MEDICAL DEVICE DAILY™

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POST-APPROVAL STUDY BEGINS IN SUMMER

Start up Tryton wins FDA approval, Cordis launch for the first branch coronary stent

By Stacy Lawrence, Staff Writer

Tryton Medical Inc. has garnered an FDA approval for its Side Branch Stent to treat coronary artery disease with lesions at major branches. This is the first approval for a dedicated bifurcation device in the U.S., according to the Durham, N.C.-based company. Cordis, part of Dublin, Ohio-based Cardinal Health Inc., has already signed a deal to be the sole U.S. distributor of the stent.

The Cordis deal dates back to last October, and the group is slated to launch the Side Branch Stent via its interventional vascular business later this month. Although the financial details are not disclosed, the pair are said to be in a long-term partnership.

See Tryton, page 3

SIGNIFICANTLY FASTER THAN IRYS

Bionano Genomics shines brightly through recent Saphyr genome mapping system launch

By Omar Ford, Staff Writer

Gene sequence specialist Bionano Genomics Inc. has launched Saphyr, its latest generation genome mapping system. The San Diego-based company said Saphyr has primary applications that include the ability to give greater insight on undiagnosed genetic

See Bionano, page 4

REGULATORY

Study says biomarkers, clinical features may be predictive of CAD

By Mark McCarty, Regulatory Editor

The search for an inexpensive, noninvasive method of predicting which patients are at risk for coronary artery disease has eluded medical science for years, but researchers believe that the use of four biomarkers and two clinical variables can yield a highly predictive method for determining the likelihood of anatomically significant CAD.

See CAD, page 5

A PATIENT-CENTRIC SYSTEM

PMDA head envisions Rational Medicine, pledges more innovation

By Kohei Kanayasu, Staff Writer

TOKYO – Japan's Pharmaceuticals and Medical Devices Agency (PMDA) is looking to play an active role in achieving "Rational Medicine" in the country.

The agency recently released the "Rational Medicine Initiative," a paper that outlines their main points of focus for the coming year. The announcement, signed by

See PMDA, page 6

MAY REDUCE ANTIBIOTIC USE BY 65%

FDA clears Biomérieux's Vidas to help assess the severity of sepsis

By Melody Watson, Staff Writer

The U.S. FDA recently reported 510(k) clearance of the Vidas Brahms PCT Assay for expanded use to help health care providers decide whether antibiotic treatment should be started or stopped in patients with lower respiratory tract infections (including community-acquired pneumonia, acute bronchitis and acute

See Biomêrieux, page 7

IN THIS ISSUE

CARDIOLOGY EXTRA

Production Editor Andrea Gonzalez and Senior Science Editor Anette Breindl on one of med-tech's key sectors

Read this week's Tuesday Special

APPOINTMENTS AND ADVANCEMENTS

Atricure Inc., a Mason, Ohio-based developer of surgical treatments for atrial fibrillation and left atrial appendage management, reported it has hired Vinayak Doraiswamy as its senior vice president of clinical, regulatory and scientific affairs. Most recently, Doraiswamy served as vice president of global clinical operations at St. Jude Medical.

Premier Eye Care, of Tampa, Fla., said Jeff Nowak has joined the company as chief solutions officer, where he is focused on addressing short and long-term business challenges and opportunities with technology solutions. Nowak joins Premier with more than 25 years of experience, including high-level operational roles at Medhok Inc., Elsevier and Wellcare Health Plans. Premier provides quality and affordable solutions for managed medical and routine eye care.

DAILY M&A

Thermo Fisher Scientific Inc., of Waltham, Mass., said it has acquired **Core Informatics**, a Branford, Conn.-based provider of a cloud-based platform that supports scientific data management. Core's offerings will enhance Thermo Fisher's existing informatics solutions and complement its cloud platform, which supports the company's genetic analysis, qPCR and proteomics systems. Core's capabilities include laboratory information management systems, electronic laboratory notebook technologies and scientific data management solutions. The business also offers an application marketplace to speed deployment and increase value for customers across a broad range of industries and scientific workflows. Financial terms were not disclosed.

FINANCINGS

Airway Therapeutics LLC, a Cincinnati-based biotechnology company that develops new interventions for acute and chronic lung diseases, has secured $6.3 million in bridge financing from new and existing investors. Cincinnati Children's Hospital Medical Center, Cincytech and Queen City Angels are among the previous investors participating in this round. The financing comes as Airway Therapeutics reports significant progress with the development of its lead product AT-100, a recombinant form of human surfactant protein D (rhSP-D). AT-100 protein replacement therapy targets bronchopulmonary dysplasia, a developmental disorder in premature neonates that leads to an arrested lung development. According to the Airway Therapeutics CEO, the proceeds will allow the company to move closer to manufacturing AT-100 for use in humans.

OSI Systems Inc., of Hawthorne, Calif., reported that its health care division, Spacelabs Healthcare, received an approximately $8 million order to provide patient monitoring solutions and related accessories to a prominent U.S. hospital group. The company expects to install, among others, it's XTR Telemetry, Xhibit Central Stations, Xprezzon and qube patient monitoring products.

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Tryton

Continued from page 1

WHAT'S NEXT FOR TRYTON?

Tryton is also planning to start a post-approval study of the stent this summer. The aim is to offer data to continue to convince U.S. health care providers that "new operators introduced to the technology can continue to generate reproducible results," Tryton President and CEO Shawn McCarthy told *Medical Device Daily*.

"We certainly will be focused on the U.S. market and demonstrating the use to physicians, and we are pursuing additional indications. We have an international business that we will continue to grow in the EU and expand into Asia," said McCarthy.

The Tryton stent gained CE mark in 2013, and the start up has been handling those marketing efforts on its own, with more than 12,000 patients having received the implant. The company plans to continue to expand in Europe on its own, but it's open to direct marketing and partnerships in Asian markets.

MAKING IT TO MARKET

It took more than eight years for Tryton to complete the U.S. regulatory path for the Side Branch Stent, starting with pre-IND meetings with the FDA. The company was initially founded in 2003 by Aaron Kaplan and H. Richard Davis. Kaplan continues to serve as Tryton CMO, while Davis is its COO.

Kaplan is a professor of medicine and the director of Dartmouth device development Symposia at Dartmouth Medical School and director of research at the Cardiac Catheterization Laboratories at the Dartmouth-Hitchcock Medical Center in Lebanon, N.H.

Davis was formerly employed with Cordis, when it was part of Johnson & Johnson prior to its 2015 sale for almost $2 billion to Cardinal Health. In addition, he was also a co-founder of vascular device company Orbusneich.

The pair had a vision of developing stent systems specifically to treat bifurcation lesions. Workarounds such as provisional stenting, the current standard of care, typically leave the side branch not stented. That can lead to complications like occlusion that then require bailout stenting.

About 20 percent to 30 percent of all patients undergoing percutaneous coronary interventions (PCI) to open blocked arteries have a bifurcation lesion. That offers a sizeable potential market for Tryton's major partner, Cordis, to reach quickly with its vast existing sales force and clientele. Coronary artery disease is the leading cause of death in the U.S.

McCarthy said that reimbursement is already in place for the stent system. "Reimbursement is already established in the U.S., both codes and payment levels," said McCarthy. He noted that the system will be reimbursed on par with current alternatives in the U.S., but that in some European countries, such as Germany, it is being paid for at a premium to other options.

A NEW STANDARD FOR BIFURCATION

The pivotal testing for the Tryton Side Branch Stent involved more than 700 patients from up to 75 centers in North America, Europe and Israel. In a post-hoc analysis of the data in patients with large side branches – appropriate for use of a stent that's greater than or equal to 2.5 millimeter stent – versus provisional stenting, the Tryton stent was found to reduce the need for additional bailout stenting, lead to statistically significant lower side branch percent diameter stenosis at nine months, and to reduce major adverse cardiovascular events and myocardial infarction rates at three years.

"Treatment of complex lesions at the site of a bifurcation has historically been inconsistent, with results varying depending on the procedure and the experience of the interventionist," Kaplan said.

He added, "A predictable bifurcation solution helps alleviate some of the stress in these procedures by limiting variability and reducing the need for bailout stenting. This important FDA decision could have a profound impact on treatment protocols and guidelines for significant bifurcation lesions in the years ahead."

The stent is deployed on the side branch artery using a standard single-wire, balloon-expandable stent delivery system. It has an open architecture, which allows for the integration of a conventional, drug-eluting stent for the main vessel. The idea is to enable complete lesion coverage.

To support its efforts, Tryton has raised more than $50 million in venture capital from investors including Rivervest Venture Partners, 3x5 Special Opportunity Fund and Canepa Healthcare.

The ultimate aim is for the Tryton stent, which will be driven entirely by Cordis in the U.S., to become the standard of care for PCI patients with a bifurcation lesion, a sizeable portion of stent patients.

"This is the new standard for treating complex bifurcations," said McCarthy. "The current standard, which is provisional stenting, is overused. Our goal is to establish a completely new standard for how physicians treat this, so this becomes the definitive treatment for complex bifurcations." //

Bionano

Continued from page 1

disorders, gene discovery, therapy development and cancer. The private firm introduced Saphyr at Advances in Genome Biology and Technology (AGBT) General Meeting held in Hollywood Beach, Fla., last month.

"The objective of anyone who is doing genome mapping is to try and elucidate the order and orientation and amount of functional elements in a genome," Erik Holmlin, Bionano CEO, told *Medical Device Daily*. "You want to know where the genes are and what chromosomes they're located on. Our tool allows researchers to study genomes and get this information."

Saphyr is an updated and stronger version of Bionano's Irys Sequencer.

"Irys was a great platform tool, and you could study genomes in great detail, but if your question required you to study a population of genomes like 50 or maybe 100, then you would struggle," Holmlin said.

The company has more than 65 of its Irys sequencers on the market. In looking to push adoption for both Iyrs and Saphyr, the firm said it was in the process of getting concrete data on the effectiveness of its gene mapping technology published.

Last month, the company highlighted data that supported the effectiveness of its technology. A group from Garvin Medical Research used optical mapping with Bionano's Irys system to generate complete human genome maps from tumor-normal pairs of both primary and metastatic prostate cancer from five prostate cancer patients. The researchers also identified a set of large structural variations (SV) within prostate cancer, of which almost 90 percent were undetectable using next generation-sequencing (NGS) alone. Use of NGS and next-generation mapping (NGM) methods allowed for verification of up to 95 percent of the large SVs.

In another study, researchers from Johns Hopkins University School of Medicine used NGM with Saphyr to determine the genomic architecture of specific regions of chromosomes associated with Facioscapulohumeral muscular dystrophy, a hereditary form of muscle disease.

Holmlin said the company could find its niche in complementing larger firm's gene sequencing technologies. He pointed to San Diego-based Illumina as an example.

Most recently, Illumina renewed its focus on gene sequencing when its stake in its liquid biopsy spin-off Grail Inc. was significantly reduced. (See *Medical Device Daily*, March 3, 2017.)

"Illumina has thousands of sequencers on the market," Holmlin said. "If we were to look at just the number of high throughput sequencers they have, it's somewhere between 1,500 and 2,000 customers. Those customers probably have around 2,500 sequencers.

He added, "We see the market opportunity for Bionano as complementing every one of those sensors."

The company is working on bringing its applications into the clinical market in China. In August of last year, the company reported a partnership with Beijing-based Berry Genomics Ltd., a noninvasive prenatal test specialist.

Under the terms of the deal, the companies are set to co-develop assays that incorporate Bionano's NGM platform. Berry will exclusively manufacture and market the assays and a related instrument system in China for clinical use following clinical validation and regulatory approval.

Holmlin noted the partnership would give Bionano's technology a greater "foothold" in the market.

Plans call for the firm to continue to seek out funding. According to its website, Bionano brought in about $53 million in a series C round in 2014. Company executives said they would expect ongoing financings to come together to support the commercialization and future development of application in the space. //

OTHER NEWS TO NOTE

Bluegrass Vascular Technologies LLC, of San Antonio, Texas, said it is entering into a partnership with **Merit Medical Systems**, a South Jordan, Utah-based manufacturer and marketer of disposable devices. The agreement will streamline European distribution of Bluegrass Vascular's recently CE mark approved Surfacer Inside-Out Access Catheter System and will provide funding to support the company's efforts to secure FDA clearance for product sales in the U.S. The Surfacer Inside-Out Access Catheter System provides reliable, efficient and repeatable central venous access to the right internal jugular vein, the optimal location for placing a central venous catheter. Terms of the agreement have not been disclosed.

Precision Medical Devices Inc., of New Brunswick, N.J., said it inked a contract with **North Carolina State University** to become its second site to do implants of its new bionic Bluetooth-controlled and Bluetooth-adjustable urethral valve device designed to optimally treat severe urinary incontinence (UI) in both humans and canines. Use of the technology will be focused on maximizing its adaptation to the challenges that are presented in treating UI in the pet canine market, challenges that far exceed the operational parameters needed to appropriately manage human cases.

CAD

Continued from page 1

The importance of a predictor of high-risk occlusion of the coronary arteries includes conventional and nontraditional risk factors, the latter of which is populated by markers such as C-reactive protein. The medical literature is peppered with papers in pursuit of a replicable approach to prediction, and cardiac troponin was proposed as one such marker in an article appearing in the *Journal of the American College of Cardiology* in February 2016.

Writing in the March 7, 2017, issue of *JACC*, Nasrien Ibrahim of Massachusetts General Hospital in Boston, along with a group of 11 others, said they used data drawn from the Catheter Sampled Blood Archive in Cardiovascular Diseases (Casablanca) study, a prospective study of clinical and biological factors that could predict significant coronary artery disease. Casablanca used a convenience sample of more than 1,250 patients who were admitted at Massachusetts General for angiographic studies of the coronary and peripheral vasculature between 2008 and 2011, although enrollees need not have undergone treatment for any diagnoses.

There was some heterogeneity in this patient population as it consisted of those referred for angiography for any one of several reasons, including infarct, unstable angina and for preoperative evaluation prior to "heart valve surgery." The threshold for "significant" stenosis of the coronary artery was set at 70 percent obstruction of the lumen in any one of several arteries, and the authors remarked that the 70 percent threshold is commonly used in similar studies.

Slightly more than 920 patients from Casablanca were selected for this analysis, with 649 used as a training set, leaving 278 enrollees for the validation set. The authors used only the training set to select the biomarkers of interest and for validation of the model, and commenced with more than 100 biomarkers and 18 clinical indicators. Those in the validation arm exhibited an association between age and CAD measures equal to or in excess of 70 percent (67.3 years of age compared to 64 years for those with less than 70 percent obstruction). With a "p" value of 0.001, this met statistical significance, as did male status, which was seen in nearly 79 percent of those whose coronary arteries met or exceeded the 70 percent threshold. In contrast, men accounted for a relatively smaller share of those whose obstruction did not reach 70 percent (129 of the 221 patients in this group).

Perhaps even more meaningful for cardiologists was the fact that among those in the validation set with at least one artery that reached 70 percent obstruction, 64 percent met the threshold in at least two arteries, while more than a third of these patients were dealing with 70 percent occlusion in three coronary arteries. Several of the typical lab measures, such as low-density lipoprotein and glucose, were high among the patients with at least 70 percent occlusion, and four biomarkers, including adiponectin and midkine, were much more conspicuous among those meeting the 70 percent threshold in at least one coronary artery.

The authors said their scoring system offered a sensitivity of 77 percent and specificity of 84 percent along with a positive predictive value of 90 percent. An elevated score based on two clinical features, male sex and percutaneous intervention in the coronary arteries, along with the four biomarkers is said to have acute myocardial infarction during a follow-up of 3.6 years.

Robert Vogel, a cardiologist in the department of cardiology at the University of Colorado in Denver, penned an editorial in the same issue of *JACC* stating that he is wary of the 70 percent threshold of obstruction as an indicator of risk. Vogel argued that the biomarkers used in this study are also used to evaluate coronary artery atherosclerosis generally, and that the study did not benchmark the performance of the biomarkers as a distinguishing factor between those with and without any disease of the coronary arteries.

Vogel continued with the observation that visual assessments of severity of stenosis "is remarkably inaccurate and imprecise," adding that such measurements correlate "only moderately" with quantitative measurements. He said visual assessments correlate poorly with digitally assessed coronary flow reserve, adding that none of the four biomarkers in question are measures of inflammation, "as would be expected" if the goal was to determine the presence of unstable disease. Vogel concluded that this study is preliminary and calls for confirmation in other studies using an independent population with a wider set of inclusion criteria.

The American College of Cardiology was unable to provide a spokesperson for comment. //

PMDA

Continued from page 1

Tatsuya Kondo, CEO of the PMDA, lists four pillars as means to achieve Rational Medicine: innovation through product approval reviews of enhanced rigor and rationality, further promotion of regulatory science, increased sophistication of safety measures through real-world data and enhanced international partnerships.

Rational Medicine is the idea that a patient-centric system should be in place from the perinatal to the final stages of life – a system under which optimal medical care from the patient's point of view, based on the latest scientific knowledge, is provided.

"I strongly feel that this idea should always be borne in mind by health care professionals, companies, government authorities and all other parties concerned," said Kondo.

"He [Kondo] believes that medical treatments that patients receive should be provided from a holistic point of view, without getting caught up in each of the medical staff's expertise, and should focus on what is rational for the patient," PMDA told *Medical Device Daily*. "He feels that doctors, nurses and pharmacists are practicing medicine based on their relative values, and the message published on Feb. 7 poses the question, 'Is that how it should be? Should we not pursue absolute rationality with patients as the axis?'"

The document – containing both Kondo's personal vision of how medicine should be and the PMDA's roadmap for 2017 – focused on how the PMDA will lead the industry, now that it has caught up with its American and European counterparts.

Founded in 2004, the PMDA is Japan's key industry regulator. It reviews and approves pharmaceuticals and medical devices, monitors post-marketing safety and is responsible for providing "relief compensation" for people suffering from adverse drug reactions and infections.

"I see the PMDA's Rational Medicine Initiative as seeking to establish a cohesive strategic direction for the country's regulatory regime," said Ang Wei Zheng, pharmaceuticals and health care analyst at BMI Research. "Content-wise, the policy paper reflects existing measures already in place. The Sakigake designation for example will allow innovative treatments to see their review period reduced from 12 months to six. Pharmaceuticals given the Sakigake designation include Merck Sharp & Dohme Corp.'s Keytruda, Astellas Pharma's ASP2215 and Daiichi Sankyo's oncolytic virus G47Δ*1."

Zheng continued, "All in all, this will see drug approval times continue to shorten over the coming years, perpetuating the significant progress made by the PMDA, which has reduced the median approval time for new active substances, falling from over 800 days in 2006 to 284 days by 2015, 351 days ahead of the U.S. FDA and 417 days ahead of the EMA (European Medicines Agency), according to the Center for Innovation in Regulatory Sciences."

Kondo's similar remarks were also published in the January issue of the monthly PMDA Updates, where he raised concerns on "uncertain factors," including the change in the U.S. administration.

U.S. President Donald Trump said during a press conference in January that his country has to get its drug industry back, as the pharmaceutical companies "supply our drugs, but they don't make them here, to a large extent." He also pledged to "create new bidding procedures for the drug industry because they're getting away with murder."

He has also pledged to "repeal and replace" the Affordable Care Act.

The U.S. Department of Health & Human Services estimated that 20 million Americans are now covered by health insurance under this act, bringing the uninsured rate to the lowest on record.

Since then, Trump has met with pharmaceutical industry members, including the CEOs of Novartis AG, Johnson & Johnson, as well as the head of the Pharmaceutical Research and Manufacturers of America (PhRMA). There, he called for increased production in the U.S. and lower drug prices; in return, he pledged to streamline the FDA approval process. //

PRODUCT BRIEFS

Masimo Corp., of Irvine, Calif., reported the availability of the RD Sedline EEG sensor, for use with Masimo Sedline Brain Function Monitoring and compatible with simultaneous use of Masimo O3 Regional Oximetry. Sedline and O3 provide simultaneous monitoring on the Masimo Root monitoring platform, helping to give clinicians more information about the brain.

Nephros Inc., of River Edge, N.J., received 510(k) clearance from the **FDA** for its Endopur Endotoxin 10 inch filter. The Endopur Endotoxin 10 inch filter is designed to provide hemodialysis quality water to dialysis machines. This new product fits into existing filter cartridge housings of the reverse osmosis water systems that provide dialysis clinics with high volumes of ultrapure water. The Endopur offers dialysis clinics an endotoxin barrier with the smallest pore size on the market.

W. L. Gore & Associates Inc., of Flagstaff Ariz., reported the Health Canada approval of the Gore Tigris vascular stent, a dual-component stent with a fluoropolymer/nitinol design. The Gore Tigris device, which gained CE mark approval in 2011, is a third generation, self-expanding stent. The device was designed to improve anatomical conformability with the natural movement of the knee when treating peripheral artery disease.

Biomérieux

Continued from page 1

exacerbations of chronic obstructive pulmonary disease) and whether antibiotic treatment should be stopped in patients with sepsis. The test, developed by Biomérieux Inc., which is headquartered in Mercy-l'Étoile, France, was initially approved to help physicians better predict a patient's risk of becoming sicker due to sepsis as well as their risk of death.

Sam Bozzette, vice president of Medical Affairs for Americas/Asia-Pacific and Global Health Economics and Outcomes at Biomérieux, told *Medical Device Daily* that "physicians need help in deciding when to initiate and when to discontinue therapy because it is often hard to tell an active bacterial infection from other conditions, like a viral infection or heart failure ... PCT is elevated in cases of severe bacterial infection, and a few other conditions such as trauma, and so by looking at initial PCT levels and then following them, clinicians can gather additional information as to whether or not they should start and how long they should continue antibiotic treatment." Bozzette added that "these new indications relate first to respiratory disease – whether a patient needs to receive antibiotics at all. This is an important question because in the U.S. at least it has been shown that half of all antibiotic prescriptions for lower respiratory tract infection aren't necessary, so this test should eliminate a big chunk of those unnecessary prescriptions. At the same time, although the guidelines currently recommend short treatment courses, many doctors are uncertain about this and providing additional information to support the decision to discontinue antibiotics is also valuable. The other indication is sepsis, which is a devastating and growing disease with a high mortality rate.

"In this situation" he said, "patients are really sick, and it is hard to tell how long you should keep giving antibiotics before the patient actually starts to be harmed by the treatment – for example, the patient may become colonized with antibiotic-resistant bacteria or develop *Clostridium difficile*-associated diarrhea. Low levels of PCT suggest that antibiotics can be safely discontinued."

Bozzette added that following the FDA clearance, he expects PCT testing to be increasingly included in treatment guidelines and for PCT testing to become more widely adopted in the approved indications.

CLINICAL EVIDENCE BASE

In clinical trials conducted in more than 1,000 patients with sepsis in intensive care, application of a PCT-based decision algorithm based on the relative decrease of plasma PCT levels over time resulted in a significant reduction in the duration of antibiotic therapy as well as the length of stay in the intensive care unit.

In more than 1,000 patients with lower respiratory tract infections who took part in randomized clinical trials, PCT measurement at relatively low concentrations was able to identify patients with clinically relevant infections who required antibiotic therapy. These trials demonstrated that using the Vidas Brahms PCT Assay along with a PCT-based decision algorithm, antibiotic use could be reduced by 65 percent in a primary care setting. In addition, there were no differences in patient outcomes compared with standard treatment.

THE VIDAS BRAHMS PCT ASSAY VS. OTHER COMMERCIAL PCT ASSAYS

When asked how the Vidas Brahms PCT Assay differs from other commercial PCT tests, Bozzette replied that "they are all pretty similar and this is because they are mostly calibrated to the Brahms standard. Our system is extremely rugged, and it is extremely reliable, using proven technology. There are more than 30,000 of them out in the field, and they will give you a result in 20 minutes. Other companies either have more cumbersome instruments or are high-volume and use expensive instruments.

"Importantly" he said, "our system is the only one so far that has demonstrated safety and effectiveness in these indications [lower respiratory tract infection and sepsis]."

COST SAVINGS FOUND WITH PCT TESTING

A cost analysis of PCT testing for diagnosing and monitoring sepsis was commissioned in 2015 by the National Institute for Health and Care Excellence in the U.K. It included several commercial PCT assays, including the Vidas Brahms PCT Assay. In a base-case analysis, cost savings were estimated to range from £368 (US$457) for children with suspected bacterial infection presenting to the emergency department (lower clinical extreme) to £3,268 (US$4,061) for adults with confirmed or highly suspected sepsis in an intensive care unit setting (lower clinical extreme).

Another economic evaluation of PCT-guided antibiotic therapy versus standard care for acute respiratory infections was performed from the perspective of a typical U.S. integrated delivery network (IDN) with a one million member catchment area or enrollment. In the inpatient setting, net savings of almost $700,000 were calculated for the IDN for 2014. For the whole insured U.S. population, PCT-guided therapy was estimated to result in annual savings of approximately $1.6 billion.

BIOMÊRIEUX'S CURRENT DEVELOPMENTS, FUTURE PLANS

Regarding current developments, Bozzette told *Medical Device Daily* that Biomérieux is "looking at a broad range of technologies to improve their PCT testing, some of them are different markers which are measured in the same way, some of them are molecular markers for host response. We are also developing rapid platforms for detection of bacteria in the blood and for determining what kind of bacteria they are, and in many cases determining what the resistance patterns are. In addition, we are looking at biomarkers in other emergency

See Biomêrieux, page 8

Biomérieux

Continued from page 7

situations. For example, people who are coming in with sepsis are at very high risk of renal failure, so a marker for renal failure could be quite useful."

When asked what the future holds, Bozzette replied that "what we want to do is make everything more comprehensive and faster, and discover better biomarkers for bacterial versus viral infections – PCT is very good but everything can be improved upon. We now have an extremely fast incubator, and we have mass spectrometry identification of organisms. We have among the quickest instruments for detecting antimicrobial sensitivity and have major projects underway to dramatically increase the speed [of the assay]. We also sell middleware to release these findings very quickly in the lab information system as well as software. We're bundling these together and trying to make a solution that exploits the potential synergies in each step." //

REGULATORY FRONT

The **Therapeutic Goods Administration** of Australia posted a notice regarding three confirmed infections of *Mycobacterium chimaera* associated with blood heater-cooler devices used in cardiovascular surgeries. The agency said other unconfirmed infections are under review, and that the agency is undertaking a product safety review. The U.S. FDA reported instances of infections associated with these devices in 2016.

The diagnostics division at the **Advanced Medical Technology Association** has penned a letter to four congressional leaders urging them to pass legislation pertaining to regulation of lab-developed tests and in vitro diagnostics. Andrew Fish, executive director of AdvaMedDx said the regulatory framework should be "modernized," pointing to the prospect that statutory reform could incorporate a risk-based paradigm that would avoid undue regulation of low-risk tests. The letter is addressed to the chairpersons and ranking members of the House Energy and Commerce Committee and the Senate Health, Education, Labor and Pensions Committee, which have jurisdiction over a bill that surfaced in 2016 that would carve out a regulatory framework specific to lab-developed tests.

CARDIOLOGY EXTRA

Keeping you up to date on recent developments in cardiology

By Andrea Gonzalez, Production Editor, and Anette Breindl, Senior Science Editor

Pacemaker function may be impacted by everyday electric appliances, tools

Electric and magnetic fields (EMF) generated from everyday household appliances, electrical tools and more, used in very close proximity to the body, can interfere with the ability of pacemakers to regulate patients' heartbeats, according to new research in the American Heart Association's journal *Circulation*. Researchers tested the impacts of EMF exposure under different conditions on 119 patients with pacemakers. The patients were exposed to an EMF similar to common exposure, i.e., EMFs at power grid frequencies (50Hz or 60Hz), then increasing the EMF until the researchers noted a pacemaker sensing failure. They found pacemakers are susceptible to EMF that can occur in everyday life, in particular when programed to maximum sensitivity or so-called unipolar sensing mode. Examples of EMF sources are powerlines, household appliances, electrical tools and entertainment electronics. In many cases, holding the appliance, tool or other EMF source at a forearm's length distance (greater than 12 inches) limits the risk of electromagnetic interference. But further measures might be needed in environments with strong EMF, such as engines used in the processing or manufacturing industry, said Andreas Napp, one of the study authors and cardiologist at RWTH Aachen University Hospital in Aachen, Germany. "Electromagnetic interferences with pacemakers in everyday life can occur, however, harmful interferences are rare using vendors' recommended device settings," said Napp. "Dedicated device programing is an effective measure to reduce the individual risk of interference. For example, doctors can reprogram pacemakers to a lower sensitivity to reduce EMF susceptibility."

Biomechanical strains in blood vessels can now be studied with new organ-on-a-chip device

Hutchinson-Gilford progeria syndrome (HGPS) is an extremely rare genetic condition that causes premature and accelerated aging. HGPS primarily affects vascular cells, which undergo biomechanical strains in blood vessels. However, the impact of these biomechanical strains on aging and vascular diseases has been challenging to study in the lab, as most models fail to mimic the biomechanics that cells experience in the body. Using a new progeria-on-a-chip model, investigators from Brigham and Women's Hospital, led by João Ribas and Ali Khademhosseini, have developed a way to recapitulate blood vessel dynamics to better understand vascular disease and aging. The new organ-on-a-chip device consists of a top fluidic channel and underlying vacuum channel, which mimics, upon pressure, the mechanical stretching that cells experience within blood vessels. The team found that cells derived from HGPS donors but not from healthy donors showed an exacerbated response to biomechanical strain, with an increase in markers of inflammation, which are strongly associated with vascular disease and aging.

New risk scale can predict serious adverse events in acute heart failure patients

More than one million patients are admitted to the hospital with heart failure each year. A prospective clinical validation found the Ottawa Heart Failure Risk Scale (OHFRS) tool to be highly sensitive for serious adverse event (SAE) in acute heart failure patients and can now be used in clinical practice to estimate the short-term risk of SAEs in acute heart failure patients. The prediction tool works even better when adding a simple blood test (NT-ProBNP). The OHFRS may therefore be useful to allow the safe discharge of patients with heart failure in the emergency department without hospital admission. That is the main finding of a study to be published in the March 2017 issue of *Academic Emergency Medicine*, a journal of the Society for Academic Emergency Medicine. The new study suggests that with adequate physician training, OHFRS will be a useful tool for making rational disposition plans in the ED and should help improve and standardize admission practices, diminishing both unnecessary admissions for low-risk patients and unsafe discharge decisions for high-risk patients and ultimately leading to improved safety for patients and more efficient use of precious hospital resources.

Hydraulic forces key to filling heart with blood

Researchers at Karolinska Institutet and KTH Royal Institute of Technology in Sweden have contributed to a recent discovery that the heart is filled with the aid of hydraulic forces, the same as those involved in hydraulic brakes in cars. The findings, which are presented in the journal *Scientific Reports*, open avenues for completely new approaches to the treatment of heart failure. The mechanisms that cause blood to flow into the ventricles of the heart during the filling, or diastolic, phase are only partly understood. While the protein titin in the heart muscle cells is known to operate as a spring that releases elastic energy during filling, this new research suggests that hydraulic forces are equally instrumental. Hydraulic force, which is the pressure a liquid exerts on an area, is exploited in all kinds of mechanical processes, such as car brakes and jacks. In the body, the force is affected by

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the blood pressure inside the heart and the size difference between the atria and ventricles. During diastole, the valve between the atrium and the ventricle opens, equalizing the blood pressure in both chambers. Therefore, the geometry of the heart determines the magnitude of the force. Hydraulic forces that help the heart's chambers to fill with blood arise as a natural consequence of the fact that the atrium is smaller than the ventricle. Using cardiovascular magnetic resonance (CMR) imaging to measure the size of both chambers during diastole in healthy participants, the researchers found that the atrium is smaller effectively throughout the filling process. If the atrium gets larger in proportion to the ventricle, it reduces the hydraulic force, and thus, the heart's ability to be filled with blood. "Although this might seem simple and obvious, the impact of the hydraulic force on the heart's filling pattern has been overlooked," says Martin Ugander, one of the authors of the study who heads a research group in clinical physiology at Karolinska Institutet. "Our observation is exciting since it can lead to new types of therapies for heart failure involving trying to reduce the size of the atrium."

Sickle cell gene therapy

Researchers have disclosed a case report of a patient with sickle cell anemia who experienced "complete clinical remission with correction of hemolysis and biologic hallmarks of the disease" after being treated with ex vivo gene therapy. Sickle cell anemia is a life-shortening disorder caused by a point mutation in the gene for beta globin, with the only cure currently being bone marrow transplant – itself a high-risk procedure even if a matched donor can be found. Researchers from the French Neck Children's Hospital and Brigham and Women's Hospital treated the bone marrow of a 13-year-old boy with Lentiglobin BB305 (Bluebird Bio Inc.) and transplanted him with the transformed cells. The boy, who had not been responsive to the standard therapy of hydroxyurea, had "no sickle cell disease-related clinical events or hospitalization" in the 15 months following his transplantation and was able to discontinue all medications, including pain medication. The team published its results in the March 1, 2017, issue of the *New England Journal of Medicine*.