BioWorld MedTech

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All-in-one lung cancer diagnostic, treatment

Auris Health inks robotic development, commercialization deal with Neuwave

By Liz Hollis, Staff Writer

With the field of robotic surgery continuing to heat up, Auris Health Inc. has entered a cooperative development and commercialization agreement with Neuwave Medical Inc., a subsidiary of Johnson & Johnson's (J&J) Ethicon Inc., focused on robotically assisted bronchoscopic ablation of lesions in the lung.

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Inside

Attorney says FDA draft re-do of Part 3 eases agency's legal burden

By Mark McCarty, Regulatory Editor

The FDA has floated a rewrite of the so-called Part 3 appeals process for combination product designation to address widespread confusion about the process, but regulatory attorney Brad Thompson of Epstein Becker Green said the proposed changes would effectively reduce the rule to a guidance, which benefits the FDA in that "guidance can't be cited as a binding requirement against FDA" in legal proceedings.

The FDA posted the draft rewrite of the product jurisdiction rule with the statement that the draft

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Raising series A funds

Ocumedic aims for the clinic with drug-eluting, clear corneal bandage

By Stacy Lawrence, Staff Writer

Ophthalmic drugs and devices have proven a strong source of revenue growth as an aging, increasingly obese population aims to prevent eyesight deterioration. Startup Ocumedic Inc. hopes to contribute to that with novel technology that could prove the foundation for a new means of ophthalmic drug administration, a clear contact lens that continuously elutes medication for up to seven days.

The Mullica Hill, N.J.-based company is in the

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Mixiii Biomed 2018

Corporate money steps in to fill med-tech funding gap for fledgling companies

By Alfred Romann, Staff Writer

TEL AVIV, Israel – Corporate venture capital investors are stepping in to fill a funding gap in the med-tech space that is keeping valuations small relatively to companies in the pharma and biotech spaces.

For corporate venture capital (VC) funds, as opposed to the more traditional VC funds, investment is driven by a relentless need to innovate and put forward differentiated products. Without such products, companies are likely to wither and stall.

See Israel, page 6

MITA says Congress must act on third party service issue

By Mark McCarty, Regulatory Editor

The FDA has completed its report on third-party servicers of imaging equipment, determining that its study of the issue does not suggest a need for more regulation of these third parties. Nonetheless, the Medical Imaging & Technology Alliance (MITA) of Rosslyn, Va., said Congress "must still take quick action to ensure third-party

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Other news to note

Emulate Inc., of Boston, is partnering with the Innovative Medicines and Early Development (IMED) Biotech Unit of Cambridge, U.K.-based **Astrazeneca** to embed its organs-on-chips technology within the laboratories of the IMED Drug Safety organization. As part of the agreement, Emulate plans to put scientists in Astrazeneca's laboratories. The aim of this agreement is to accelerate the development of organs-on-chips technology and testing within the context of a pharmaceutical organization. Astrazeneca began collaborating on Emulate's organs-on-chips technology in 2013.

Denver-based **Matrix Analytics** is rebranding as Eon. The rebrand marks the expansion of Eon's offerings beyond Lungdirect to a suite of software solutions that will help improve the treatment of complex conditions. Lungdirect, which will be rebranded to Eondirect, is a cloud-based software application for lung cancer screening and incidental nodule management that integrates with hospital electronic medical records.

Hangzhou, China-based **Venus Medtech** has entered a definitive investment agreement with Dcp Capital. The investment will be used by Venus to accelerate the upgrading and internationalization of existing valve products, support the company to enter into the clinical research stage for its new mitral/tricuspid valve disease treatment technology, and lay a foundation for the company to enter the international heart valve market. Venus's first generation transcatheter aortic valve replacement product, Venusa-Valve percutaneous interventional aortic valve system, is the first interventional prosthetic valve product approved by the CFDA.

Regulatory front

The **FDA** will convene a June 14 meeting of the anesthesiology and respiratory devices advisory committee to obtain feedback on the application for the Pneumrx Elevair endobronchial coil system by Pneumrx of Mountain View, Calif. The application proposed an indication for use of improvement in quality of life, lung function and exercise capacity for patients with severe emphysema. The agency said it will post meeting materials at least two days prior to the meeting, which will take place at the Gaithersburg Holiday Inn in Gaithersburg, Md.

The **FDA** said N95 masks used in surgical procedures will henceforth be exempt from premarket notification requirements, although this action is limited to single-use masks. The agency, which undertook the action unilaterally, said products other than those under the procode MSH that fall under the category of surgical apparel, will still be subject to the requirement. The rule is effective immediately.

The U.K. **Medicines and Health Care Products Regulatory Agency** said in its workplan for 2018 and 2019 that the agency "is already operating in a financially challenging context," and that it will "be undergoing operation transformation over the next three years" in order to replace "aging systems." MHRA said it will seek to avail itself of a total of £9.1 million for device regulation, with £1 million to be expended "for capital investment in further efficiencies." The agency said it will "continue to plan for the U.K.'s preferred exit outcome of close cooperation with the EU," a reference to the ongoing Brexit.

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Auris

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The agreement revolves around the development of systems for robotic control, navigation and application of microwave ablation delivered by bronchoscopes. A bronchoscope with a small camera and an accessory channel would permit tools to enter the lungs through the mouth. The co-development agreement also covers technology optimization and procedure development.

"From the beginning, our vision has been to create a platform capable of enabling advanced diagnosis and therapy for a spectrum of disease, using the least-invasive approach," said Frederic Moll, co-founder and CEO of Redwood City, Calif.-based Auris. "Through this collaboration, we believe we are taking a significant first step together toward making the goal of diagnosing and treating lung cancer, all through the body's natural openings, an eventual reality."

Word of the deal comes about two months after the company reported that the FDA had cleared its Monarch robotic platform for diagnostic and therapeutic bronchoscopic procedures. (See *BioWorld MedTech*, March 27, 2018.) The platform has an interface that is managed with a gaming-like controller. It is accompanied by a computer-aided navigation program that uses 3D modeling of an individual lung.

Ethicon's Neuwave Flex microwave ablation system, the only FDA-cleared flexible microwave ablation probe, builds on the Neuwave percutaneous microwave ablation system. The Flex system is indicated for soft tissue ablation in percutaneous procedures, open surgical procedures, as well as in procedures in which the target tissue is accessed by a lumen or scope, such as an endoscope.

"For those treating people with suspicious nodules in the lung, the holy grail is to one day be able to detect and treat the disease in a single procedure," said Kazuhiro Yasufuku, associate professor of surgery at the University of Toronto. "When this option becomes a reality, we may see many patients seek early screening and minimally invasive treatment."

Lung cancer is the leading cause of cancer deaths worldwide. "Four hundred and fifty people die every day in the U.S. due to lung cancer. It is the number one cancer killer of both men and women in the world. Lung cancer screening has given us an opportunity to save some of these people by diagnosing the cancer early, while we have a chance to cure it. Despite the benefit, we still are limited by the current technology in making a diagnosis," said Michael Simoff, director of Interventional Pulmonology at Henry Ford Health System in Detroit, at the time of the FDA clearance of the Monarch platform. "The development of new advanced technology, like the Monarch platform, could allow us the opportunity to make the diagnosis early, which translates directly to saving lives."

Timelines, future plans

In terms of timelines, Josh DeFonzo, chief strategy officer at Auris, told *BioWorld MedTech* that development will start in the coming months. "[O]nce we begin collaborating, we will have a better sense of timelines." He added that no financial details were being disclosed.

"We are open to partnerships that help us advance our goal of addressing a spectrum of disease in a minimally invasive manner," DeFonzo said when asked about potentially linking up with other companies. He added that no additional details about plans for future applications with Monarch were being shared.

Competitive landscape

Formerly named Auris Surgical Robotics Inc., the company is in a competitive field led by Intuitive Surgical Inc. Intuitive has more than 4,000 systems for use in laproscopic hernia repair, colon, gynecology, urology, thoracic and general surgeries. Moll helped co-found Intuitive.

In addition, Mazor Robotics Ltd., which has teamed up with Medtronic plc, is developing a robotic surgical system for brain and spinal procedures. On Monday, the company posted first quarter results. Wells Fargo analysts noted that systems revenue of $6.6 million missed their estimates by about $2 million, due in part to lower net systems being place in the quarter than what was modeled.

"The company will no longer provide a breakdown of system placements for competitive reasons, but noted that the installed base stood at over 200 as of the end of Q1," the analysts noted. "By our math, Mazor likely placed 15 net systems in 1Q18, up from 10 in 1Q17 and 16 in 4Q17, which is four systems shy of our estimate." Overall, revenue of $15.5 million exceeded the analysts' estimates.

Globus Medical offers a range of products for spinal surgery. It jumped into this field with its Excelsius GPS, a robotic guidance and navigation system – a move that appears to have boosted the company's revenues. It disclosed first quarter revenues of $174.4 million, above the consensus of $167.9 million. Analysts from William Blair noted that the results, which were discussed May 2, were driven in part by interest in the Excelsius GPS.

"We remain compelled particularly by the company's emerging technologies opportunity and believe that management has been putting in place the proper foundation to accelerate growth from here, though we acknowledge that the growth required to meet the company's goal of $1 billion in sales by 2020 is still fairly aggressive," wrote William Blair analysts.

The company reported the first spine surgeries with the platform Oct. 10, 2017, after noting it had received clearance for it two months earlier.

U.K.-based startup CMR Surgical, which changed its name in Cambridge Medical Robotics Ltd. in February, is planning to launch its next-generation universal surgical robotic system, Versius, later in the year. It closed a $46 million series A funding last fall to help with this effort. (See *BioWorld MedTech*, Sept. 20, 2017.) Its robotic surgical system, aims to replicate the actions of a human wrist movement in holding a surgical instrument. The system could be applicable in a range of minimal access surgeries, as well as offering a less expensive treatment option. ♦

FDA

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is intended "to enhance regulatory clarity and efficiency," listing several estimates of the cost savings to regulated entities associated with the elimination of the Part 3 appeal to the Office of Combination Products (OCP). The rewrite was driven in part by the 21st Century Cures Act, and the draft says that sponsors have evinced confusion on several points in the 26 years since Part 3 was codified.

The agency says that the rule would revise Part 3's subsection 3 to the extent that it would make clear that applicants are not required to seek a product designation from OCP unless the classification of the product is unclear or in dispute. There has been some confusion on the part of industry as to whether a product designation application was necessary even in instances in which there was no question as to the product's appropriate classification, the FDA said.

However, the proposed rule would excise subsection 3.8, the feature of Part 3 that provides for requests for reconsideration made by the sponsor to the OCP product jurisdiction officer. The FDA said applicants are not permitted to include new information relating to the combo product in question in these requests, and thus "further evaluation of the same data and information by OCP is unlikely to result in a change of decision."

The FDA noted that such requests for reconsideration have proven inefficient for industry, and have led to confusion as to whether the sponsor can make a request for supervisory appeal under another portion of the Code of Federal Regulation.

Thompson told *BioWorld MedTech* that many of the provisions the agency is proposing to rewrite or eliminate had played a role in the agency's two losses in the D.C. district court in *Prevor v. FDA*. The questions in *Prevor* revolved around whether the agency had failed to comply with its own procedures in declaring the product a drug rather than a device, and Thompson said most of the features of the proposed rewrite of Part 3 suggest that the agency "seems to be intent on dropping provisions which the plaintiff found useful in that case."

It might also bear pointing out, however, that the September 2017 FDA product classification guidance suggests an ingrained orientation toward product classification as a drug, with only secondary regard for a product's primary mode of action as demonstrated by that guidance's statement, "conceptually, all FDA-regulated medical products meet the definition of 'drug' . . . due to the broader scope of the drug definition." (See *BioWorld MedTech*, Oct. 5, 2017.)

Thompson said his primary concern regarding the effect of the proposed rule is that "a regulation is binding and guidance is not." In addition to the fact that a guidance does not bind the agency's hands in legal proceedings the way rules do, he said the impact is that "the regulated community in general loses the certainty of having a binding regulation in place," thus implicitly reviving the guidance/rulemaking debate that has gained substantial traction among regulatory attorneys over the past few years.

Thompson said the agency's observations regarding confusion in relation to several portions of Part 3 are conspicuous in that

> *"If a regulation is confusing, the most natural solution would be to rewrite it in a way that is not confusing, as opposed to simply dropping the provisions.*
>
> Brad Thompson
> Regulatory attorney, Epstein Becker Green

"if a regulation is confusing, the most natural solution would be to rewrite it in a way that is not confusing, as opposed to simply dropping the provisions." He added that the removal of an opportunity to request a reconsideration at OCP "is particularly unusual because it is simply an optional pathway." The removal of the reconsideration request presumes that members of OCP are "incapable of making a mistake," and that administratively, "it's handy to have a way to fix [those determinations] without an appeal to a higher authority," he said.

Only sponsors need apply

The draft said that in the past, "some entities who are not the sponsor for the product have attempted to obtain a product classification or assignment determination," and that clarification that Part 3 is applicable only to sponsors "is consistent" with the statute as amended by the Cures Act. Thompson said this could be problematic in that a trade association might seek clarification regarding a designation, but that as written, the draft rule would make that product designation known only to the sponsor of a specific application. Thompson said one area in which this is particularly pertinent is "in the context of software used with pharmaceuticals."

The draft rule noted that the regulation currently permits the constituent parts of a combo product to be reviewed under separate applications, but that the Cures Act directs "that combination products shall be reviewed under a single application whenever appropriate." Again, purportedly to reduce confusion, the FDA said it would excise the portion of the regulation that permits review of the components individually, and Thompson said, "this is a very critical issue." He aid that the agency again seems intent on wholesale elimination of regulatory language in lieu of the more difficult work of lending clarification, adding, "I would like to understand FDA's thinking here more."

Section 3.5 of Part 3 reviews inter-center agreements at the FDA, and the proposed rule says that the agency would remove this section as well, because the current suite of inter-center agreements might not represent "the most accurate jurisdictional statements." The agency said it would review existing inter-center agreements "to determine what action, if any, to take with respect to them."

Thompson acknowledged that the inter-center agreements have collected dust, but that "it would seem to me the solution to that is to update them" rather than to replace

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Ocumedic

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midst of raising a $4 million series A funding round to support ongoing preclinical testing and to move into a phase I/II trial with an anti-inflammatory version that is designed to treat postoperative vision surgery patients as well as those with corneal abrasions. Additional indications, including dry eye and glaucoma, have also been studied preclinically using applicable off-patent drugs for sustained delivery.

Getting it right

Ocumedic isn't the first company to pursue the concept of what is essentially a drug-eluting contact lens. In fact, it's been an unrealized research goal for decades. But a few fundamental drug delivery problems have long remained unsolved, and Ocumedic believes it has surmounted these basic obstacles.

"Controlled release from contact lenses has been the subject of discussion and investigation for 50 years. A lot of people have been attempting to deliver drugs in a metered time delay producing good pharmacokinetics. These previous methods suffered from either poor control of the release profile or inadequate drug loading, with the overwhelming majority of the researchers demonstrating both problems," Ocumedic President and CEO Keith Ignotz told *BioWorld MedTech*.

"With the Ocumedic method, the memory for the drug is produced during polymer synthesis where monomers are complexed noncovalently to the drug and cross linked into a hydrogel matrix," he continued. "Upon removal of the drug, the macromolecular memory sites remain within the hydrogel with an affinity for the drug. So, the drugs heightened interaction with these memory pockets enhances it's loading, slows its transport within the hydrogel despite comparable free volume of drug transport. Basically, we can literally dial in the release of the drug through the lens over time, delivering a therapy at a concentration of drug payloads for the duration."

The underlying, in-licensed technology was originally developed by Mark Byrne when he was at Auburn University. He has since moved to Rowan University, where he is a founding head and professor of biomedical engineering, and is the CTO of Ocumedic.

Better than drops?

The idea is to improve upon medicated eye drops, which typically wash out of the eye often without having reached their intended target. The initial iteration to hit clinical testing will be based on an undisclosed, off-patent anti-inflammatory drug to treat postoperative and abrasion patients in order to boost healing.

"Patients who undergo eye surgery for cataracts, LASIK [Laser-Assisted In Situ Keratomileusis]or who suffer corneal abrasions can experience longer healing times, complications, and even infections if proper care, including administering eye drops, is not properly followed," said Byrne. "Our research shows the new contact lens technology is expected to lead to higher efficacy for patients compared to topical eye drops by improving compliance and mitigating concentration peaks and valleys associated with multiple drops."

"Our research shows the new contact lens technology is expected to lead to higher efficacy for patients compared to topical eye drops by improving compliance and mitigating concentration peaks and valleys associated with multiple drops.

Mark Byrne
CTO, Ocumedic Inc.

The company is currently working on preclinical testing in New Zealand white rabbit, a standard ophthalmic animal model. Ocumedic is also in the midst of putting together a Request for Designation submission to the FDA, a necessary step for combination drug/device products that enables the Center for Drug Evaluation and Research (CDER) and Center for Devices and Radiological Health (CDRH) to determine which agency will take the lead on evaluating the technology.

Once there's clarity on which agency will take precedence, the company plans to start a phase I/II trial in roughly eight to 12 human subjects. The trial would aim to establish good pharmacokinetics, as well as reductions in pain and inflammation in the eye. Ignotz expects that once Ocumedic has phase I/II trial results in hand, it might then be able to use that to secure a commercial and development partner.

If Ocumedic succeeds with its first anti-inflammatory product, it expects to proceed into dry eye with a sustained-release lens using Allergan's Restasis (cyclosporine ophthalmic emulsion), which has gone off-patent. It's also done preclinical testing with prostaglandins to treat glaucoma. Ignotz said that Ocumedic has done preclinical testing using nine different drugs thus far.

Market path

The drug-eluting lens could have a relatively simple commercialization path, since they are expected to be covered by established reimbursement codes. Ignotz said there's already an existing CPT reimbursement code for a bandage contact lens that includes physician application. Ophthalmologists typically handle eye surgeries, so they would conceivably be responsible for any immediate pre- or post-surgical care.

But optometrists, who in the U.S. are usually in charge of routine eye care and refer patients to ophthalmologists, would potentially be responsible for any subsequent applications or for corneal damage use. Under Medicare, physician fees for procedures could offer a meaningful contribution to optometrist office income. The lens is expected to be priced in-line with competitor eye drops, but aims to offer a significant treatment advantage.

Antibiotic and anti-inflammatory drops used to be the standard of care after these eye surgeries, but ophthalmologists have moved away from antibiotic drops to a one-time, post-

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Israel

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Bruce Rosengard, VP for global external innovation at Johnson & Johnson, emphasized that point when discussing his company, the largest health care company in the world and one that has a relentless focus on growth. Johnson & Johnson's global medical device sales topped $25 billion in 2016, when they grew 3.8 percent. That year, the company marked 34 consecutive years of earnings increases and 55 consecutive years of dividend increases.

"We have to be constantly adding to our portfolio, otherwise we lose momentum and fail to grow," said Rosengard. "We are driven constantly by the need for growth. And how does growth come? It comes from innovation."

"When you have a higher level of innovation and you move at greater speed you end up with a differentiated product," said Rosengard. "The challenge, of course, is when you are not high enough on the innovation scale. The world is flat. Innovation is coming from everywhere."

But, while there is plenty of innovation around, most of that innovation makes it nowhere, said Rosengard.

The Medical device market "is a very different business and it has a very different set of challenges." And, "probably the biggest challenge is the early stage funding gap for medical devices."

One challenge is that the initial returns and incremental returns that drugs can generate are much larger than for medical devices.

A second challenge is the changing nature of the industry. In the (now increasingly distant) past, developing a new device was much easier and cheaper than developing a new drug but the new high-tech devices are more complex, take a long time to develop and often require trials that are long and expensive.

A third challenge is competition from areas such as digital health, with require very little investment and can provide exits quickly are more attractive and easier to understand for investors.

Corporate investors that have a strategic need to tap into new ideas and new devices and may have less of a need to focus solely on financial returns to keep shareholders happy may help both individual companies and the industry as a whole to address this funding gap.

Virtually all the large global companies have some kind of corporate investment arm that typically operates at arm's length from the parent company but, in most cases, aims to address the long-term strategic needs of the parent.

Takeda Pharmaceuticals, for example, has Takeda Ventures that undertakes early stage investments in oncology, gastroenterology and neuroscience. Bristol-Myers Squibb and Novartis both have investment arms, the latter with $800 million to invest and with a clear focus on financial returns. Johnson & Johnson has an investment arm that invests between $200 to $400 million around the world.

The growing interest on corporate venture capital was in clear evidence in Tel Aviv during the annual Mixiii Biomed conference. All those companies were present at the conference. They were a good match for the hundreds of startups that populate Israel's crowded and innovative med-tech space.

For small companies, securing funding from a corporate investor may "enhance the overall dynamics of the transaction," said Gil Bar-Nahum, managing director of investment bank Jefferies International. "If a big corporate is putting in a big chunk of money, I think other people are going to look at it."

Zeev Zehavi, VP of venture investments at Johnson & Johnson Innovation, highlighted one of the unique features of the fund: "We were very much focused on medical devices but as our business expanded our investments were pretty much split between medical devices, pharmaceuticals and biotech."

"We have a strategic objective but also have a financial objective," said Zehavi. "When we make an investment, in many cases, we want to have a window into the opportunity."

This is a similar view that Takeda Ventures takes.

"We look to utilize venture investment to provide a strategic lever to support and inform technical R&D," said Michael Martin, the global head of Takeda Ventures.

And both Israeli companies and the Israeli government want to tap into more of that need for strategic investment and the capital necessary to fill the funding gap.

In 2017, Israel was home to some 473 deals in the med-tech space with an average value of $57 million per deal, said Aharon Aharon, the CEO of the Israel Innovation Authority. ♦

Financings

Charlottesville, Va.-based **Caretaker Medical LLC**, which focuses on continuous noninvasive blood pressure and wireless vital signs monitoring, completed a $3.4 million investment round led by Irishangels, Kofa Healthcare, and Jaffray Woodriff, with participation from both new and existing individual investors. Proceeds will accelerate the company's global commercialization activities for the FDA-cleared, Wireless Caretaker continuous "beat by beat" noninvasive blood pressure and vital signs monitor.

Appointments and advancements

Clinical Innovations, of Salt Lake City, has hired Michael Behling as its new CFO. He joined Clinical Innovations as interim CFO in February. Behling previously served as CFO at Lasko Products.

Tampa, Fla.-based **Laser Spine Institute**, which focuses on minimally invasive spine surgery, appointed Kathleen Donald as chief marketing officer. Prior to joining Laser Spine Institute, Donald was general manager at Dassault Systemes' 3Dexcite.

MITA

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servicers of medical devices register with the FDA and report adverse events."

The FDA report, mandated by the Food and Drug Administration Reauthorization Act (FDARA), said the evidence available to date does not suffice to determine "whether or not there is a widespread public health concern" related to third-party servicing of imaging systems, at least not that would justify the imposition of "additional/different burdensome regulatory requirements at this time."

The agency said the evidence supports the argument that these third parties provide high-quality, safe and effective servicing" of those imaging systems, and that the majority of complaints and adverse events relating to non-OEM serviced systems revolves around the remanufacture of these systems, not mere servicing.

Still, the agency said it will prod third-party servicers to adopt quality management principles and will seek to clarify the regulatory distinction between servicing and remanufacturing. The report characterizes servicing as activities that return or maintain a finished device's safety and performance specifications whereas remanufacturing "significantly changes the finished device's performance, safety specifications, or intended use." Due to some confusion over the respective meanings of these terms, the agency said it will publish guidance that will lend clarity to the question and allow the FDA to prioritize its use of resources pertaining to the related imaging systems.

The agency said it will emphasize cybersecurity for these systems as well, but said that any extension of medical device reporting mandates to these third parties would not likely yield useful information. Any collection of data that would yield significant insight into this question would require "a multi-stakeholder enterprise," the agency said.

MITA responded with a statement on the same day of the FDA report, saying the association "strongly supports the FDA decision to promote the adoption of quality management principles in equipment servicing." Nonetheless, MITA said Congress "must still take quick action to ensure third-party servicers of medical devices register with the FDA and report adverse events," despite the agency's lack of conviction on the MDR question.

Patrick Hope, MITA's executive director, said, "We agree the evidence available to the FDA is not sufficient to conclude whether or not a public health concern is warranted," but the uncertainty surrounding the FDA report supports the notion that legislation in the House "requiring third-party servicers to register and report is an important first step and a common-sense approach." The Medical Device Servicing and Accountability Act would require third parties to register with the agency, maintain complaint-handling systems, and file MDRs with the FDA.

Hope said, "Plain and simple, this is about patient safety. Patients should not have to risk taking a leap of faith regarding the upkeep" of an imaging system, adding, "if a medical imaging device malfunctions due to improper servicing, a diagnosis could be missed, care could be delayed, or the patient could be severely injured or even killed." Passage of the Medical Device Servicing and Accountability Act "would be a major first step toward solving this problem," Hope concluded. ♦

Product briefs

CAS Medical Systems Inc., of Branford, Conn., received 510(k) clearance from the U.S. FDA for its Fore-Sight tissue oximetry OEM module, an original equipment manufacturer (OEM) version of its next-generation Fore-Sight Elite tissue oximeter. The OEM module permits the tissue oximetry values derived by Fore-Sight technology to be displayed on a monitor manufactured by a third party, rather than requiring a standalone Fore-Sight monitor.

Coremedic GmbH, of Tübingen, Germany, reported the start of a first-in-human study to evaluate new minimally invasive valve repair technology. The prospective, multicenter trial is intended to establish the safety and effectiveness of the Chordart system. The study was approved to enroll up to 40 subjects at up to six European centers. Chordart is a transfemoral chordal repair system for the treatment of degenerative heart disease with mitral valve insufficiency. The first patient to receive the Chordart was treated at the Vilnius University Hospital in Lithuania. According to the company, the patient recovered from the intervention and is continuously doing well. A 30-day follow-up showed no complications.

Istar Medical SA, of Wavre, Belgium, reported six-month results of their first-in-human micro-invasive glaucoma surgery trial for the Miniject device in a standalone setting. The trial showed that the implantation of Miniject resulted in an average 39 percent intraocular pressure (IOP) reduction to a mean of 14.2 mmHg at six months. In addition, 87.5 percent of patients were able to discontinue topical medication usage and remained medication-free at six months. The trial is a prospective, international, multicenter study in which a Miniject was implanted in 25 patients with mild-to-moderate, primary open angle glaucoma uncontrolled by topical hypotensive medication. The aim of the study is to assess the safety and performance of the Miniject device measured by IOP reduction under medication from baseline to six months. Subsequent safety and performance will be measured up to two years postsurgery.

K2m Group Holdings Inc., of Leesburg, Va., launched its Mojave Pl 3D expandable interbody system in the U.S. Designed with K2M's Lamellar 3D titanium technology, Mojave Pl 3D incorporates a porous structure in conjunction with rough surfaces, with the goal of allowing for bony integration throughout the endplates. The Mojave Pl 3D expandable interbody system, which received a 510(k) clearance from the FDA in June 2017, is a 3D printed fusion device designed to allow for independent control of the anterior and posterior heights in the lumbar spine.

FDA

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them "with very general explanatory instructions." He said specific precedents for inter-center work on combo product applications are far more instructive to applicants, and that the FDA has been loathe to provide jurisdictional updates due to concerns regarding disclosure of confidential information found in combo product applications.

"We would encourage the agency to solve that problem so that the agency can share more with regard to jurisdictional updates," Thompson said, adding, "this is a key issue for the combination product industry."

Mark Brager, spokesman for the Advanced Medical Technology Association, told *BioWorld MedTech*, "while we are still evaluating the proposed rule, we support FDA's efforts to update, clarify and streamline regulatory requirements."

The Biotechnology Innovation Organization and the Pharmaceutical Research and Manufacturers of America declined to comment for this story. The agency is taking comment on the draft rule through July 14 under docket number FDA-2004-N-0191. ♦

Ocumedic

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procedure injection. Ocumedic is designing its product to work in tandem with that. About 6 million people in the U.S. have eye surgery annually including 4 million for cataract, 1 million post-corneal abrasion surgeries and 800,000 LASIK procedures.

"Now we have a standalone kind of application here, where there's still a great need for an anti inflammatory to reduce the pain and discomfort due to either cataract, LASIK or corneal abrasion," said Ignotz. "We also looked at the growth of cataract procedures over the next several years; because of an aging population that is forecasted to double. And there are procedures like SMILE [SMall Incision Lenticule Extraction] in LASIK, as an alternative to LASIK, that are becoming more popular with the growth in corneal modeling."

Founded in 2009, thus far Ocumedic has been largely supported via research grants. It's tapped roughly $1.85 million in grants from the NIH and the National Science Foundation. It recently raised an undisclosed amount from the Rowan Innovation Venture Fund and the Keiretsu Forum, which is also backing the planned $4 million series A round that Ocumedic is currently working to put together. ♦

Product briefs

Lifeplus Inc., of Menlo Park, Calif., reported the launch of Lifeleaf, a noninvasive continuous blood glucose monitoring multisensor wearable device. In addition to blood glucose monitoring, the patent-pending multisensor device monitors heart rate, blood pressure, respiration rate and oxygen saturation. Lifeleaf is currently active in five trials around the world. According to the company, the Lifeleaf wearable will be available later this year.

Mc10 Inc., of Lexington, Mass., said its Biostamp Npoint system received FDA 510(k) clearance and will be available beginning June 2018. Biostamp Npoint is a wireless, biometric data collection platform intended for use by health care professionals and researchers for the continuous collection of physiological data.

Photocure ASA, of Oslo, Norway, launched Blue Light Cystoscopy with Cysview for a new indication of surveillance cystoscopy of bladder cancer. The new FDA approved indication was a result of a phase 3 study using blue light rigid and flexible cystoscopes from Karl Storz Endoscopy of America Inc., which showed that Blue Light Cystoscopy with Cysview significantly improves detection of patients with recurrent bladder cancer.

Pi-Cardia Ltd., of Beit Oved, Israel, said it started its first-in-human study with its Leaflex Performer catheter system. The Leaflex Performer is a trans-femoral catheter that uses two mechanical structures for scoring valve calcification at multiple locations, restoring leaflets flexibility and improving valve hemodynamics. The Leaflex catheter is aimed to be a cost-effective standalone treatment or a preparatory step for improving the outcome of valve implantation in heavily calcified aortic valves, bicuspid aortic valves and calcified mitral valves. Initial trial results demonstrate safety, feasibility and a hemodynamic improvement, which is significantly superior to that previously achieved with balloon valvuloplasty.

Rapid Medical Ltd., of Yokneam Illit, Israel, reported the first patients have been enrolled in the TIGER (Treatment with Intent to Generate Reperfusion) study. This is a multicenter study of the performance of Tigertriever, the company's thrombectomy device for the acute treatment of ischemic stroke. The TIGER study is an IDE clinical study for purposes of supporting the company's 510(k) submission to the FDA. The study will take place in up to 25 stroke centers throughout the U.S.

Reva Medical Inc., of San Diego, launched the Fantom bioresorbable scaffold in Turkey with implants conducted during the first week of introduction at three separate hospitals. The procedures were conducted in Istanbul and Antalya at the Mega Medipol University Hospital, Memorial B. Evler Hospital, and Medical Park Hospital. Fantom procedures were successfully conducted at all three centers with excellent acute patient outcomes. Reva has a commercial distribution partnership with Kardionet Healthcare and Foreign Trading Ltd. in Turkey.

Varian Medical Systems Inc., of Palo Alto, Calif., reported two patients with brain cancer were the first patients in South Korea to be treated using the company's Hyperarc high definition radiotherapy, a new type of radiosurgery treatment, at the Ajou University Hospital. Hyperarc is designed to automate and simplify sophisticated treatments such as stereotactic radiosurgery and make them available to more cancer patients.

Ventripoint Diagnostics Ltd., of Toronto, received market clearance from the FDA to sell its Vms+ machine with the four-chamber heart analysis system. The intended use is for the analysis of ejection fraction (function) and volumes of any chamber of the heart, where they are warranted or desired, using conventional 2D ultrasound.

Orthopedics Extra

Keeping you up to date on recent developments in orthopedics

By Holland Johnson, Executive Editor

Spinal surgery for osteoporosis no better than injections

Vertebroplasty was found to be no more effective for pain relief than a sham procedure in older patients with osteoporosis, according to a trial published May 9, 2018, by *The BMJ*. Vertebroplasty involves injecting a special cement into the fractured bone to stabilize it and to relieve pain. But previous studies have reported conflicting results and there is ongoing debate about its benefits, risks, and cost-effectiveness. To try to resolve this uncertainty, researchers compared pain relief in patients undergoing vertebroplasty or a placebo procedure, where patients are given local anaesthetic injections, but no bone cement. The trial involved 180 adults aged older than 50 years, with 1-3 painful vertebral compression fractures of up to nine weeks old. Participants were randomly assigned to either vertebroplasty (91 patients) or the sham procedure (89 patients). The primary outcome measure was mean reduction in pain scores at one day, one week, and one, three, six, and 12 months after the procedure. Clinically significant pain relief was defined as a decrease of 1.5 points in visual analogue scale (VAS) score from the start of the study (baseline). The mean reduction in VAS pain score was statistically significant in both groups at all follow-up points compared with baseline. However, these changes in VAS scores did not differ significantly between the groups over the 12 month follow-up period. The researchers concluded that vertebroplasty had no effect on quality of life or on disability. While they said that there is a place for vertebroplasty "when efficacy outweighs the risks," these results "do not support using percutaneous vertebroplasty as standard pain treatment in patients with acute osteoporotic vertebral compression fractures."

Key brain-to-spinal cord connections for voluntary movement mapped

Researchers trying to help people suffering from paralysis after a spinal cord injury or stroke mapped critical brain-to-spinal cord nerve connections that drive voluntary movement in forelimbs, a development that scientists say allows them to start looking for specific repair strategies. The study is an important step to help motor function recover after an injury or disease damages the central nervous system, the scientists reported in the May 2018 issue of *Cell Reports*. Little has been known about how the corticospinal network of nerve connections between the brain and spinal cord are organized and function together. To map this connectivity in the current study, the scientists studied these circuits in laboratory mice. The researchers were able to track corticospinal connections from the brain's cerebral cortex near the top of the head down to the spinal cord by working from previous studies. They also traced the organization and function of corticospinal circuits using mouse genetics, and a viral tracer that allowed investigators to highlight and capture images of these links. The connections trace down through what's called the brain's internal capsule, then arrived at the caudal medulla of the brain just above the spinal cord. From there they entered the spinal cord, continuing to protrude downward and make additional connections. The research team was able to develop a map of corticospinal neurons that control forelimb and sensory nerve impulses. They also identified specific neurons that control different skilled movements. The article is titled "Corticospinal circuits from the sensory and motor cortices differentially regulate skilled movements through distinct spinal interneurons."

Higher protein intake benefits adult bone health

A new expert consensus endorsed by the European Society for Clinical and Economical Aspects of Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases and the International Osteoporosis Foundation has reviewed the benefits and safety of dietary protein for bone health, based on analyses of major research studies. The review, published in *Osteoporosis International*, found that a protein-rich diet, provided there is adequate calcium intake, is in fact beneficial for adult bone health. It also found no evidence that acid load due to higher dietary protein intakes, whether of animal or vegetable origin, is damaging to bone health. The review found that hip fracture risk is modestly decreased with higher dietary protein intakes, provided calcium intakes are adequate and that bone mineral density (BMD) appears to be positively associated with dietary protein intakes. Additionally, it found that protein and calcium combined in dairy products have beneficial effects on calciotropic hormones, bone turnover markers and BMD and that the benefit of dietary proteins on bone outcomes seems to require adequate calcium intakes. The article is titled "Benefits and safety of dietary protein for bone health – an expert consensus paper endorsed by the European Society for Clinical and Economical Aspects of Osteopororosis, Osteoarthritis, and Musculoskeletal Diseases and by the International Osteoporos."

Osteoporosis drug may benefit heart health

The osteoporosis drug alendronate was linked with a reduced risk of cardiovascular death, heart attack, and stroke in a May 9, 2018, *Journal of Bone and Mineral Research* study of patients with hip fractures. The association was seen for up to 10 years after fracture. In the study, patients newly diagnosed with hip fracture from 2005 through 2013 were followed until late 2016. Among 34,991 patients, 4,602 (13 percent) received osteoporosis treatment during follow-up. Alendronate was associated with 67 percent and 45 percent lower risks of one-year cardiovascular death and heart attack, respectively. It was associated with an 18 percent reduced risk of stroke within five years and a 17 percent reduced risk of stroke within 10 years. Protective effects were not evident for other classes of osteoporosis treatments. The article is titled, "Association of alendronate and risk of cardiovascular events in patients with hip fracture."