6 billion, rounding out the top 5.

In terms of capital spending, BASF spent \$3.8 billion, a 45.0% decrease, although the company was still the largest among the top 50 in capital spending. DowDuPont spent \$3.6 billion, a 6.2% decline. Sasol, Sinopec and ExxonMobil rounded out the top 5 with capital spending of \$3.6 billion, \$3.4 billion and \$3.3 billion, respectively.

Source: Chemical & Engineering News

Energy

Executives in the oil sector are setting their sights on building new multi-billion dollar liquefied natural gas (LNG) plants after a four-year lull in investments. Increasing oil prices and healthy demand from countries such as China and India indicate that the industry is ready for new LNG projects. A major turning point that facilitated this change was China's increase in LNG imports in recent years in order to fight pollution by reducing the use of coal.

Qatar is the largest LNG producer globally, and is making plans to increase its facilities by approximately 33% to be able to produce 100–108 million tonnes per annum (mtpa) by 2023–2024. Companies such as Exxon Mobil, Royal Dutch Shell, Total and ConocoPhillips are expected to collaborate on this Qatari project, as well as other long-term partners.

According to experts, the LNG market needs more than 200 mtpa of new supply until 2030, and expansions to liquefaction capacity are expected to sharply decline in late 2019 due to newly commissioned plants reaching their maximum capacity. The US is expected to be the greatest driver of growth.

Source: Reuters



China

Last fall, Beijing decreased the red tape involved in obtaining drug approvals, and the change is already producing results, with many patients in China now able to receive cutting edge medicines before they are introduced in the US. Companies such as AstraZeneca and Eli Lilly are bringing their therapeutics to pharmacies in Shanghai and Beijing nearly a year before they will be available in the US. Experts predict that within two decades China's health care market will be comparable, if not bigger, than the US's. This is largely due to the spike in medical insurance amongst Chinese citizens that began around 2016; as of 2017, nearly 1.2 billion Chinese are enrolled in public medical insurance.

China's FDA was known for its red tape-laden drug approval process, with the Administration itself stating that between 2001 and 2016, less than 33% of 433 new treatments that were approved in developed countries were available in China. But in October 2017, the Chinese FDA removed a criterion requiring companies to re-conduct all clinical drug trials in China before it approves the drugs. This move greatly changed the pharmaceutical industry, as now companies are able to simultaneously introduce drugs in China and the US. Since 2014, China's FDA has decreased the backlog number of drugs waiting for approval 78.9% to just four thousand left to greenlight.

Source: Bloomberg

Germany

As part of the new Framework Program for Research and Innovation, the German government is helping foster the microelectronics sector in Germany. Through this program, the government is also helping support the European Commission's Strategy for Micro- and Nanoelectronic Components and Systems, established in 2013. The Program targets small, medium and large companies in the microelectronics sector, as well as other related industries, to help further grow the semiconductor and IoT industry. The Federal Ministry of Education and Research is providing up to €400 million (\$455.3 million) for the Program through 2020.

Hardware, integrated circuits and sensors are some of the components that provide microelectronic chips with as many functionalities as possible. To continue innovation in this field, the Program lays out five strategic research goals: developing electronics systems equipped with a multitude of functionalities, such as network capability, reliability and energy efficiency, all while working towards further miniaturization of chips; creating new approaches in power electronics for efficient energy utilization; developing computer algorithms and simulations in order to design complex chips; developing new efficient chip manufacturing capabilities; and strengthening existing chipbased security.

Source: Federal Ministry of Education and Research

Japan

According to the latest R&D survey by Nikkei, 231 leading companies in Japan are poised to increase spending on R&D in the current fiscal year (through March 2019). Nearly 44% of respondents indicated they are planning record outlays, with the survey showing an expected rise of 4.5% in R&D spending by major Japanese companies to total ¥12.5 trillion (\$112 billion) in the current fiscal year.

Companies are largely investing in cutting edge technologies, such as artificial intelligence, to drive innovation, especially in the automotive sector, in which R&D spending will grow 6.4% to over \(\frac{4}{2}\).0 trillion (\(\frac{5}{3}\)6.2 billion). The basic materials sector is expected to increase R&D spending 6.5% and the machinery sector will see its R&D expenditures increase 9.9%. Mitsubishi Chemical expects to spend \(\frac{4}{1}\)60 billion (\(\frac{5}{1}\).4 billion), while Hitachi plans to



develop artificial intelligence and software to further bolster Lumada, the company's IoT platform, increasing its budget for innovation projects by more than 60% since 2015.

Automotive companies ranked as Japan's top R&D spenders, with companies such as Toyota, Honda and Nissan planning to invest record amounts into R&D this fiscal year to remain competitive with other global companies. Instead of keeping R&D in-house, many automotive companies are aiming to foster collaborations externally.

Source: Nikkei Asian Review

Broad-based Companies

Company Announcements

In August, **Becton, Dickinson** (BD) named Simon Campion as executive vice president of BD and president, BD Interventional segment, effective Sept. 4. He had been serving as worldwide president of BD's Surgery business.

Becton, Dickinson Biosciences' fiscal third quarter revenue grew 9.7% to \$314 million, up 6.8% on a currency-neutral basis. Biosciences sales were led by the research reagents and advanced bioprocessing businesses, as well as sales growth of newer instruments. On its quarterly conference call, the company announced a write down for the discontinuation of the BD CLiC system.

In August, **QIAGEN** signed a master collaboration agreement with Japanese clinical testing lab company **SRL**. The agreement will enable rapid implementation by SRL of QIAGEN's companion diagnostic workflows upon approval of the drugs and tests by Japan's **Pharmaceutical and Medical Devices Agency**. Initial projects involve QIAGEN companion diagnostics paired with new drugs under development in Japan for solid tumors and leukemia.

In the second quarter, **Teledyne Technologies**' Environmental Instrumentation revenue rose 10.9% to \$85.7 million, including \$5.3 million in **Scientific Systems** sales (see **IBO** 7/15/17). On its quarterly conference call, the company stated that its expects Environmental Instrumentation sales to grow 4%-4.5% organically for the year.

In August, **Merck KgaA** announced the retirement of Walter Galinat as a general partner of E. Merck KG and Executive Board member, effective September 30. As a member of the Executive Board of Merck KGaA, he is currently responsible for the Darmstadt site (global company headquarters), Environment, Health, Safety, Security and Quality (EQ), Procurement and In-house Consulting.

PerkinElmer disclosed in a quarterly financial filing that it acquired **Shanghai Spectrum International** (see **IBO** 5/31/18) for \$15.4 million in cash.

Sales and Orders of Note

In June, **Ireland's Queen's University Belfast** announced the opening of a laboratory at the School of Chemistry and Chemical Engineering equipped with 18 instruments from **Agilent Technologies**, including MS systems, LCs and GCs, and molecular spectroscopy systems.

Life Science Consumables

Company Announcements

In July, **SYGNIS** changed its name to **Expedeon**.

In August, **Maravai Life Sciences** completed a new debt financing, which finances its existing debt at a lower interest rate and provides Maravai access to an additional \$50 million of capital.



Gene-based Consumables

Company Announcements

In June, the **US Patent and Trademark Office** granted Dr. Emmanuelle Charpentier, co-founder of **ERS Genomics**, the **University of California** and **University of Vienna**, their first US patent with claims covering the use of CRISPR/Cas9 technology for gene editing. The patent covers the use of an optimized guide RNA format in all environments including human cells. The Office deemed the claims in this patent unrelated to the ongoing interference appeal between the Charpentier/UC/Vienna group and the **Broad Institute/MIT/Harvard** group.

Merck Life Science announced in June that **Tongji University** in Shanghai, China, has joined the company's CRISPR Core Partnership Program. The Program has more than 70 partners.

In July, **Oxford Gene Technology**, a **Sysmex** company, announced it is now directly selling its Cytocell FISH products through Sysmex affiliates in Europe.

DNA Script, which is developing an enzymatic DNA synthesis technology, was awarded \$2.7 million in July in non-dilutive financing from the Concours d'Innovation program of investment bank **Bpifrance**. To date, DNA Script has raised a total of \$27 million.

In July, **KromaTiD** joined the **National Institute of Standards and Technology Genome Editing Consortium**. KromaTiD's dGH is a commercial structural genomic platform capable of de novo detection of random, low-frequency and complex structural variations in batches of gene-edited cells.

In July, **Streck** signed a three-year distribution agreement with Argentinian distributor **Cromoion**.

Product Introductions

In June, **Thermo Fisher Scientific** introduced the Invitrogen TaqMan & SYBR Green Fast Advanced Cells-to-CT Kits for high-throughput expression analysis directly from cultured cells without RNA purification and without risking sensitivity.

Sales and Orders of Note

In July, the **US Department of Agriculture Food Safety and Inspection Service** awarded **3M Molecular Detection** a contract for pathogen detection instruments and kits, making the technology the primary method used by the organization for the detection of Salmonella, Listeria monocytogenes and E. coli O157 (including H7).

Cell-based Consumables

Company Announcements

In June, **Sphero AG** partnered with immunoassay provider **ALPCO** to provide assays certified to work with its 3D InSight Islet Microtissues. Under the agreement, Sphero will include ALPCO STELLUX Chemiluminescent insulin and proinsulin ELISAs as part of its 3D InSight Diabetes Discovery Platform.

In June, **RoosterBio** joined the new **NSF Engineering Research Center for Cell Manufacturing Technologies** (CMaT), which aims to enable scalable manufacturing and broad use of potentially curative therapies that utilize living cells as drugs. RoosterBio provides adult human marrow-derived stromal cells and paired bioprocess media systems.



Emulate, which develops Organs-on-a-Chips technology, announced in June that it secured a \$36 million Series C financing round led by **Founders Fund**.

In July, **AMSBIO** and the **University of Strathclyde** launched ScreenIn3D, a joint venture company set up to develop a novel microfluidic screening platform using 3D spheroids. The company's OncoScreen uses patient-derived tissue.

In August, **Porvair** released an extended range of BactiGrowth specially packaged plates designed to enable high-yield growth of bacteria, yeast, mammalian or insect cell lines. Volumes span 300 µL to 10 mL per well.

Product Introductions

In June, **Eppendorf** introduced CCCadvancedTM FN 1 motifs cell cultureware, featuring a ready-to-use growth surface with synthetic fibronectin-derived motifs to support cell attachment by mimicking native extracellular matrix proteins. The surface supports human-induced iPSCs.

In July, **Fluidigm** launched a T-ATACseq application for its C1 system. The new assay measures transposase accessible chromatin and T cell receptor reporter gene expression from each cell.

Irvine Scientific released in July the PRIMEXV NK Cell CDM, calling it the first commercially available chemically defined media, animal component-free medium for the ex vivo expansion of NK (natural killer) cells.

In July, **Axol Bioscience** debuted its human iPSC-derived atrial cardiomyocytes, which are ready to use in seven days from thaw.

Corning launched in July the Corning 1536-well Spheroid Microplate. The design allows scientists to generate, culture, assay and analyze 3D multicellular spheroids in one microplate.

In August, **Bio-Techne** introduced a new range of Tocris Bioscience-branded stem cell research compounds, which are suitable for use as ancillary materials in the development of stem cell therapies. The first compounds released are SB 431542 and DAPT, which are widely used in stem cell differentiation and reprogramming protocols, which will be followed by Y27632, CHIR 99021 and XAV 939.

Protein-based Consumables

Company Announcements

Thermo Fisher Scientific signed an agreement in July with **BenchSci** to utilize machine learning to mine antibody data published in peer-reviewed scientific journals that will then be displayed on its product-specific webpages.

Under a licensing and supply agreement signed in July, **Cygnus Technologies** agreed to provide **Gyros Protein Technologies** with reagents for host cell protein analysis, enabling the development of new Gyrolab immunoassay kits and applications for biotherapeutics development and manufacturing.

In July, **SomaLogic** obtained a license to apply **GNS Healthcare**'s REFS (Reverse Engineering & Forward Simulation) causal machine learning technology to SomaLogic's SOMAscan-derived protein data sets.

In August, Canada's **Center for the Commercialization of Antibodies and Biologics** for a new business segment in August, which announced distribution agreement with MédiMabs for its reagent antibodies.

Product Introductions

In July, **Abcam** launched a new antiPDL1 antibody clone MKP1A07310 (clone 7310) developed in collaboration with **Merck KGaA**. The antibody is important in assessing the expression of PDL1 in tumors from patients who might be



able to benefit from PD 1/PDL1 checkpoint immunotherapy.

Ultivue launched in July the UltiMapper portfolio of reagents for high-throughput whole-slide, protein biomarker spatial detection and analysis in tissue. With a high level of multiplexing, the reagents can be used with instrumentation and software solutions currently found in most IHC labs. Ultivue's InSituPlex technology combines DNA-barcoded antibodies with fluorescent DNA barcodes in a single-slide staining, signal amplification and imaging step assay.

In July, **Bio-Rad Laboratories** debuted a range of recombinant monoclonal antiranibizumab antibodies that are highly specific for the monoclonal antibody drug ranibizumab (Lucentis) or the complex of ranibizumab with its target, vascular endothelial growth factor A (VEGFA).

In August, **Gyros Protein Technologies** introduced the Gyrolab CHO-HCP E3G Kit for impurity analysis in the CMC (chemistry manufacturing and controls) bioprocess workflow of biotherapeutics. The kits were developed as part of its licensing and supply agreement with **Cygnus Technologies**, using Cygnus' 3G CHO-HCP ELISA reagents.

Molecular Spectroscopy

Company Announcements

In April, **KLA-Tencor** acquired **Keysight Technologies**' nano-indenter product line.

In June, **Nanoscience Instruments** expanded its distribution agreement for **KLATencor**'s Nano Indenter G200 and T150 UTM systems.

Nanomechanics, a provider of nano-indenter products, announced in July its acquisition by KLA-Tencor.

In June, **Princeton Instruments** (PI) added its proprietary spectral and imaging data format (.SPE) to **Eigenvector Research**'s upcoming versions of the PLS_Toolbox and Solo software. The .SPE data format used by PI's LightField software is a flexible data format that stores spectral and imaging data. By convention, .SPE files include metadata detailing experiment information of instrument settings as well as the history of the data processing applied.

Picarro partnered in June with **Southern Cross**, which offers field services to utilities, to provide outsourced leak management, including data-enabled asset management solutions.

Bruker disclosed in a quarterly **SEC** filing that it paid \$27.0 million plus the potential of additional consideration to purchase **Anasys Instruments** (see \underline{IBO} 4/30/18).

In July, **AMETEK Grabner Instruments** and **Agilent Technologies** entered into an OEM agreement. Grabner developed the MINISCAN IR LOG, based on Agilent's handheld FTIR systems, an analyzer for monitoring the condition of lubricating oils and greases.

Product Introductions

FOSS introduced in May the FoodScan 2, an NIR system for analyzing solid and semi-solid dairy products, with time to results in as little as 15 seconds. Color can be measured simultaneously with compositional tests by employing NIR transmission and transflectance technology in one unit. Models are available for lab and production settings.

In June, **Bruker** released a new version of its ParaVision 360 imaging software for preclinical MRI, enabling essential or simultaneous PET/MR measurements and analysis. ParaVision 360 includes the unique IntraGateUTE method, which offers artefact-free images of a beating heart.

Bruker introduced in June the B.I.QUANT-PS metabollte quantification solution, part of the B.I.BioBankTool, for its



AVANCE IVDr NMR 600 MHz system. The software offers delivers automatic quantification of 26 disease-relevant metabolites and in the same experiment also enables lipoprotein subclass analysis.

In July, **PerkinElmer** debuted the FL 6500 Pulse Xenon and FL 8500 Continuous Wave Fluorescence Spectrometers. The FL 6500 features scan speeds up to 60,000 nm. The FL 6500 fluorescence spectrometer is designed for testing samples that are susceptible to photo bleaching.

Wasatch Photonics expanded in July its Cobra OCT spectrometer line. The new models operate at visible wavelengths and provide depth-resolved, localized oxygenation mapping concurrently with the acquired optical coherence tomography image.

Sales and Orders of Note

In July, **Rigaku Analytical** announced that Project Global Shield, a **World Customs Organization** (WCO) program, has chosen its Progeny ResQ 1,064 nm handheld Raman analyzers for global customs operations. The WCO will use a minimum of 38 systems. The program is designed to combat illicit use of precursor chemicals used to manufacture improvised explosive devices by monitoring cross-border movements.

In July, CDMO **Almac** installed a **Bruker** 500 MHz NMR system and Prodigy Cryoprobe at is global headquarters in Craigavon, UK, representing a £375,000 (\$493,421) investment in additional NMR instrumentation.

In August, **Bruker** announced orders for two 1 GHz AVANCE ultra-high field NMR systems from the UK's **University of Warwick** and **University of Birmingham**. The orders also include CryoProbes and AVANCE NEO console upgrades to existing 800 and 950 MHz systems at several universities across the UK.

Agilent Technologies announced in July the **UK Border Force** is using its Resolve handheld Raman System to detect bulk chemicals. This deployment is part of a multimillion-pound framework agreement between the **UK Home Office** and Agilent.

Laboratory Products

Laboratory Equipment

Company Announcements

In March, Labtech International acquired MSE, a UK manufacturer of centrifuges, from Henderson Biomedical.

In July, **Esco** broke ground on its 215,278 ft² (20,000 m²) Jiangsu Innovation Center, a manufacturing and innovation complex located in China. The Center is scheduled to be completed by the end of next year.

ERWEKA announced in July the establishment of a US subsidiary in Edison, New Jersey.

In July, **Edstrom Industries** announced the combination with its **Triple Red** subsidiary under the name **Avidity Science**. Both companies provide laboratory water solutions.

Product Introductions

In July, **Edstrom Industries** launched the Avidity Science line of pure water systems for laboratory applications, which includes Type 1, 2 and 3 pure water systems. Production rates ranges from 10 L/hour to 80 L/hour. All models are available through **Thomas Scientific**.

Boekel Scientific introduced in July the Gen2 Refrigerated Incubator for BOD testing, microbiologic work, and



plant and animal incubation. The system can accurately control temperatures at 200 C° below ambient temperature and features approximately 4 ft³ of space in the interior chamber.

In July, **PHC Holdings** debuted in Japan the VIP ECO series, a new -85°C ultra-low temperature freezer using natural refrigerants and new inverter compressors. This product series comprises models MDF-DU702VHS1-PJ/DU502VHS1-PJ (single-phase 100 V) and is specially designed for pharmaceutical companies, research and medical institutions.

VELP Scientific released in July the AREX-6 Connect PRO, calling it the first hot plate stirrer connected to the cloud, allowing real-time monitoring of speed and thermoregulation, as well as data logging.

In August, **Shimadzu** launched the AP225W semi-micro analytical balance, its highest-end model, capable of measuring up to 220 g and a minimum reading of 0.01 mg.

Sales and Orders of Note

In July, **VWR** was awarded a five-year laboratory supplies and services contract by **E&I Cooperative Services**, a nonprofit purchasing cooperative focused on education needs. The agreement continues an ongoing relationship.

Laboratory Automation

Company Announcements

In July, **Labcyte** announced an agreement with the **Center for Excellence in Engineering Biology**, a nonprofit organization that is managing initial planning and coordination of efforts for the **Genome Project-write** (GP-write). Labcyte will provide preferred pricing, in-kind support to researchers at qualified laboratories involved with GP-write and early access to certain new products. GP-write will oversee a reduction in the costs of engineering and testing of large genomes in cell lines by more than 1,000-fold within 10 years.

Reported Financial Results



\$USD in Millions	Period	Ended	Sales	Chg.	Op. Prof.	Chg.	Net Prof.	Chg.
Agilent Technologies	Q3	31-Jul	\$1,203.0	8.0%	\$225.0	11.9%	\$236.0	34.9%
Agilent Technologies (Life Sciences and Applied Markets)	Q3	31-Jul	\$540.0	5.9%	\$123.0	12.8%	NA	NA
Agilent Technologies (Diagnostics and Genomics)	Q3	31-Jul	\$237.0	8.7%	\$44.0	18.9%	NA	NA
Agilent Technologies (CrossLab)	Q3	31-Jul	\$426.0	10.4%	\$102.0	13.3%	NA	NA
Bio-Rad Laboratories	Q2	30-Jun	\$575.9	14.1%	\$43.8	NM	\$268	5223.6%
Bio-Rad Laboratories (Life Science)	Q2	30-Jun	\$217.8	21.4%	\$40.0	NM	\$12.2	NM
Bruker	Q2	30-Jun	\$443.7	6.9%	\$48.8	38.2%	\$31.5	31.3%
Bruker (BSI)	Q2	30-Jun	\$402.4	11.0%	\$47.2	46.1%	NA	NA
Fluidigm	Q2	30-Jun	\$26.4	10.5%	(\$12.8)	22.5%	(\$16.2)	4.1%
MTS Systems	Q3	30-Jun	\$194.7	0.5%	\$16.3	-2.1%	\$9.0	-15.4%
MTS Systems (Test)	Q3	30-Jun	\$116.1	-6.7%	\$3.9	-55.5%	NA	NA
NanoString Technologies	Q2	30-Jun	\$25.0	-27.7%	(\$18.8)	-466.9%	(\$20.6)	-352.3%
Pacific Biosciences	Q2	30-Jun	\$21.6	7.5%	(\$21.7)	10.8%	(\$22.5)	11.7%
Perkin⊟mer	Q2	1-Jul	\$703.4	28.6%	\$88.1	18.7%	\$64.1	-68.6%
PerkinElmer (Discovery & Analytical Solutions)	Q2	1-Jul	\$430.6	12.4%	\$64.7	26.5%	NA	NA
PerkinElmer (Diagnostics)	Q2	1-Jul	\$272.7	66.5%	\$38.8	5.0%	NA	NA
Techcomp	Q2	30-Jun	\$83.3	4.8%	\$1.3	38.4%	\$1.4	68.0%
Other Currencies in Millions					3			
Eppendorf	H1	30-Jun	€ 336	2.3%	€67	6.5%	NA	NA
HORIBA	H1	30-Jun	¥99,966	14.5%	¥14,057	44.9%	¥10,503	62.6%
HORIBA (Scientific)	H1	30-Jun	¥12,535	8.9%	-¥0.5	-23.9%	NA	NA
HORIBA (Process & Environmental)	H1	30-Jun	¥9,248	14.5%	¥0.9	170.4%	NA	NA
Merck KGaA	Н1	30-Jun	€ 7,199	-2.1%	€ 895	-32.2%	¥588	-38.0%
Merck KGaA (Life Science)	Н1	30-Jun	€ 3,030	1.8%	€ 527	15.3%	NA	NA
Shimadzu	Q1	30-Jun	¥85,655	13.0%	¥5,739	47.8%	¥4,352	79.2%
Shimadzu (Analytical & Measuring Instruments)	Q1	30-Jun	¥51,652	12.0%	¥5,679	19.9%	NA	NA

 $NA = not \ available; NM = not \ material \ Click \ to \ enlarge$

