Revision Optics scores panel-free win at FDA with Raindrop approval

By Liz Hollis, Staff Writer

This fall, patients with presbyopia are slated to have a new treatment option after the FDA gave a green light Wednesday to Lake Forest, Calif.-based Revision Optics’ implantable Raindrop near vision inlay. It marks the first time the agency has approved a device that changes the shape of the cornea to improve vision.

The clear inlay – which is made of a hydrogel material – is indicated for use in patients who are between 41 and 65 and have not undergone cataract surgery and need reading glasses with +1.50 to +2.50 diopters of power. In patients with presbyopia, the lens becomes hardened and has trouble focusing on close-up objects. The inlay aims to reshape the curvature of the cornea, thus correcting the refractive error.

Medtronic files for FDA approval of ‘artificial pancreas’ technology

By Omar Ford, Staff Writer

Medtronic PLC’s lengthy journey to get its artificial pancreas on the market is finally coming close to fruition, and an FDA approval could occur sometime next year. A spokesperson for Medtronic, told Medical Device Daily, the Dublin, Ireland-based company recently filed for a PMA submission of its hybrid closed-loop system, a device that measures diabetics’ glucose levels and automatically administers insulin.

Brazilian med-tech industry beset by both political and economic crises

By Sergio Held, Staff Writer

BOGOTA, Colombia – Brazil’s political and economic crises are taking a heavy toll on the country’s med-tech industry. The Brazilian Alliance of the Innovative Industry of Health (ABIIS for its Portuguese acronym) highlighted the challenges facing the industry in a recent newsletter.

DIAGNOSTICS EXTRA

Staff Writer Omar Ford on one of med-tech’s key sectors

Read this week’s Friday Special
reached an agreement on terms for the settlement of the lawsuits between the companies, as well as the withdrawal from related proceedings in the U.S. Patent and Trademark Office. Nuvasive will make a one-time payment of $45 million to Medtronic, and the parties will release each other from any and all liabilities arising out of the litigation. As part of the settlement and in exchange for the one-time payment, Nuvasive and Medtronic also agreed to certain licenses and other rights, including a standstill of patent litigation and a dispute resolution process to address allegations of patent infringement going forward.

**PRODUCT BRIEFS**

The FDA approved Concordia International Corp.'s Photofrin 630 photodynamic therapy (PDT) laser. The Oakville, Ontario-based company said PDT with Photofrin is a light-based cancer treatment that combines its photosensitizing drug called Photofrin (porfimer sodium) with a specific type of light administered by a laser to attack cancer cells. The laser, which is designed to treat esophageal cancer, Barrett’s Esophagus, and non-small cell lung cancer. Concordia is also evaluating Photofrin as a rare disease product candidate through a phase III trial.

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**Exosome Diagnostics Inc.**, of Cambridge, Mass., entered into a collaboration with **Takeda Pharmaceuticals International Co.**, of Osaka, Japan, to develop an exosomal RNA sequencing platform for biomarkers. As part of the agreement, Exosome Diagnostics will establish a gene expression pipeline with Takeda that will use its exosomal RNA isolation technology, RNA-Seq biomarker discovery platform, proprietary algorithms, signal enhancement technology, and additional ancillary technologies for analysis of exosomal RNA. The goal of the pipeline is to develop a platform for serial analysis of gene expression patterns in patients with cancer, as well as additional disease states beyond oncology.

**Lantheus Holdings Inc.**, of North Billerica, Mass., reported the first commercial shipment of Xenon Xe 133 Gas (Xenon 133) using unprocessed radiochemical Xenon 133 supplied by the Institute for Radioelements (IRE) in Belgium. The commercial availability of Xenon 133 sourced from IRE supports Lantheus’ commitment to ensuring the medical community has continued reliable access to Xenon 133 through 2016 and beyond. Earlier this month, Lantheus received approval from FDA for IRE to be a supplier of unprocessed radiochemical Xenon 133 for processing and finishing by Lantheus. IRE’s supply will supplement and eventually replace Lantheus’ current Xenon 133 supply when the National Research Universal reactor in Canada no longer provides a regular supply of medical isotopes to the marketplace in October.

**Nuvasive Inc.**, of San Diego and **Medtronic plc**, of Dublin, reached an agreement on terms for the settlement of the previously disclosed patent infringement lawsuits between the companies, as well as the withdrawal from related proceedings in the U.S. Patent and Trademark Office. Nuvasive will make a one-time payment of $45 million to Medtronic, and the parties will release each other from any and all liabilities arising out of the litigation. As part of the settlement and in exchange for the one-time payment, Nuvasive and Medtronic also agreed to certain licenses and other rights, including a standstill of patent litigation and a dispute resolution process to address allegations of patent infringement going forward.

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**Medical Device Daily presents Patent Highlights**, an excerpt of the most important med-tech patents from this week’s Cortellis Patents Gazette. See the attachment at the end of this edition.
Revision  
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error that contributes to vision problems. Presbyopia is a normal part of aging, with bifocals and reading glasses serving as common treatment options. “Given the prevalence of presbyopia and the aging of the baby boomer population, the need for near vision correction will likely rise in the coming years,” said William Maisel, deputy director for science and chief scientist at CDRH. The inlay will give patients a new option for the surgical, outpatient treatment of the condition.

In a 373-subject study backing the PMA submission, 92 percent of patients included in the analysis had 20/40 vision or better at near distances with the inlay-implanted eye after two years, the FDA said.

The implantation procedure takes about 10 minutes, according to Revision. It involves the surgeon using a laser to create a flap in the cornea of the patient’s non-dominant eye. The surgeon inserts the implant and returns the flap into place. John Kilcoyne, president and CEO of Revision, said he expects commercialization activities to begin in the third quarter through a direct field salesforce. Further, he anticipates that a large number of patients – potentially 30 million – could see benefits from the device.

“We will do a national rollout on a very controlled basis during the first six months,” Randy Alexander, chairman of Revision, told Medical Device Daily. He added that the company hasn’t settled on pricing details at this time, but patients could expect costs to be in line with a Lasik procedure.

The FDA did not send the device for review by an advisory committee panel, thereby reducing the amount of time it will take to get the product to market. While the company had hoped for an approval later this year, a panel review likely would have pushed the process into 2017, said Mike Crompton, Revision’s vice president of regulatory affairs and quality assurance/chief compliance officer.

An FDA spokesperson told Medical Device Daily the agency didn’t refer the PMA application to the Ophthalmic Devices Panel, “because there were no new issues associated with this review since the information contained in the application substantially duplicates information previously reviewed by this panel. Therefore, the agency determined no new panel input was needed.”

Crompton told Medical Device Daily that the company had significant interaction with the FDA over the last few months, with the agency working hard to meet or exceed the MDUFA III review goal.

With the decision, Crompton believes the agency has struck the appropriate balance between gathering data in the pre-versus postmarket settings. He labeled the postapproval commitments “realistic” and “not unduly burdensome,” saying the company will continue to follow the cohort from the IDE study for an additional two years.

In addition, the company will conduct a study in the commercial setting that involves 528 eyes, tracking patients for 60 months. Crompton said this kind of monitoring was “realistic for the commercial setting.”

Revision also is studying Raindrop in patients who have undergone cataract surgery, with an IDE already having full approval. Eight sites already are involved in the three-year study, which began last year, with a target enrollment of 400 patients.

While not going into specifics, Alexander told MDD that the company will explore other conditions with its inlay. He added that the Raindrop launch is one of the most exciting he’s been involved in, given that there’s a big market for the problem that has few solutions for patients.

In addition to the U.S., the inlay has the CE mark, and has regulatory signoffs in South Korea, Australia, and New Zealand. Revision has attracted the attention in terms of big name investors. In July 2013, it announced it had raised $55 million in an equity financing, with existing investors Canaan Partners, Proquest Investments, InterWest Partners, and Domain Associates participating. New investors Johnson & Johnson Development Corporation and Rusnanomedinvest also came on board.

Revision does have some company in the presbyopia space. The FDA accepted the PMA application for Raindrop last November, about seven months after it approved Acufocus’ Kamra inlay. (Medical Device Daily, April 22, 2015.) Acufocus CEO Jim Mazzo told Medical Device Daily last year that the approval represented a “huge win” for the ophthalmology field, given its product was first-of-its-kind.

Unlike Raindrop, the Acufocus device does not reshape the cornea, but rather blocks peripheral light rays while allowing central light rays to pass through a small opening, with the goal of making nearby objects less blurry.

It wasn’t smooth sailing for Irvine, Calif.-based Acufocus, which experienced a rough hearing in front of an FDA advisory committee panel.

The panel gave an adverse vote on safety (5-4) but determined that it had demonstrated effectiveness in a 7-1 decision. In addition, the panel gave a favorable vote (4-3) that the benefits outweigh the risks. (See Medical Device Daily, June 10, 2014.)

PRODUCT BRIEFS

Nexstim Plc received a CE mark for it Navigated Brain Therapy (NBT) system for the relief of chronic neuropathic pain. Nexstim, of Helsinki, Finland, said the NBT system is based on navigation software that enables it to target the stimulating e-field using a patient’s own MRI scans.

Medtronic

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blood glucose levels in real time and automatically adjusts the amount of insulin it delivers.

The approval submission was based largely on strong data from a pivotal trial presented at the American Diabetes Association (ADA) Scientific Sessions, held in New Orleans, in June. Kyle Rose, a Canaccord Genuity analyst said results from the pivotal study were “likely the biggest product specific data presented” at this year’s ADA.

Results of the study show, compared to a two-week, pump plus continuous glucose monitoring (CGM) without automation phase, adolescents and adults spending three months on the hybrid closed loop system saw; a 0.5 percent reduction in insulin, bringing patients; a 44 percent reduction in time spent with low blood glucose; and a 40 percent decline in time spent in dangerous hypoglycemia.

Of the 124 patients in the trial, about 80 percent wanted to still use the device through the FDA’s continued access program, according to data presented at ADA.

Medtronic first gained access to the artificial pancreas technology through its $3.7 billion acquisition of Minimed Inc. nearly 15 years ago. Minimed’s main product was an external pump, worn on a patient’s belt, to administer insulin continuously to people with Type I diabetes. Since the Minimed acquisition, Medtronic’s other critical milestones in developing the artificial pancreas system include introducing an integrated insulin pump and CGM in 2006 and the introduction of low glucose suspend technology in 2009.

The current system up for FDA approval includes a glucose sensor that’s attached to the body and measures sugar levels just under the skin; an insulin pump that’s strapped to the waist; and an infusion patch with a small needle that’s connected to the pump with a catheter.

RENEWED FOCUS IN DIABETES MARKET

To date, the company has had a fairly successful track record with its diabetes program. In the most recent quarter ending May 31, Medtronic’s diabetes business took in $496 million in revenues. The unit accounted for about seven percent of Medtronic’s business and grew 10 percent last year, with insulin pump sales growing 30 percent outside the U.S.

“Medtronic clearly has a renewed focus on its diabetes franchise underscored by 20 planned new product launches in the next five years compared to just four new products in the prior five-year period,” said Rick Wise, an analyst with Stifel.

“Management outlined an extensive new product cadence over the next five years including pumps both new pumps and sensors. The company confirmed first closed loop insulin pump filing at the end of [June]. As well, Medtronic plans to launch multiple improved continued glucose monitoring sensors over the next five years including the 10-day wear, Harmony 1 in F2019.”

During ADA, Medtronic shed more light on those projects - specifically on the Sugarwise app it’s developing with Cambridge, Mass.-based IBM Watson Health. The app is expected to launch this summer for those using Medtronic’s Minimed Connect. The app will analyze past insulin, glucose, and food data and provide insights based on the patterns it recognizes.

While Medtronic might have a significant lead over firms developing closed-loop systems, it isn’t alone in its efforts to develop technologies for the diabetes treatment and management space. The market is set to reach $1.01 billion by 2024, according to a report published by Grand View Research Inc.

Just last week, Senseonics Inc., of Germantown, Md, received CE mark approval for its Eversense (CGM) system, featuring an implanted glucose sensor that lasts up to 90 days, or about six times longer than non-implantable systems currently on the market.

Earlier this month, San Diego-based Dexcom Inc. reported the FDA would hold a public advisory committee meeting to discuss a change to the intended use of its G5 Mobile (CGM) device. The change would allow the company to market the G5 as a CGM patients can base treatment decisions on.

Last year, Dexcom made another significant movement in the space, and revealed a partnership with Google Life Sciences to develop the next generation of a miniaturized glucose meter that could eventually replace the fingerstick method. (See Medical Device Daily, Aug. 12, 2015.) //

DAILY M&A

Luminex Corp., of Austin, Texas said it has completed its previously acquisition of Nanosphere Inc., of Northbrook, Ill. for $58 million. Its tender offer of $1.70 per share for all of the shares of Nanosphere expired as of midnight on June 29. According to Luminex, as of the expiration of the tender offer, a total of 45,252,609 shares were validly tendered and not withdrawn, representing a total of nearly 86 percent of Nanosphere’s outstanding shares. The company first revealed merger plans in late May.

Opko Health Inc., of Miami, reported that it will acquire Transition Therapeutics Inc., of Toronto. Under the terms of the agreement approved by the boards of both companies, Transition Therapeutics security holders will receive about 6.4 million shares of Opko common stock. Based on the moving average price of Opko common stock for the five trading days preceding the signing of the agreement, the transaction is valued at approximately $60 million, or $1.55 per share of Transition Therapeutics common stock, based on current outstanding shares.

CRE
Continued from page 1

assay that tests patient specimens for specific genetic markers associated with CRE. By testing a specimen taken directly from a patient (usually with a rectal swab), the new Xpert Carba-r is expected to drastically reduce the turnaround time of CRE detection compared to traditional cultural methods.

This regulatory milestone follows a March FDA clearance for Sunnyvale, Calif.-based Cepheid Inc.’s Xpert Carba-r test, but at that time the test could only be used to test pure bacterial isolates. David Persing, Cepheid’s chief medical and technology officer, said the test delivers a result in as little as 48 minutes whereas traditional enriched culture methods typically take between three and five days.

That means clinicians can assess high-risk patients for colonization status at, if not prior to, admission, Persing said. That helps hospitals to take preventative measures sooner, if necessary, to reduce infection risk to the patient, the broader patient population, and staff.

Carbapenem antibiotics are widely used in hospitals to treat severe infections, the FDA said, and CRE cases have been reported in almost all states within the U.S. According to the CDC, CRE infections are most commonly acquired in healthcare settings.

CRE are usually resistant to many other antibiotics in addition to carbapenems, the FDA said, and when bacteria become resistant to carbapenems, few treatment options may remain. Some CRE bacteria have become resistant to almost all available antibiotics, the agency said, which presents a significant public health threat.

Not only does it take up to five days to grow the bacteria from fecal material in cultures, but additional testing is often required to confirm that carbapenemase, an enzyme that inactivates carbapenem antibiotics, is present. However, Cepheid’s test should also be followed with bacterial cultural testing for epidemiological typing, antimicrobial susceptibility testing, and for confirmatory bacterial identification.

Cepheid’s test is designed to detect the presence of the five most prevalent genetic markers associated with carbapenemase, but it does not detect the bacteria, carbapenemase activity, or other possible non-enzymatic causes of carbapenem resistance, the FDA said.

In a recent series of special reports on the global threat of superbugs, Medical Device Daily’s Senior Science Editor Anette Breindl clarified that there is not yet a completely untreatable superbug. But that does not mean the mounting fear of these highly-resistant bugs are not justified. (See Medical Device Daily, June 21, 2016.)

“Surveillance is a key infection prevention activity for monitoring and controlling the spread of CPOs in hospitals and long-term care facilities,” said Lance Peterson, director of microbiology and infectious diseases research at Northshore University Health System. “Xpert Carba-r is the first real time [polymerase chain reaction] test for [carbapenemase-producing organisms] in the United States that can be performed on demand, thus facilitating surveillance studies.”

Xpert Carba-r adds to the Cepheid’s portfolio of Xpert tests. Other products in the portfolio target antimicrobial resistance. The test runs on the company’s GeneXpert System, and Cepheid said it will begin shipping Xpert Carba-r with the extended claim in July.

The FDA said data from two clinical studies supported its decision to clear the Xpert Carba-r for marketing. A prospective study used rectal swabs from 755 patients in hospitals or long-term care facilities to compare results from the Xpert Carba-r assay with results from reference cultures and automated real-time PCR sequencing. A second study designed to test the clinical performance of the Xpert Carba-r assay used 432 rectal swabs that were artificially prepared with specific concentrations of bacteria containing the genes detected by the test. The results of these studies demonstrated similar performance between the new assay and the culture method. //

FINANCINGS

Redwood City, Calif.-based Capnia Inc., which develops diagnostics, devices and therapeutics addressing unmet medical needs, entered into an agreement with an investor to purchase up to $13.8 million of series B convertible preferred stock. The sale of the preferred stock is expected to take place in two separate closings. Upon the first closing, which is expected to occur on or about July 5, 2016, the company will receive gross proceeds of about $3.2 million. Upon the successful completion of the second closing for up to $10.6 million, the full $13.8 million of preferred stock will be convertible into 13.78 million shares of the company’s common stock, based on a fixed conversion price of $1.00 per share on an as-converted basis. In addition, subject to shareholder approval, the company will amend its outstanding series D warrants to purchase 2,702,704 shares of common stock to reduce their exercise price to $1.75 per share. The company expects to receive gross proceeds from the offering of $13.8 million, with approximately $7.8 million of the proceeds from the offering being used to redeem 7,780 shares of series A convertible preferred stock held by the same investor. The balance of the proceeds, after offering expenses, will be used for general working capital purposes. Maxim Group LLC acted as exclusive placement agent for the transaction.
Regulatory
Continued from page 1

The AHRQ report, part of the agency’s Hospital Cost and Utilization Project (HCUP) series, stated that the $38 billion in costs that year, nearly two thirds (63 percent) of which was covered by the Medicare and Medicaid programs. Private payers made up 28 percent of the total, while uninsured care accounted for the remaining five percent.

The HCUP analysis demonstrated that septicemia rang up a bill of $23.7 billion in 2013 via nearly 1,300 hospital stays, while charges for treatment of osteoarthritis came in at a fairly distant second at $16.5 billion for roughly 1,020 stays. The cost of live birth placed third, but the fourth through sixth places were all occupied by treatment of cardiovascular conditions.

The category of “complication of device, implant or graft” was associated with more than $12.4 billion in spending in 2013, while acute myocardial infarction was right behind, accounting for nearly $12.1 billion. Congestive heart failure was predictably in the top 10, absorbing more than $10.2 billion in costs, which was good for sixth place.

The report’s authors pointed out that cardiovascular and respiratory system conditions accounted for nine of the 20 most expensive conditions paid for by Medicare – a group that includes COPD, pneumonia and heart valve disorders – while another three were associated with orthopedic issues and procedures. Cardiovascular and respiratory system made up seven of the 20 most expensive conditions paid for by private payers, although osteoarthritis, live births, and “back problems” were the top three.

Among the 20 most expensive hospital-treated conditions covered by private payers were maintenance chemotherapy and secondary malignancies, but neither of these showed up in the top 20 for Medicare or Medicaid. The report stated that private payers paid out nearly $1.2 billion “in aggregate hospital costs” for secondary malignancies, an amount nearly matched by maintenance chemotherapy, which generated in excess of $1.1 billion in aggregate hospital costs in 2013.

SSA FINALIZES NEUROLOGICAL DISORDER RULE

The Social Security Administration announced recently it has finalized a 2014 draft rule for evaluation of neurological disorders associated with disability claims, a rule that goes into force 90 days after the formal appearance of the rule in the Federal Register. The SSA noted that it had received in excess of 3,000 comments to the proposed rule, nearly a third of which arrived after the agency extended the comment period beyond the original 60-day window. The final rule noted that the SSA will take both medical and non-medical evidence in support of a claim of disability, but said that the use of MRI, CT or electroencephalography must be consistent “with the prevailing state of medical knowledge and clinical practice.”

FDA TOUTED AS CABINET-LEVEL AGENCY

Hierarchies are always interesting, but a recent panel discussion involving former FDA commissioners gave some insight into the thinking of half a dozen former FDA commissioners, who are apparently of the view that the FDA should report directly to the president of the United States instead of having to go through the Health and Human Services hierarchy.

The six former FDA commissioners, speaking at the Aspen Ideas Festival in Colorado recently, expressed their individual and collective frustration with their inability to get into the president’s ear. The latest commissioner, Robert Califf, is said to have passed on a chance to respond to such suggestions, but those who preceded him were less reticent.

David Kessler, the author of the notion of making warning letters publicly available, is quoted as having said at the session, “there are 150 people between you and the president, and they all think they’re your boss.” Kessler served as the commissioner between 1990 and 1997. Andrew von Eschenbach, who had directed the National Cancer Institute prior to taking the FDA job in 2005, cited a “structural problem” in that the agency is funded by the appropriations mechanism that also handles the Department of Agriculture despite being part of the HHS portfolio.

HQO SAYS NO TO ARGUS II

Health Quality Ontario (HQO) announced that the agency’s technology advisory committee recommended against coverage for the Argus II retinal prosthesis by Second Sight Medical Products Inc., of Sylmar, Calif. The agency noted that the device is the only implantable device approved by Health Canada for retinitis pigmentosa, leaving many residents of Ontario with no access to the device.

CMS approved a new technology add-on payment for the device for the fiscal year 2014 inpatient prospective payment system along with a pass-through payment for outpatient care, which seems to have had little influence on the outcome for the HQO advisory committee. However, the agency added that the device is not covered in any of the other Canadian provinces and territories, either.

The agency cited 10 reports on the device in the literature, the bulk of which addressed the Argus II International Study, although none of those entries in the literature captured outcomes for more than 30 enrollees. The HQO indicated that the evidence in support of improvement in visual function was moderate, while another study examining quality of life was also rated as moderate.

The HQO said the advisory committee recommended the agency review its stance again in a year. //
Brazil

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problems in a recent report.

According to data from the Brazilian Institute of Geography and Statistics (IBGE in Portuguese), the production of the Brazilian med-tech industry during the first quarter of 2016, fell by 11.2 percent in comparison to its performance during the first quarter of 2015.

“The economic crisis experienced in Brazil in several sectors has reached the segment of medical devices,” said the ABIIS. José Márcio Cerqueira, executive director at ABIIS, added that the “fiscal crisis stalled the payment capacity of the federation, the states and the municipalities to the Unified Health System [SUS in Portuguese]. The services [in the SUS] are impaired, as well as replacement supplies, vaccines, diagnostic tests in-vitro and medicines.”

Data from the IBGE shows a cumulative fall of 4.7 percent in med-tech production over the past 12 months. And it is not just production of medical devices and supplies that have been affected. IBGE’s consumption index suggests a decline of 14.2 percent in the first quarter of the year, compared to the same period in 2015 while the drop over the past 12 months adds up to around 13 percent.

“Unemployment has also reduced the number of beneficiaries of health plans and hence the capacity of service providers that cater to the private sector to invest in medical devices,” said Cerqueira.

According to the IBGE, Brazil’s unemployment rate has surged to over 11 percent, the worst figure since the index was launched in 2012. Surprisingly, however, employment in the Brazilian med-tech sector specifically is still showing mixed results.

Data from the Ministry of Labor and Social Security indicated that during the first quarter of the year, 194 jobs were created in the space for a total of 135,766. However, ministry data also suggested that 3,320 jobs were lost in the last 12-months, implying a loss of 2.4 percent of the jobs in the med-tech sector.

“If there is a slowdown in the sector, with a fall in economic indexes, there are naturally layoffs,” said Cerqueira. “However, if we assess the overall scenario, the index is not so bad,” he added.

For Cerqueira, the unique qualifications that med-tech professionals require also impact the performance of the space.

“The segment of medical devices employs people with high qualifications, and it is not uncommon to hear from companies that they have difficulties finding qualified professionals in the market, which indicates that there are unfilled vacancies,” he said.

While unemployment and industry data hint at the difficulties the country is experiencing, international trade figures confirm the desperate moment that the Brazilian med-tech industry and distributors are facing.

“In the first quarter of 2016, [the] sector accumulated a value of $1.2 billion in imports, down 14.5 percent from the same period in 2015 in all product groups, while in the 12-month period the decline reached 16.3 percent,” said ABIIS.

“Exports totaled $179.6 million in the first quarter of this year, representing a 21.9 percent decline over the same period of last year,” it added.

And it is not just the country’s ongoing political and economic crisis that is hurting the space. Cerqueira said the challenges are everywhere.

“[There are] pressures from all sides: complex and expensive regulations, serious problems with the delay in the release of medical devices at ports and airports, [the] tightening of prices for service providers who buy medical technology, delays in payments and restrictions on purchases for investment and replacement due to the crisis,” he explained.

After an indictment on corruption charges, on May 12, the Brazilian lawmakers took all power away from President Dilma Rousseff. Vice President Michael Temer assumed power and is acting as president of the country for 180 days, during this time, legislators will decide if Rousseff is guilty. If Rousseff is found guilty, Temer will hold the power until 2019, but if Rousseff is declared innocent, she will resume her post before the end of the year. //

FINANCINGS

Spirometrix Inc., of Pleasanton, Calif, a company developing novel breath analysis devices for applications in disease diagnosis and management, closed on $17.4 million in the first round of a series C financing. The financing was led by Shanghai Fosun Pharmaceutical (Group) Co., Ltd., with participation from return backers NGK Spark Plug Co., LTD (NTK); South Valley Angels; Iconical; Ohio Innovation Foundation; and, Carmen Innovation LLC.

APPOINTMENTS AND ADVANCEMENTS

Nonin Medical Inc., of Minneapolis, Minn., reported Matthew Prior has been named vice president of business development. Prior has served at Nonin for over 8 years and was previously the company’s vice president of product development. He holds a doctorate in physics from Duke University. Greg Rausch has been named vice president of product development. Rausch has served at Nonin for over six years and was previously the company’s director of advanced technology. Jill Wroblewski has been named senior director of marketing. Wroblewski has served at Nonin for over nine years and was previously the company’s director of business development.
Researchers identify molecular roots of lung damage in preemies with GI disease

Johns Hopkins researchers report they have figured out a root cause of the lung damage that occurs in up to 10 percent of premature infants who develop necrotizing enterocolitis, a disorder that damages and kills the lining of the intestine. The finding, they say, led them to identify and successfully test a potential treatment for the lung damage in a mouse, which may one day be offered to human infants. A summary of the research was published online June 15 in the Journal of Immunology. Necrotizing enterocolitis is marked by severe inflammation of the large and small intestine and bowel, striking an estimated 5 to 10 percent of babies born prematurely. The disease kills intestinal tissue and can damage other organs, leading to lifelong growth impairment and other disability. Some 40 percent of infants with necrotizing enterocolitis develop lung damage, and nearly 50 percent of patients who develop necrotizing enterocolitis will die, according to the study’s authors. Some that survive may not be able to breathe on their own for many months; others remain permanently disabled. In a bid to alter the grim numbers, a team from the Johns Hopkins Children’s Center built on an earlier discovery showing that one of the main drivers of necrotizing enterocolitis is a receptor on the surface of intestinal cells called Toll-like receptor 4, or TLR4. This receptor acts like a switch, which detects bacteria in the intestine and then releases chemicals to summon the immune system to attack. When the switch is turned on, necrotizing enterocolitis develops. To see if this same bacterial receptor was important for related damage in the lungs, the researchers in the new study genetically engineered mice that lacked this receptor in their intestinal lining. When they introduced gut bacteria from a mouse with the rodent form of necrotizing enterocolitis into the intestines of the mice without the TLR4 receptor, those mice didn’t develop lung damage. The investigators then created mice without the bacterial receptor in the cells lining the lungs. When they added gut bacteria from mice with necrotizing enterocolitis into those mouse intestines, the animals also failed to show lung damage. The researchers say other experiments showed that inflammation-promoting molecules like HMGB1 need to be released first from the intestines, which then leads to lung damage in mice with necrotizing enterocolitis. Because the main culprit behind the initiation of lung damage in mice was the TLR4 receptor, the researchers wanted to see if blocking this receptor from working in the lungs could stop lung inflammation and lung damage. In a study published last year, Hackam’s team reported the creation of a set of compounds that stuck to the TLR4 receptor in the same spots that detect bacteria, preventing the receptor from putting the immune system on alert. For the new study, the researchers tested one of those compounds, called C34, by aerosolizing it and having the preemie mice with necrotizing enterocolitis breathe it in daily through a tiny syringe for four days. The treated mice had less inflammation in the lung tissue, and their lung cells also turned on less inflammation-promoting chemicals.

Data competition and new diagnostic tools

Big data has a bright future in personalized medicine, as demonstrated by an international competition centered at Rice University that suggested ways forward for treatment of patients with leukemia. In the DREAM 9 challenge, 31 teams of computational researchers applied competing methods to a unique set of patient data gathered from hundreds of patients with acute myeloid leukemia at the University of Texas MD Anderson Cancer Center. Rice bioengineer Amina Qutub is principal investigator of the open-source paper published in PLOS Computational Biology. Rice served as the competition hub, in line with the university’s strategic initiative to foster bioscience collaborations with fellow Texas Medical Center institutions. DREAM, which stands for Dialogue for Reverse Engineering Assessment and Methods, is a platform for crowdsourced studies that focus on developing computational tools to solve biomedical problems. Essentially, it’s a competition that serves as a large, long-standing, international scientific collaboration. Acute myeloid leukemia presented a worthy challenge since there is no single genetic cause of the disease, which makes it hard to select treatments for patients suffering from the deadly cancer of the blood, Qutub said. The DREAM 9 patient data set was collected by Steven Kornblau, a leukemia doctor and professor at MD Anderson. The data was distributed to DREAM 9 participants online through Sage Bionetworks’ Synapse web portal and through Biowheel, a cloud-based technology launched by the Qutub Lab. Biowheel is an interactive tool to visualize and group high-dimensional data of all kinds. It was developed by Rice graduate student Chenyue Wendy Hu, undergraduate alumnus Alex Bisberg and Qutub. National Library of Medicine postdoctoral fellow David Noren and research scientist Byron Long, also of the Qutub Lab, are lead authors of the paper. For DREAM 9, each team was presented with training data from 191 patients that included demographic information like age and gender and more complex proteomic and phosphoprotein data that describes signaling protein pathways believed to play a role in the disease. The competition used a test data set from 100 patients that didn’t include outcomes, such as whether patients responded to therapy, relapsed, survived or died. The

Continues on next page
primary challenge was to see how well the teams’ algorithms could predict how patients responded to chemotherapy. The eventual goal is to give clinicians a predictive tool to develop individualized treatment plans.

**Which burn victims will develop sepsis?**

University of Birmingham researchers have created a potentially life-saving new test that will allow clinicians to predict which burn victims will develop sepsis during their treatment. Their findings, published in *Annals of Surgery*, show that using just three biomarkers of neutrophil function on the day of injury can determine which patients with major burn injuries are likely to become septic. In addition to its potential as a diagnostic marker for sepsis, the data highlights burn-induced neutrophil dysfunction as a potential therapeutic target to reduce susceptibility to bacterial infections and sepsis. The ground-breaking research was funded by the Healing Foundation Birmingham Centre for Burns Research, a partnership including University of Birmingham and University Hospitals Birmingham NHS Foundation Trust. Three potentially novel biomarkers of sepsis in burn injury were tracked — immature granulocyte (IG) count, neutrophil phagocytosis and plasma cell free DNA — with the combination of measurements displaying good discriminatory power to predict later development of sepsis, especially at one day after injury. The team will now look to carry out a trial in patients to see if the use of this new test will help to reduce the incidence of sepsis by allowing doctors to give antibiotics to patients promptly.

**Paper strips used to test for malaria, cancer?**

What if testing yourself for cancer or other diseases were as easy as testing your blood sugar or taking a home pregnancy test? In a few years, it might be. Chemists at The Ohio State University are developing paper strips that detect diseases including cancer and malaria — for a cost of 50 cents per strip. The idea, explained Abraham Badu-Tawiah, is that people could apply a drop of blood to the paper at home and mail it to a laboratory on a regular basis — and see a doctor only if the test comes out positive. The researchers found that the tests were accurate even a month after the blood sample was taken, proving they could work for people living in remote areas. The assistant professor of chemistry and biochemistry at Ohio State conceived of the papers as a way to get cheap malaria diagnoses into the hands of people in rural Africa and southeast Asia, where the disease kills hundreds of thousands of people and infects hundreds of millions every year. But in the *Journal of the American Chemical Society*, he and his colleagues report that the test can be tailored to detect any disease for which the human body produces antibodies, including ovarian cancer and cancer of the large intestine. The technology resembles today’s “lab on a chip” diagnostics, but instead of plastic, the “chip” is made from sheets of plain white paper stuck together with two-sided adhesive tape and run through a typical inkjet printer.

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WO2016100055-A1: “Drug delivery device with live button or user interface field.”

Assignee: Amgen Inc
Inventors: Gibson, Scott, R.; McCullough, Adam, B.
IPC Codes: A61M 5/145; A61M 5/32; A61M 5/142
Publication Date: 23-Jun-2016
Earliest Priority Details: US201494516, 19-Dec-2014

Drug delivery devices which have an activation button or user interface that indicates when the device is ready to deliver or inject and suggests the next step in the delivery or injection process. The device comprises a sensor that detects contact between the device and a body of a patient and which then activates the user interface or causes activation of the injection drive. Published alongside WO2016100781 in which McCullough describes a drug delivery device with proximity sensor. McCullough’s prior patenting has included descriptions for controllable drug delivery systems (WO2015187797), which may incorporate a sensor coupled to the drug delivery device and a controller coupled to the sensor, so as to determine the operational state of the drug delivery device.

The application’s disclosure suggests its potential use in the delivery of wide variety of APIs, but if one were to hone in on etanercept and pegfilgrastim, then one could draw a possible association to Amgen's Prefilled SureClick® Autoinjector for delivering Enbrel® (etanercept) and its Onpro™ On-body Injector for delivering Neulasta® (pegfilgrastim).

Assignee: Cerner Corp Pty Ltd
Inventors: Crough, Daniel Craig; Quick, Megan Kathleen; Ryan, Hugh H.
IPC Codes: G06N 7/00; G06F 19/00
Publication Date: 23-Jun-2016
Earliest Priority Details: US2014581052, 23-Dec-2014

Computerized system for predicting blood glucose levels. In November 2014, Cerner Corp, the electronic health records company and mHealth platform vendor which is headquartered in Kansas City, Missouri, announced a multi-year agreement with Livongo Health™ (headquartered in Mountain View, California) to connect diabetes screening data collected from "smart" consumer devices with Cerner health care clients. It was said that this could mean more effective self-management of diabetes and a better use of time with their clinician, and provide care teams with near real-time access to patient information, enabling quick interventions when a patient might be headed toward trouble.

Livongo's diabetes management program consists of connected devices, a smart cloud, and a virtual care team. The device, called In Touch, serves as both a connected glucometer and a pedometer and allows easy sharing of the data. It is a standalone cellular-connected device with a color touchscreen. The program also offers unlimited test strips at no extra charge. Using a combination of data from the device, electronic health records, and medication records Livongo performs data analytics and pushes out insights and alerts to the user, their friends and family, or their care team.

Prior patenting from Cerner Innovation can be seen to include descriptions of a health care biometric surveillance and online communication interface that could incorporate data from and feedback to a blood-glucose meter, see US20130030835.
An analyte measurement system which uses a test strip which has a coating on it which allows the capacitance of the test strip to be measured is described. The value of the capacitance determines the compatibility of the test strip to the analyte measurement device.

In the illustrations, batch 3374418 has a mercaptoethane sulfonate coating and batch 3310251 a mercaptopropane sulfonate coating. The difference in capacitance (Cap) of the strips is distinguishable (fig 3A), but strips with either coating give the same response in a glucose analysis test (fig 3B).

This continues Cilag’s interests in test strips which can be recognised by a test meter see for example WO2012028841. The present team of inventors appears to be based at LifeScan International (see also WO2016097051-A1 on possible improvements to glucose meters in this issue).
US20160175494-A1: “Medical devices for delivering a bioactive to a point of treatment and methods of making medical devices.”

Assignee: Cook Group Inc
Inventors: Gemborys, Colleen
IPC Codes: A61L 31/04; A61L 31/16; A61L 31/10; A61L 31/14; A61L 31/00
Publication Date: 23-Jun-2016
Earliest Priority Details: US201493684, 18-Dec-2014

Device for delivering a bioactive agent to a target site of treatment and methods for their production. The methods described provide flexibility in the performance of treatment procedures, as they may be undertaken well in advance of a treatment procedure or even be performed bedside in a hospital, immediately before use of the resulting medical device. It states that in cancer treatment procedures, this allows a caregiver to select a desired chemotherapeutic or immunotherapeutic bioactive for local delivery, make and immediately use the device.

It is claimed that the substrate comprises a biocompatible foam formed of expanded collagenous materials, such as expanded extracellular matrix (ECM) materials, with there being a particular focus on ECM materials derived from expanded small intestine submucosa. Whilst various bioactives are contemplated, there is a clear a focus on anticancer agents being delivered either singularly (eg paclitaxel or doxorubicin) or in combination (with only FOLFIRI (folinic acid with fluorouracil and irinotecan) and FOLFOR (folinic acid with fluorouracil and oxaliplatin) being specifically named).

Published alongside US20160175495 (Medical devices for local bioactive delivery) and US20160175559 (Medical devices for local delivery and retention of bioactive agents). The disclosure cites prior Cook patenting, eg US8741354 (Composite ECM materials and medical products formed therefrom) and US8329219 (Methods for producing ECM-based biomaterials), as being incorporated by reference in their entirety.
**WO2016100970-A2**: “Multi-catheter infusion system and method thereof.”

Assignee: Hospital for Special Surgery NY  
Inventors: Memtsoudis, Stavros  
IPC Codes: A61M 25/02  
Publication Date: 23-Jun-2016  
Earliest Priority Details: US201494514, 19-Dec-2014

Multi-catheter infusion system comprises a cannula having a first end connected to a drug delivery system (14), and a second end connected to a plurality of catheters in fluid communication with the cannula for delivering a drug to a target area of a patient. The drug delivery system (14) is capable of delivering a drug eg an analgesic, anti-inflammatory agents, antibiotics, nutrients, medications, hormones and the like, to the multi-catheter infusion system. The multi-catheter infusion system is said to be easily removed as there is no active anchoring.

The invention states that such an improved multi-catheter infusion system would allow for targeted administration of local anesthetics or other drug fluids, eg to provide prolonged and titratable analgesia while minimally affecting patient mobility. It further suggests that periarticular analgesia and wounds covering large areas may be especially amenable to such a technique.

Represents the first patenting from Dr Stavros Memtsoudis, who is board-certified in both anesthesiology and critical care medicine, and who joined the Hospital for Special Surgery after completing subspecialty training in critical care medicine, cardiac, and thoracic anesthesiology.

Assignee: INSERM Institut National de la Santé et de la Recherche Médicale; Université de Bordeaux
Inventors: Guillemot, Fabien
IPC Codes: C12M 1/26; C12N 5/071; B41J 2/00; C12M 1/00; C12M 3/00; B29C 67/00
Publication Date: 23-Jun-2016
Earliest Priority Details: FR201462570, 17-Dec-2014

Method for producing biological tissue by laser printing. The bioprinting invention can be used to produce: implantable tissue for use in regenerative medicine; individualized fabrics from patient's cells to be used to select treatments and develop customized, therapeutic solutions in vitro; and, predictive models that reproduce the physiology of healthy human tissues or disease affected tissues to test the potential efficacy or toxicity of molecules, ingredients and drug candidates. Bone tissue is seen to be named by way of a non-limited example.

Presumably the invention represents amendments and enhancements to Guillemot's previous description of a bioprinting station in WO2011107599 that comprised a bioprinting device adapted to deposit a pattern of biological material, a biological material dispenser, a positioning system, an electronic control unit, and an imaging system.

Dr Fabien Guillemot is the founder of Poietis, a bioprinting company which is seeking to harness Laser-Assisted Bioprinting technology to fabricate complex and customized tissues for regenerative medicine and pharmaceutical applications. Poietis, founded in 2014 between INSERM and the University of Bordeaux, has attracted attention as it aims to become the first company in the world to 3D bioprint human skin using a proprietary laser-assisted 3D bioprinting technology. Currently, Poietis is said to be using two specially designed laser-assisted 3D bioprinters developed by l'INSERM and ALPhANOV Laboratory, and that it is working on developing its own dedicated 3D bioprinting machine (perhaps this is what is being described here).
**WO2016097051-A1**: “Hand-held test meter with test strip electrode to ground-reference switch circuit block.”

Assignee: Lifescan Scotland Limited  
Inventors: Hamer, Malcolm; Nelson, Jonathan  
IPC Codes: G01N 27/327  
Publication Date: 23-Jun-2016  
Earliest Priority Details: US201493043, 17-Dec-2014

Three co-published applications describe possible improvements to Lifescan's range of glucose meters.

In **WO2016097051** (illustrated), a system is included whereby the meter can connect or disconnect the reference electrode in the test strip to the ground reference in the meter thereby determining if the test strip is correctly placed in the meter (and connecting), and if not providing an alert to the user.

In **WO2016100011**, the meter is provided with an array of electrodes which allows it to accommodate and hence measure results from different sizes of test strips.

In **WO2016097344**, a method for varying the bias applied by the meter to the test strip is provided. This permits the meter to measure glucose concentrations over a wider range and with improved accuracy. This work appears to have been done in collaboration with Flextronics in Milan.

See also **WO2016097054-A2** in this issue from Cilag but appearing to originate with members of LifeScan on methods for recognising test strips.
**US20160178526-A1:** “Optical sensor device for repetitive assays in biological fluids.”

Assignee: Light Pointe Medical, Inc.
Inventors: Nomura, Hiroshi
IPC Codes: G01N 21/77; G01N 33/66
Publication Date: 23-Jun-2016
Earliest Priority Details: US2014575781, 18-Dec-2014

![Fig. 3](image1.png)

![Fig. 5](image2.png)

The application describes a series of flat optical waveguides (fig 3; 34) arranged in an annulus and having a bevelled edge (33) which also bears an analyte specific reagent. In use (fig 5), the waveguide (53a) is deflected (53b) to come into contact with a drop of biological fluid (51). An example analyte is glucose.

This continues the interests of the company in devices for the analysis of biological samples see for example US9267897.
**WO2016098060-A1: “Multi-use injection system.”**

Assignee: Medaxor Pty Ltd  
Inventors: Aeschlimann, Andreas  
IPC Codes: A61M 5/20; A61M 5/178  
Publication Date: 23-Jun-2016  
Earliest Priority Details: AU2014905150, 19-Dec-2014

The application describes a multi-use pen injector which is fitted with a microprocessor capable of monitoring the use of the pen, transmitting details of that use to a remote location (e.g., a doctor) and receiving instructions for the user of the pen from the remote location.

The application continues the interests of the inventor and company in injector pens, see WO2016038498. Interestingly, Medaxor shares the same address as MiniFAB, a contract engineering firm specialising in microfluidics.
**US20160175520-A1: “Infusion devices and related methods and systems for preemptive alerting.”**

Assignee: Medtronic Minimed, Inc

Inventors: Palerm, Cesar C; Myers, Jeffrey C

IPC Codes: A61M 5/168

Publication Date: 23-Jun-2016

Earliest Priority Details: US 2014578174, 19-Dec-2014

The application describes improved alerting processes for users of insulin pumps. The improvements are intended to decrease the frequency of non-actionable alerts and hence improve patient compliance/action on receipt of an alert. Two of the four flow diagrams describing the alerting processes are illustrated.

The application forms a pair with US20160174911 which contains provisions for the alerts to be automatically updated. This continues the company’s interests in alerting systems coupled to medical devices, see for example WO2011028411.
**WO2016100307-A1**: “Method and apparatus for improved wound healing.”

Assignee: Mower, Morton, M  
Inventors: Mower, Morton, M  
IPC Codes: A61N 1/30  
Publication Date: 23-Jun-2016  
Earliest Priority Details: US 201493143, 17-Dec-2014

The application describes a wound dressing (102) with embedded into it one (or more) anodes (104) and one (or more) cathodes (106) which are placed in contact with the wound and provide a current through the wound. The dressing may also include ointments such as silver sulfadiazine.

This continues the inventor’s interests in electrotherapy see for example WO2015195795.  
He is associated with Johns Hopkins School of Medicine.
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