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CytoSorbents to treat cytokine storm with CytoSorb application

By OMAR FORD
***Medical Device Daily* Staff Writer**

The overproduction of cytokines by the immune system, often called "cytokine storm" is often present in many life threatening illnesses that are seen in the intensive care unit such as sepsis, burn injury, trauma, lung injury and pancreatitis. Cytokine storm often causes excessive inflammation that can trigger organ failure, the leading cause of death in the ICU. The current standard of care therapies are typically supportive care with little to no active therapies to battle the cytokine storm.

But one publicly traded med-tech company said that it has designed a solution, currently approved in Europe, that could help with the treatment of cytokine storm while potentially preventing or treating organ failure, and is now vying to get the product approved in the U.S. to treat sepsis.

See CytoSorbents Page 4

New AF technique shows promise for difficult-to-treat patients

By AMANDA PEDERSEN
***Medical Device Daily* Senior Staff Writer**

It's been almost a year since cardiac ablation device maker **nContact** (Morrisville, North Carolina), previously called nContact Surgical, dropped the surgical part of its name to reflect the company's evolution towards closed chest approaches to treat heart arrhythmias. The company's epicardial ablation technology has enabled a new epicardial-endocardial technique, known as the Convergent Procedure, which was recently evaluated by doctors in North Carolina to treat patients with atrial fibrillation (AF).

The 12-month physician study, published in the *Heart Rhythm Journal*, reported outcomes of 66% arrhythmia-free survival after a single procedure at one year in difficult to treat patients at **First Health of the Carolinas Moore Regional Hospital** (Pinehurst, North Carolina) and

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International report

Fujifilm and Mauna Kea enter strategic agreement in China

A *Medical Device Daily* Staff Report

Mauna Kea Technologies (MKT; Paris), a developer of optical biopsy products including Cellvizio, reported that Cellvizio has received State Food and Drug Administration (SFDA) approval in China. Concurrently, MKT has entered into a strategic partnership with **Fujifilm China** (Shanghai), a subsidiary of **Fujifilm** (Tokyo). The partners will work together to develop the Cellvizio market throughout China in various indications.

"We are pleased to add Cellvizio to our broad portfolio of endoscopic products that we offer physicians throughout China," said Koji Yokota, president of Fujifilm China. "Optical biopsies allow physicians to diagnose and treat their patients in real time and are a true differentiating factor

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Washington roundup

FTC advises Federal Circuit on standard-essential patents

By MARK McCARTY
***Medical Device Daily* Washington Editor**

The Federal Trade Commission has chimed in again on patents for technological standards, explaining in a Dec. 5 statement that it has filed a friend-of-the-court briefing to the Court of Appeals for the Federal Circuit addressing a case between **Apple** (Cupertino, California) and **Motorola** (Schaumberg, Illinois) dealing with the former's iPhones and iPads.

FTC's Edith Ramirez had testified earlier this year to Congress that patent holders have often charged more for licensing their products after those items become part of a technological standard, a practice she said could be addressed by the U.S. International Trade Commission,

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AHC Media

Agreements roundup

Theragenics to load/package Oncura brachytherapy seeds

A *Medical Device Daily* Staff Report

Theragenics (Buford, Georgia), a device company serving the surgical products and prostate cancer treatment markets, said it has signed a value-added loading services agreement with **Oncura** (Arlington Heights, Illinois), a unit of **GE Healthcare** (Chalfont, UK), to provide worldwide brachytherapy loading services to Oncura.

Under the three-year agreement, Theragenics will load and package Oncura manufactured brachytherapy seeds in prescription loaded needles, custom strands and other configurations. Oncura's iodine-125 brachytherapy seeds are used primarily in the treatment of early stage prostate cancer.

"This agreement is our first significant effort to provide value-added services for brachytherapy seed products manufactured by other suppliers," said Christine Jacobs, chairman/CEO of Theragenics. "Our fully integrated, ISO certified brachytherapy manufacturing and servicing capabilities are unique in the industry and allow us to branch out in new ways to find growth. Oncura, an acknowledged leader in brachytherapy for years, has recognized our unique capabilities and has entrusted us with loading services for their customers located around the world. We are thrilled to be expanding our relationship in this manner with Oncura and GE Healthcare."

Theragenics operates two business segments: its surgical products business and its brachytherapy seed business.

In other agreements and contracts news:

• **Galileo Analytics** (Washington) reported that the **American Society of Clinical Oncology** (ASCO; San Francisco) has selected the Galileo Cosmos platform to serve as an analytic component of the CancerLinQ prototype, the first phase of the society's multi-phase effort to build a rapid-learning system in cancer care.

Galileo will provide real-time visual data mining and advanced analytics within the de-identified data of the breast cancer-specific prototype. The ability to visually explore complex data and perform sophisticated analytics in real-time is at the essence of CancerLinQ.

ASCO's vision for CancerLinQ is a comprehensive, knowledge-generating computer network, which will pull in data from a variety of sources and make that data accessible and understandable to health care providers, researchers and patients. Through CancerLinQ, ASCO seeks to speed the generation of new knowledge and understanding, so the cancer community can learn from all patients, not just the small percentage who participate in clinical trials.

The development of the prototype will allow ASCO to determine and overcome technological barriers to creating a more robust system encompassing all types of cancer, as well as identify requirements around the use of data standards.

• **Vystar** (Atlanta), maker of the Vytex natural rubber latex, reported two significant relationships with durable medical equipment providers, **Specialized Sleep Diagnostics** (Atlanta), and **SleepRx** (Skokie, Illinois), for the southeastern U.S. region. Vystar says that with these two new relationships, its SleepHealth division will now offer a full range of sleep-related equipment and supplies to patients at sleep centers.

Vystar also entered into an agreement with SleepRx, which will offer similar DME supplies to patients in a SleepHealth managed clinic located primarily in South Carolina. ■

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Med-Tech Notes

Univita expands Bridges program

Univita Health (Scottsdale, Arizona) reported the national expansion of its evidence-based Bridges transition care program to support at-risk patients transitioning from the hospital to home. The program's home-based services and care coordination are designed to improve patient outcomes and reduce costly readmissions in line with the recently enacted Hospital Readmissions Reduction Program (Section 3025) under the Affordable Care Act.

"In partnering with health plans, we have seen success at reducing hospital readmissions by more than 30%. By expanding our transition care services to directly work with both hospitals and health plans throughout the United States, we are even better positioned to bridge the gap in care between the hospital and the home," said John Mach, MD, president of Univita's complex case management division. "The ability to expertly manage a patient's medical, cognitive and functional needs in the home has proven to be effective in promoting a full recovery and reducing hospital readmissions."

Working jointly with hospital medical staff and the patient's health plan, Univita's specially trained nurses consult with each patient and their family preceding the surgery, as well as in the hospital post-surgery to confirm understanding of the medications, discharge materials and follow-up instructions.

Univita provides home-based care management.

Alameda Medical gets STEMI designation

Alameda County Medical Center (Oakland) was designated a STEMI Receiving Center (SRC) and Cardiac Arrest Receiving Center (CARC) by the Alameda County Emergency Medical Services Agency.

Hospital officials estimate Highland will receive between 75 and 100 STEMI heart attack patients annually that in the past had to be transported to other hospitals. With the STEMI designation, the hospital says these patients will be able to receive care faster – a key factor in survival.

Alameda County Medical Center provides comprehensive, high quality medical treatment and compassionate care to all residents of Alameda County.

Molded Devices refines dip molding process

Dip molding may not be a term that readily comes to mind when surgeons begin complicated procedures. et without this process, many medical devices used daily in hospitals could not meet stringent certification requirements. Dip molding defines any process where a mold is dipped into a polymer for molding a part. The process begins with aluminum or steel mandrels, or molds, on a handling rack. The rack is preheated then dipped into a substance such as Plastisol, latex, neoprene, urethane, or other material for a specified amount of time. The newly formed parts are then cured, dip-quenched and stripped off the mandrels and delivered to medical equipment manufacturers in the quantity required.

Over the years, **Molded Devices** (Riverside, California) said that it has refined its dip molding process to eliminate drip marks and other similar flaws.

Molded Devices said that it is one of only a few companies in the United States that can offer dip molding, dip coating (a similar process in which a metal part is dipped directly into Plastisol or other material), and injection molding capabilities.

Medical Metrics to support MoM trials

Medical Metrics (MMI; Houston), a provider of imaging core lab services for orthopedic clinical trials, has been selected by five orthopedic device manufacturers to support multiple cross-sectional, post-market, FDA surveillance studies of metal-on-metal (MoM) hip implants. MMI will independently evaluate radiographs and MRI to assess long-term outcomes in patients implanted with MoM hips. Over 2,000 subjects will be evaluated at one to ten years post-implantation.

Grants roundup

BrainStorm Cell Therapeutics receives 3 million NIS grant

A *Medical Device Daily* Staff Report

BrainStorm Cell Therapeutics (New York), a developer of adult stem cell technologies for neurodegenerative diseases, said that its Israeli subsididary, Brainstorm Cell Therapeutics Ltd (Petach Tikvah, Israel), was awarded a 3 million NIS grant from Israel's Office of the Chief Scientist (OCS) for the year 2013. The grant is intended to support BrainStorm's research and development program for its stem cell therapy candidate NurOwn.

"We are thankful to the OCS for its continued support of our Research and Development program. The non-dilutive capital funding from the OCS will help facilitate continuation of our clinical trials in Israel, as well as our preparations for clinical trials in the USA," said Adrian Harel, BrainStorm's CEO.

The OCS has supported BrainStorm Cell Therapeutics Ltd. since 2007, providing grants of a total of $18 million until today. The company is required to pay royalties to the OCS, amounting to 3% - 3.5% of revenues derived from sales of the products funded with these grants, but only up to the amount equal to 100% of the grants received plus LIBOR interest. ■

CytoSorbents

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CytoSorbents (Monmouth Junction, New Jersey) has developed CytoSorb, a device that uses polymer beads that capture cytokines to help stabilize the patient in the ICU, preventing this inflammatory response and allowing the patient to heal. Current sepsis treatments are based on the thesis of keeping the patient stable, but they don't address the underlying problem – those cytokines.

CytoSorb attaches to any typical hemodialysis machine, which is common practice in the ICU, and requires no additional equipment to operate. It is simply an adjunct filter that is specifically designed to capture cytokines and other mid-sized toxins in these polymer beads, preventing them from creating an uncontrolled inflammatory response in a body that has undergone massive injury or infection.

The company said that CytoSorb therapy is gentle, well-tolerated, and has been used in more than 650 human treatments without serious device-related adverse events.

Aside from a slight reduction of platelets as seen with all extracorporeal therapies, standard hematology and chemistry panels were unaffected.

The product received CE mark approval last year and the company is now gearing up for a trial in the U.S. (*Medical Device Daily*, April 1, 2011). The company launched the product in Germany, Austria and Switzerland in 3Q12.

"We currently have an IDE approval to run a small sepsis trial in the U.S. and we're looking to take the safety and efficacy data we've obtained in our European studies and bring it back to the FDA to negotiate a pivotal trial in the U.S," Dr. Phillip Chan CEO of CytoSorbents told *Medical Device Daily*. "Hopefully the trial will begin late next year or sometime in 2014."

Data from the European Sepsis Trial suggest that CytoSorb treatment has a protective benefit, particularly in patients with high cytokine levels. The company said that as expected, there is a correlation between clinical outcome and highly elevated levels of IL-6 (≥1,000 pg/mL) and/or IL-1ra (≥16,000 pg/mL), which are both known independent predictors of mortality in sepsis.

In these patients, CytoSorb cytokine reduction showed; both improvement in respiratory function with fewer patients on mechanical ventilation at 28 days: 33% vs 88% control, p=0.09), and fewer days in the ICU (24 vs 28 days control). Data also reveals statistically significant absolute reduction in 28-day all-cause mortality (0% vs 63% mortality control, p=0.03, n=14), and a trend to benefit in 60-day mortality (17% vs 63% control, p=0.14, n=14).

"This is why CytoSorb is potentially such a revolutionary product," Chan said. "CytoSorb has now demonstrated the ability to safely control cytokine storm in critically ill patients, with promising early clinical efficacy data in survival and treating organ failure"

As to when the device could be available on the U.S. market, Chan remarked that it could be a few years out.

"In the U.S. we're looking at a 2016 or a 2017 timeframe in terms of getting a pivotal trial done, moving through what should be an accelerated approval process, and hopefully getting CytoSorb to the market," he said.

The company has recently landed a great deal of support.

In September, CytoSorbents was awarded $1 million in Phase I & II Small Business Innovation Research awards from the U.S. Army to develop its technology to help treat burn injury and trauma patients with rhabdomyolysis.

In August, the company said that the U.S. Defense Advanced Research Projects Agency (DARPA), awarded it a $3.8 million five year contract to remove cytokines and toxins as part of DARPA's "Dialysis-Like Therapeutics" program to treat sepsis.

CytoSorbents is a critical care-focused publicly traded company using blood purification to treat life-threatening illnesses. The company went public in 2006. ■

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Financings roundup

Investors to acquire nearly $7.2M in OncoSec Medical security shares

A *Medical Device Daily* Staff Report

OncoSec Medical (San Diego), a company developing its advanced-stage ImmunoPulse DNA-based immunotherapy and NeoPulse therapy to treat solid tumor cancers, said that it has entered into definitive agreements with institutional investors to purchase about $7.2 million of securities in a registered public offering.

OncoSec has agreed to sell to institutional investors an aggregate of 28 million shares of its common stock at 25 cents per share. Additionally, investors will receive warrants to purchase up to 14,400,000 shares of common stock at an exercise price of 26 cents per share for a term of four years.

The gross proceeds of the offering are expected to be approximately $7.2 million. Net proceeds, after deducting the placement agent's fee and other estimated offering expenses payable by OncoSec, are expected to be approximately $6.5 million.

OncoSec intends to use proceeds from the offering for general corporate purposes, including clinical trial expenses and research and development expenses.

Dawson James Securities, acted as the exclusive placement agent for the transaction. Burrill LLC and Noble Financial Capital Markets acted as financial advisors to OncoSec in connection with the transaction.

The offering is expected to close on Dec. 17, subject to customary closing conditions. ■

nContact

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UNC Heart & Vascular Clinic at the **University of North Carolina-Chapel Hill**. The patients enrolled in the study had multiple risk factors and were considered the most difficult patient cohort to date, the researchers noted.

Jim Whayne, VP of research and clinicals at nContact, told *Medical Device Daily* that the study continues the evolution of this multi-disciplinary approach and highlights how multi-disciplinary treatments can benefit healthcare. "I think that's one of the trends we're seeing throughout medicine is taking best practices of several disciplines and combining them into a collaborative effort," Whayne said.

The study included 101 patients, all of whom had AF with disabling associated symptoms and had previously failed medical management with a class I or class III antiarrhythmic medication. Most of the patients in the study, 84%, had persistent or long-standing persistent AF and with an average CHADSVASC score of 21. Patients were followed with 24-hour Holter monitors at three, six, and 12-month intervals.

"The Convergent Procedure was used with success in the most difficult-to-treat patient cohort to date," said Paul Mounsey, MD, PhD, professor and director of electrophysiology in the Department of Medicine, Division of Cardiology at the University of North Carolina-Chapel Hill. "To see such an improvement in survival outcome analysis is significant, given it is one of the most stringent reporting standards. Survival outcome analysis is an unusual standard for the primary endpoint of a paper. Utilizing more traditional endpoints such as freedom from AF, the outcomes would have been 79% at one year."

Epicardial access is gained through a small midline incision in the abdomen allowing entrance through the diaphragm to the atrium. By utilizing direct endoscopic visibility and epicardial ablation, the posterior wall can be electrically isolated. The wall is considered a key location for arrhythmogenic substrates in persistent and long standing persistent patients. Isolating the posterior wall of the atrium is a key advantage of the surgical portion of the procedure.

The primary advantage of the Convergent Procedure is using a multi-disciplinary approach to ensure more comprehensive and complete treatment. In the combined approach, all areas of the heart can be reached and addressed, while a system of diagnostic checks and balances can be used to ensure electrical isolation of the posterior and pulmonary veins as well as lesion completeness to predict outcome.

Whayne said a key component of the technique is the direct endoscopic visualization that enables the physician to see the lesions they are creating, allowing for precise and appropriately-placed lesions.

"The Convergent Procedure has been an important addition to my practice, enhancing my ability to treat and provide a better standard of care for the more persistent AF patient population," Mounsey said. "The Convergent Procedure is the least invasive epicardial-endocardial procedure for the treatment of atrial fibrillation as it does not require chest incisions, ports or lung deflation, which can increase recovery times significantly."

nContact's lead technologies the EPi-Sense and Numeris Coagulation systems with VisiTrax, have CE mark approval in Europe for the coagulation of cardiac tissue for the treatment of atrial fibrillation and atrial flutter. In the U.S., these systems are indicated for endoscopic coagulation of cardiac tissue. ■

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HIT roundup

TriZetto launches integrated software, services solution

A *Medical Device Daily* Staff Report

The TriZetto Group (Denver) reported the availability of an integrated software and services solution for consumer operated and oriented plans (CO-OPs), offered at a monthly subscription price. The solution will provide the technology and staffing infrastructure that these nonprofit health plans need to administer benefits and care and enroll members by October 2013 for January 2014 effective dates.

TriZetto's platform will give CO-OPs the flexibility to administer value-based benefits and reimbursement arrangements and the functionality participate in state health insurance exchanges.

"TriZetto alone offers three advantages to CO-OPs," said Rob Scavo, TriZetto's regional accounts market president. "One, a reliable technology and staffing infrastructure used by hundreds of healthcare payer organizations, including most of the country's nonprofit health plans. Two, a solution that manages population health transparently and engages consumers and providers in making the most informed decisions about care. Three, a nimble, flexible and functionally rich platform that deploys quickly, enables participation in state exchanges and supports innovative, emerging models of care delivery. With TriZetto's solution, CO-OPs can get a quick jump out of the starting blocks." ■

International

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in endoscopy. Cellvizio will complement and enhance our own proprietary suite of advanced endoscopic imaging devices and systems."

Fujifilm benefits from an exponential growth in its endoscopy market in China and has established strong distribution network all over the country. There are 800 advanced endoscopy centers in tertiary referral hospitals in China, which will constitute the primary target for Cellvizio.

"Fujifilm is the ideal partner to help us penetrate the Chinese market and offer physicians across the most populous country in the world access to Cellvizio," said Sacha Loiseau, CEO of Mauna Kea Technologies. "Chinese endoscopists have been eagerly waiting for Cellvizio to be available in China. SFDA approval is a significant milestone for the company and strengthens our footprint around the globe, since Cellvizio is now available in more than 40 countries and used by hundreds of physicians."

Dehaier in medical equipment procurement accord

Dehaier Medical Systems (Beijing), a developer of medical devices and homecare medical products, reported that it has obtained a medical equipment procurement agreement valued at approximately RMB 2 million. The procurement agreement is with **Beijing Kanglian Medicine Co.** and is part of the **China Development Bank**'s (CDB) Rural Medical and Healthcare Infrastructure Project in Longhua County, Hebei province.

Ping Chen, chairman/CEO of Dehaier said, "Dehaier has implemented several Rural Medical and Healthcare Infrastructure Projects with Beijing Kanglian Medicine Company. This cooperation has given us valuable experience in bidding, implementation and after-sales service for these government-initiated projects. In accordance with the CDB's mandate to support rural medical and healthcare construction, the CDB plans to offer preferential loans worth RMB 7 billion in the aggregate to county medical institutions and clinics, which will facilitate purchases by county hospitals of medicine and medical equipment. Looking at current policies and trends, we believe the government will continue to invest more capital and resources into medical and healthcare infrastructure programs. For this reason, we will keep focusing on this area for future opportunities."

MediPendant coming to China

Medical Alarm Concepts (King of Prussia, Pennsylvania) reported it has signed a marketing and operations agreement with **JTT-EMS LTD** (Shijiazhuang, China) to bring the MediPendant personal medical alarm to the People's Republic of China. This agreement follows the recent shipments of product to Denmark and the consummation of an agreement with a large alarm company in Scotland, both with plans to begin marketing the MediPendant in 1Q13.

The parties have started the planning process with an initial strategy of offering the MediPendant in select cities in China. They plan to provide monthly monitoring services within a new joint venture business arrangement.

"JTT-EMS is a well established operation that employs several personnel who are very familiar with the features and functions of the MediPendant," said Ronnie Adams, CEO of Medical Alarm Concepts. "We believe this joint venture allows us a ground floor opportunity in one of the fastest growing and largest markets in the world. China is our third international opportunity, and we are very excited about our international expansion plans."

The MediPendant is a second-generation personal medical alarm and the only product in its category that allows for voice prompts and monitored, two-way communications directly through the pendant. Older generations of technology require the user to be in close proximity to the base station in order to speak and listen to the operator.

Covidien's Solitaire approved by Health Canada

Covidien (Dublin, Ireland), a provider of healthcare products, reported that the Solitaire FR Revascularization Device has been approved by Health Canada. The Solitaire FR device is used to restore blood flow to the brain in patients suffering from acute ischemic stroke.

An acute ischemic stroke can occur when a blood vessel that carries oxygen and nutrients to the brain is blocked by a clot and the flow of blood to the brain is interrupted. According to the Canadian Stroke Network's Burden of Ischemic Stroke (BURST) study, the healthcare costs for patients in just the first six months after they have a stroke is more than $2.5 billion a year in Canada.

"Stroke is a widespread public health issue, with approximately 50,000 Canadians experiencing a stroke annually," said Stacy Enxing Seng, president, Vascular Therapies, Covidien. "Solitaire FR is intended to transform the way this potentially fatal and often debilitating condition is treated."

The Solitaire FR device received CE mark approval in Europe and has been sold in that region by Covidien since November 2009. Solitaire FR is also available in the U.S., where it received FDA clearance in March. ■

Washington

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even if ITC needed a statutory assist for the authority to do so (*Medical Device Daily*, July 25, 2012). Ramirez cited interoperability as a situation in which such practices might arise, and mentioned *Apple v. Motorola* in this context.

FTC's latest statement argues that it is "ordinarily inappropriate for a court to issue an injunction barring the sale of products incorporating standardized, patented technology when the patent holder has previously committed to license the patent on fair and reasonable terms." The agency asserted further that a district court "correctly applied the governing legal principles when it dismissed Motorola's request for an injunction that could have blocked Apple from selling iPhones and iPads" in the U.S. over a standard-essential patent (SEP).

The statement indicates that FTC's *amicus* brief spells out the means by which owners of SEPs can use the threat of injunctions "to distort competition by insisting on high royalties and other favorable licensing terms" that the market would not have borne prior to the establishment of the standard. This kind of patent hold-up can be nettlesome where interoperability is concerned because "it becomes very difficult to change a technology in the standard without impairing interoperability" once the standard is adopted, FTC claims. The holder of the patented article can attempt to base its charges for licensing "not on the value of its invention, but on the costs and delays of switching away from the standardized technology," the agency says.

The FTC statement explains that a pair of factors arising in the Supreme Court decision in *eBay v MercExchange* should be considered by CAFC in its review of *Apple v Motorola*, one of which is a demonstration that that the patent holder "would be irreparably harmed without an injunction" against unlicensed practice of the patent. Part of this consideration is also the question of whether monetary relief – described parenthetically as "an ongoing royalty" – would suffice. However, FTC argues that both factors are "generally inconsistent with the underlying basis of" the reasonable and non-discriminatory terms for licensing of patented standards.

The other factor from *eBay* cited in the FTC statement was a consideration of whether the patent holder would suffer greater damage in the absence of an injunction than the purported infringer would upon the imposition of an injunction. FTC weighs in on behalf of the infringer, citing both the possibility that the infringer would be forced out of the market and that the public would be adversely affected "by losing access to the affected products."

FTC said its brief concludes that that the district court "properly applied *eBay* in determining that Motorola was not entitled to an injunction."

FDA inks draft guidance for home use devices

FDA has issued a draft guidance addressing design considerations for devices intended for home use, explaining that the scope of the guidance encompasses "both prescription and over-the-counter medical devices that are intended for home use." The guidance also addresses devices that are "likely to be used in the home" even if that setting is not the only setting intended setting for the device's use.

Among the considerations noted in the section dealing with device design are childproofing and tamper resistance, but the guidance also notes that airport security measures may also expose devices to a variety of radiant energy sources, including backscatter X-ray and millimeter wave technologies. Another consideration is the cognitive capability of the user, with the explanation being that some users "might have some type of cognitive impairment that could affect how they interact" with the device. FDA suggests that manufacturers "consider the amount of experience the users might have with a type of device and with similar devices, and how able and willing they might be to learn and adapt to using a new device."

Under the section dealing with design controls, FDA reiterates its concern over human factors engineering (HFE), stating that a validation study could be handled in an environment intended to simulate home use rather than a study in the home. The draft also makes reference to the guidance document on HFE from 2000, a tacit acknowledgement that the 2011 draft has not yet been finalized, although the home use devices draft includes a link to the 2011 HFE draft.

The passage dealing with medical device reports (MDRs) is remarkably brief given the frequency with which MDRs appear in warning letters. The draft includes nothing beyond boilerplate language regarding the necessity of filing such reports and a listing of contact information.

GAO: Medicare overspending on ESRD

The Government Accountability Office (GAO) took aim at Medicare drug spending for end-stage renal disease (ESRD) and found what it believes is a problem with the way the Centers for Medicare & Medicaid Services manages the program. According to GAO, CMS could have shaved as much as nearly $900 million off the cost of ESRD services last year with a little additional bundling.

GAO's Dec. 7 report says that use of ESRD drugs last year was roughly 23% below the amount spent in 2007, a difference said to have been driven "largely by a decline in the utilization of" erythropoiesis-stimulating agents (ESAs). The report speculates that CMS may have overpaid for dialysis care in 2011 because the bundled payment rate in use last year "was based on 2007 utilization levels."

The report says that Medicare spending on dialysis would have been between $650 million and $880 million lower last year "if the bundled payment rate were re-based

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Product Briefs

• **Biosensors International** (Singapore) reported enrollment of the first patient in LEADERS FREE, a study involving BioFreedom, the polymer-free drug-coated stent (DCS) from Biosensors. LEADERS FREE is the world's first prospective, randomized double-blind trial exclusively involving patients at high risk of bleeding. The study has been designed to confirm that BioFreedom is as safe as a bare-metal stent (BMS) in this patient group, and can deliver the anti-restenotic benefit of a drug-eluting stent (DES), with only a one-month course of DAPT. BioFreedom represents the latest development in Biosensors' stent technology, featuring a micro-structured abluminal surface which permits the controlled release of Biolimus A9 (BA9) without the use of a polymer. BA9 is a highly lipophilic anti-restenotic drug developed by Biosensors specifically for use with stents. The first patient has been enrolled by the study's Principal Investigator Dr Philip Urban at the Hôpital de la Tour, Geneva."The results of this study will be particularly important as we hope that they will show, for the first time, that a drug-coated stent can be more effective than a bare metal stent in a subgroup of patients not previously studied, yet just as safe", Urban commented. "This study could therefore potentially change clinical practice by permitting the use of a drug-coated stent in conjunction with one month's DAPT duration." LEADERS FREE is in the process of enrolling about 2,500 patients identified as having a high risk of bleeding from 60 sites across Europe, Asia and South America, with follow-up for two years. Patients in both arms of the study are being prescribed only one month of DAPT. The co-primary endpoints of the study are: 1) non-inferiority of BioFreedom compared with BMS as measured by specific safety factors (cardiac death, myocardial infarction, and definite/probable stent thrombosis) after one year and; 2) superiority over BMS in terms of clinically-driven TLR at 12 months. Investigators anticipate completing the enrollment process by early 2014. Primary endpoint data is likely to be presented during 2015.

• **Cerus** (Concord, California) reported that the FDA has accepted its proposed modular premarket approval application (PMA) shell for review of the Intercept blood system for plasma. A PMA shell is an outline of the application process that defines the structure, content and timing of each module. FDA and the applicant need to agree on a shell prior to initiation of a modular PMA submission. "Our PMA shell proposal was designed to leverage our existing regulatory dossier from European approvals and to begin the Intercept plasma regulatory submission in Q1 of 2013," said Carol Moore, Cerus' VP, regulatory affairs, quality and clinical. "FDA's agreement with our proposal means that we can target completing all four modules in 2013, putting us in a position to receive U.S. approval as early as 2014." Cerus recently announced its intention to pursue a modular PMA submission after dialogue with the FDA indicated that the company could proceed with an application for multiple indications of plasma use, not just the thrombotic thrombocytopenic purpura (TTP) indication for which Cerus received orphan drug designation last year.

• **Lumetrics** (Rochester, New York), a manufacturer of measurement technology began shipment of the first four of its CLAS wavefront aberrometer products. Lumetrics acquired this patented technology from Abbott in June of 2012. These products formerly had been sold under the WaveFront Sciences name. Lumetrics has spent the past six months integrating the WaveFront products into their manufacturing system, ordering components, and developing technology to repeatably build and test systems. The first products released were the CLAS-XP wavefront sensors used to characterize optics and laser beams. The systems are intended to reduce inspection costs, improve yields, and satisfy stringent requirements for new and existing products.

People in the News

• **The DePuy Synthes Companies** (Raynham, Massachusetts) of **Johnson & Johnson** (New Brunswick, New Jersey) reported that Max Reinhardt has been named worldwide president of DePuy Synthes Spine. Reinhardt has been with the company since 2002, most recently as VP of worldwide marketing. DePuy Synthes Spine is part of the DePuy Synthes Companies, which offer treatments and solutions that span joint reconstruction, trauma, spine, sports medicine, neurological, craniomaxillofacial, power tools and biomaterials.

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to reflect the 2011 utilization level of ESRD drugs." GAO indicated more savings may be in the offing, remarking that preliminary data hint that "potential savings could be larger in future years if the level of ESRD drug utilization at the end of 2011 declines further."

CMS officials are said to have signaled that there is no immediate plan to re-base ESRD rates, in part because the agency is not legally empowered to do so. GAO suggested Congress consider a mandate to the Secretary of Health and Human Services to re-base ESRD bundled payment rates "as soon as possible and on a periodic basis thereafter, using the most current available data." ■

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MDD's Diagnostic Extra

Additional Developments in One of Med-Tech's Key Sectors

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Keeping you up to date on recent developments in diagnostics

UCLA researchers demonstrate prostate cancer can be diagnosed via biopsy . . . Ground-breaking research by a **University of California Los Angeles** (UCLA) team of physicians and engineers demonstrates that prostate cancer can be diagnosed using image-guided targeted biopsy. Traditionally found only by blind biopsy, a procedure that dates from the 1980s, prostate cancer now appears detectable by direct sampling of tumor spots found using Magnetic Resonance Imaging (MRI) in combination with real-time ultrasound, according to the UCLA study released Dec. 10, 2012 early online for the January 2013 issue of *The Journal of Urology*. The study indicates that the MRI and ultrasound fusion biopsy, which is much more accurate than conventional blind biopsy, may lead to a reduction in the numbers of prostate biopsies performed and allow for early detection of serious prostate cancers. The study involved 171 men who were using active surveillance to monitor slow growing prostate cancers or men who had persistently elevated prostate specific antigen (PSA) – a protein produced by the prostate that can indicate the presence of cancer – but had prior negative biopsies. The UCLA biopsies were done in about 20 minutes in an outpatient clinic setting under local anesthesia. Elevations in serum PSA level trigger nearly all of the one million prostate biopsies performed in the U.S. every year. Annually, about 240,000 new cases of prostate cancer are discovered. Thus, about 75% of the biopsies are negative for cancer. However many of those men with negative biopsies but elevated PSA levels may still harbor malignant tumors that were missed by conventional biopsies, said study senior author Leonard Marks, MD, a professor of urology and director of the UCLA Active Surveillance Program. "Early prostate cancer is difficult to image because of the limited contrast between normal and malignant tissues within the prostate," Marks said. "Conventional biopsies are basically performed blindly, because we can't see what we're aiming for. Now, with this new method that fuses MRI and ultrasound, we have the potential to see the prostate cancer and aim for it in a much more refined and rational manner." The new targeting process is the result of four years of work funded by the National Cancer Institute and based in the Clark Urology Center at UCLA. Since the mid-1980s, prostate cancer has been diagnosed using trans-rectal ultrasound to sample the prostate. Unlike most other cancers, prostate cancer is the only major malignancy diagnosed without actually visualizing the tumor as a biopsy is done, Marks said. With the advent of sophisticated MRI, imaging the prostate improved and provided a picture of tumors within the organ. However, trying to biopsy the prostate with the patient inside the MRI has proved to be cumbersome, expensive and time consuming. Thus the fusion process evolved, permitting the targeted biopsy to be done in a clinic setting.In this study, the volunteers undergo MRI first to visualize the prostate and any lesions. That information is then fed into a device called the Artemis, which fuses the MRI pictures with real-time, three-dimensional ultrasound, allowing the urologist to see the lesion during the biopsy."With the Artemis, we have a virtual map of the suspicious areas placed directly onto the ultrasound image during the biopsy," Marks said. "When you can see a lesion, you've got a major advantage of knowing what's really going on in the prostate. The results have been very dramatic, and the rate of cancer detection in these targeted biopsies is very high. We're finding a lot of tumors that hadn't been found before using conventional biopsies."

Researchers develop novel 3-D culture system for inflammatory breast cancer . . . Inflammatory breast cancer (IBC) is a very rare and aggressive disease that progresses rapidly and is associated with a very low survival rate. To understand how this type of cancer spreads, it's crucial to characterize the interactions between cancer cells and their 3-D environment. Researchers at **Fox Chase Cancer Center** (Philadelphia) have developed a novel, 3-D culture system that mimics the environment surrounding these cancer cells. This model could be used to test new anticancer drugs capable of inhibiting the spread of IBC tumors. "The tumor microenvironment plays a pivotal role in tumor development and progression, and it also plays a big role in restricting tumorigenesis," says senior study co-investigator Edna Cukierman, PhD, Associate Professor of Cancer Biology at Fox Chase. "So understanding the interactions between the tumor and the environment will help us to come up with new ways to target the tumor." K Alpaugh, a co-author in this collaborative work, will present the study findings at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium on Dec. 8, 2012. For the study, Cukierman, a tumor

microenvironment expert, and her colleagues in the lab of Massimo Cristofanilli, MD, Professor at Fox Chase and a leading expert in inflammatory breast cancer, used tumor-associated stromal cells from patients with advanced IBC to build a 3-D structure consisting of cell-derived extracellular matrix – scaffold that provides structural and biochemical support to cells. After culturing a plethora of established and patient-derived cancer cells in the stromal 3D system, the researchers categorized them into two groups. While some cells showed a significant increase in proliferation and resembled those seen in aggressive tumors, others were more similar to cells in less-aggressive tumors. These two types of cells modified the extracellular matrix in distinct ways, indicating that there is a dynamic interplay between cancer cells and the microenvironment. Moreover, exposure to the matrix caused all of the cancer cells to increase their expression of the protein epithelial cadherin (i.e., E-Cadherin), whose levels are often elevated in IBC tumors. These findings suggest that the microenvironment may promote the proliferation, growth and invasion of IBC tumors.

News study shows greater accuracy in predicting Alzheimer's by combining diagnostic tests . . . Employing a combination of imaging and biomarker tests improves the ability of doctors to predict Alzheimer's in patients with mild cognitive impairment, according to researchers at **Duke Medicine** (Durham, North Carolina). The findings, which appeared in the journal *Radiology*, provide new insight into how to accurately detect Alzheimer's before the full onset of the disease. Duke researchers studied three tests - magnetic resonance imaging (MRI), fluorine 18 fluorodeoxyglucose positron emission tomography (FDG-PET), and cerebrospinal fluid analysis – to determine whether the combination provided more accuracy than each test individually. The tests were added to routine clinical exams, including neuropsychological testing, currently used to diagnose Alzheimer's disease. "This study marks the first time these diagnostic tests have been used together to help predict the progression of Alzheimer's. If you use all three biomarkers, you get a benefit above that of the pencil-and-paper neuropsychological tests used by doctors today," said Jeffrey Petrella, MD, associate professor of radiology at Duke Medicine and study author. "Each of these tests adds new information by looking at Alzheimer's from a different angle." Alzheimer's disease affects more than 30 million people worldwide, and the number is expected to triple by 2050. Research suggests that Alzheimer's begins years to decades before it is diagnosed, with patients experiencing a phase with some memory loss, or mild cognitive impairment, before the disease's full onset. Patients with mild cognitive impairment are at a higher risk for having Alzheimer's, but not everyone will progress to developing the disease. While there is no cure for Alzheimer's, new treatments under study are likely to be most effective at the disease's earliest stages. Researchers are working to improve early detection of Alzheimer's, even before patients experience symptoms, but the disease remains difficult to diagnose and patients are often misclassified. "Misdiagnosis in very early stages of Alzheimer's is a significant problem, as there are more than 100 conditions that can mimic the disease. In people with mild memory complaints, our accuracy is barely better than chance. Given that the definitive gold standard for diagnosing Alzheimer's is autopsy, we need a better way to look into the brain," said P. Murali Doraiswamy, MBBS, professor of psychiatry and medicine at Duke and study author.

Sequenta reveals LympoSIGHT data at ASH . . . Sequenta (San Francisco) and their collaborators presented data from four new clinical studies in which the LymphoSIGHT method demonstrated superior sensitivity in measuring minimal residual disease (MRD) in bone marrow and peripheral blood from acute lymphoblastic leukemia (ALL) patients. The presentations were made at the 2012 **American Society of Hematology** (ASH; Washington) annual meeting in Atlanta this week. Combined with two studies previously published in BLOOD, a total of six clinical studies have firmly established the value of the LymphoSIGHT method for MRD assessment in adult and pediatric ALL patients and demonstrated more comprehensive MRD coverage compared to flow cytometric and allele-specific oligonucleotide polymerase chain reaction (ASO-PCR) methods. LymphoSIGHT is the core technology that serves as the basis for Sequenta's commercial product, ClonoSIGHT. "The studies presented at ASH, representing more than 300 ALL patient samples, form the basis of a strong clinical validation of our approach to MRD testing," said Sequenta CEO Tom Willis. "These and other ongoing studies make our ClonoSIGHT assay the only clinically validated sequencing approach to immune cell monitoring." "The value of MRD in making treatment decisions in ALL is now well established," said David Miklos, MD, PhD, Assistant Professor of Medicine at **Stanford University** (Stanford, California). "Sequenta's approach represents the future of MRD testing, allowing clinicians to monitor all disease clones in virtually all patients even when they are present at very low levels." ■

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