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The MDD Interview

Dubreuil tills product development soil for concepts to grow at Farm

1st of 2 parts

By JIM STOMMEN, *MDD* Contributing Writer

Marc Dubreuil is director of business development at **Farm**, a Hollis, New Hampshire-based consultancy that focuses on medical and life sciences product development. He has held numerous positions within the plastics and manufacturing industries, and has a strong background in the product development process.

Marc's focus in business development activities includes orthopedics, arthroscopy, neurology, robotics, dental, and the venture capital and academic communities. Past clients include most of the medical companies within the Fortune 100.

MDD: What are the trends in product design? I'm wondering how the process has changed, particularly over the past few years?

Dubreuil: The most beneficial change for us is that design is finally is getting the respect it deserves, and it's because consumers are finally realizing the role that great design can play in their lives. Companies like Apple and Dyson are designing holistic product experiences that are supremely well-executed and have awakened consumers to the difference between a well-designed and a badly-designed product. Consequently, people are looking for good design in all areas of their lives, and that awareness has flowed into our clients' understanding of what should constitute good medical device design.

As for trends in the process itself, there's a greater structure in medical product development today than there ever was in the past, and our clients have become much smarter about the development path. Most of the bigger companies have instituted product development and

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Elixir looks to future of bioresorbable scaffolds

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

Elixir Medical (Sunnyvale, California) started out in 2005 in the interventional cardiology space with the goal of having the broadest portfolio of drug eluting stents (DES) on the market to address as many patients as possible, Elixir CEO Motasim Sirhan told *Medical Device Daily*. Today it seems the company is right on target with its goal.

So right from the get-go the company's portfolio included a bioresorbable eluting stent, Sirhan said, referring to the company's DESolve novolimus eluting bioresorbable coronary scaffold system. The scaffold is designed to resorb in the body within one to two years after implantation and return the patients' coronary vessel to *de novo* state.

Bioresorbable scaffold technology had thus far been

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Washington roundup

FDA warns Axiobionics for unauthorized claims, designs

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

FDA's efforts to clamp down on claims that are not cleared or approved were renewed in the Dec. 6 warning letter to **Axiobionics** (Ann Arbor, Michigan), which cited the maker of electrical stimulation garments for promoting the devices for use in patients with stroke and cerebral palsy. The warning letter advises that the devices were cleared for claims including "relaxation of muscle spasms" and "prevention or retardation of disuse atrophy." The devices were deemed adulterated as a result, but a Dec. 19 search using the term "palsy" returned a hit on a company web brochure mentioning stroke and cerebral palsy.

The 510(k) application in question (K944543) was

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Don't miss today's MDD Extra: Orthopedics

INSIDE:

AHC Media

Financings roundup

Dynatronics gains approval for reverse stock split

A *Medical Device Daily* Staff Report

Dynatronics (Salt Lake City) reported that the shareholders approved a one-for-five reverse stock split of its common stock. About 93% of the votes cast were in favor of the reverse split which becomes effective today.

"After careful analysis, our board of directors determined that the best course of action for shareholders was to maintain our Nasdaq listing where we have traded for the past 28 years," said Kelvyn Cullimore, Jr. , chairman/president of Dynatronics. "Our research showed that staying on Nasdaq provides greater liquidity through higher trading volumes, as well as tighter spreads between bid and ask prices, more market makers and overall better investor confidence compared to trading in the over-the-counter market as a result of being delisted from Nasdaq."

The company has a number of positive developments which management believes should bode well for the company's future performance. "This week, we are completing the expansion of our California operation into a new, larger facility in Livermore, California to better serve our west coast customers," reported Cullimore. "Beginning today, we will be operating from that new facility which will allow greater operating efficiencies than our previous facility. In addition, our new SolarisPlus line of therapy devices is being well received by the market. October was a very profitable month for the company and should result in earnings for the quarter ended December 31st improving significantly over the same period last year."

The company is also working on expanding its distribution channels over the coming quarters and will introduce a record number of new products in fiscal year 2013.

Dynatronics manufactures, markets and distributes advanced-technology medical devices, orthopedic soft goods and supplies, treatment tables and rehabilitation equipment for the physical therapy, sports medicine, chiropractic, podiatry, plastic surgery, dermatology and other related medical, cosmetic and aesthetic markets.

In other financings activity, **Square 1 Bank** (McLean, Virginia), a partner to entrepreneurs and the venture capital community, said it has provided $1.75 million in debt financing to **BioSurplus** (San Diego), a provider of equipment management solutions and pre-owned scientific instruments to the life sciences industry. Loan proceeds will go towards fueling expansion for BioSurplus, and to repay existing indebtedness.

"BioSurplus has built a successful business with a history of exceptional performance, offering solutions for every stage of the laboratory equipment life cycle," said Scott Foote, senior vice president and managing director of Square 1 Bank's Life Sciences West division. "We are delighted to contribute to BioSurplus' growth in the life sciences industry." ■

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Agreements/contracts

OpGen provides microbial maps for 100K Genome

A *Medical Device Daily* Staff Report

OpGen (Gaithersburg, Maryland) has entered into a scientific and technical partnership with the **University of California, Davis**, (UC Davis) in cooperation with the FDA-supported 100K Genome Project to create high resolution microbial genetic maps.

The 100K Genome Project is a collaboration that was initiated by the FDA, UC Davis, and **Agilent Technologies** (Santa Clara, California) to sequence the genetic code of at least 100,000 infectious organisms and accelerate the diagnosis of foodborne illnesses. UC Davis will integrate OpGen's Argus Whole Genome Mapping System into its current DNA sequencing workflow for sequence assembly and validation of the genomes.

Through the integration of OpGen's Whole Genome Mapping technology, The 100K Genome Project will create a new gold standard for high-quality microbial reference genomes. These data will be used in the surveillance and management of international foodborne microbial outbreaks, and to establish a high-fidelity global reference database for microbial genomes. The 100K Genome Project will publish the genomes that are completed and validated using OpGen's Whole Genome Maps to a database, providing access to the genomic maps for public health agencies throughout the world. The FDA is advocating rigorous quality control standards for this reference database whereby genomic information should be validated by two independent methods.

"OpGen's technology allows us to complete sequencing and provide quality control of genomes drafted by data produced using short read next-generation sequencing methods," said Bart Weimer, PhD, professor, department of population and reproduction, School of Veterinary Medicine, University of California, Davis, and director of The 100K Pathogen Genome Project. "Whole Genome Mapping provides an independent method to detect sequence variations and misassemblies, and aids us in closing the gaps. Final Whole Genome Maps will assist health agencies in outbreak management of food borne diseases which cause tremendous risk to public health."

OpGen's Argus Whole Genome Mapping System is technology that can provide a high-resolution, complete visual map of a whole genome and individual chromosomes. The company says its unique single molecule analysis technology provides a whole genome view that complements genome assembly and enables scientists to identify highly repetitive regions, tandem repeats and translocations that are very difficult to identify and clarify with sequencing alone. Sequencing projects can now be finished and validated with less investment in time, cost and computational effort.

OpGen makes rapid, accurate genomic and DNA analysis systems and services.

In other agreements/contracts news:

• **Moneris Solutions** (Schaumburg, Illinois) has formed a strategic partnership with **Henry Schein MicroMD** (Boardman, Ohio), a provider of practice management and electronic medical records management software for medical practices and a subsidiary of **Henry Schein** (Melville, New York), a provider of healthcare products and services to office-based dental, medical and animal health practitioners.

Moneris will integrate its eSelectPlus payments gateway with encrypted card reader functionality into the upcoming new release of Henry Schein MicroMD's Practice Management (PM) software, enabling Henry Schein MicroMD customers to process patient credit and debit card payments directly through their MicroMD PM software. By eliminating the need for a traditional credit card terminal or stand-alone payment system, the new integrated solution will substantially reduce payment processing and equipment costs; the integrated card reader, which encrypts cardholder data before it reaches the Henry Schein MicroMD PM, helps protect patient account information and keep practices within the scope of PCI-DSS compliance.

Moneris will soon integrate its eSelectPlus gateway into Henry Schein MicroMD's on-line statement presentment and bill-pay solution, enabling Henry Schein MicroMD customers to offer patients the security and convenience of receiving and paying their medical bills electronically.

Moneris Solutions is a payment processor.

• The **Premier** (Charlotte, North Carolina) healthcare alliance reportednew multi-source agreements for blood bank analyzers, reagents, consumables and service have been awarded to Bio-Rad Laboratories (Hercules, California); Immucor (Norcross, Georgia); **Ortho Clinical Diagnostics** (Raritan, New Jersey); and **Quotient Biodiagnostics** (Newtown, Pennsylvania).

In addition, Premier reported new agreements for orthopedic soft goods have been awarded to **Clear Advantage Collar** (Charlotte, North Carolina); **Corflex** (Manchester, New Hampshire); **DeRoyal Industries** (Powell, Tennessee); and **DJO** (Vista, California).

Premier maintains a clinical, financial and outcomes database.■

HIT roundup

Retroscreen Virology selects Deltek's cloud ERP solution

A *Medical Device Daily* Staff Report

Deltek (Herndon, Virginia), a provider of enterprise software and information solutions for professional services firms and government contractors, reported that **Retroscreen Virology** (London), a fast-growing virology healthcare business, has selected Deltek's cloud ERP solution Deltek First, to support and enhance its significant growth. Retroscreen will use Deltek's project-centric cloud ERP solution to manage key aspects of its business and improve its overall business performance.

Retroscreen is a virology healthcare business that provides clinical services, focused on the viral challenge model (VCM), and pre-clinical analytical services, primarily to pharmaceutical and biotechnology companies. Retroscreen has grown and developed the VCM for evidencing the efficacy of antiviral and viral therapeutics in flu, cold and RSV viruses.

Instead of having different systems to manage core tasks such as resource management, management accounting, financial reporting and project planning, Retroscreen purchased Deltek First so it has one, integrated solution which eliminates the need for further investments and integration of new systems in the future. Based on web service technology and built with projects at its core, Deltek First will deliver complete information about Retroscreen's business ensuring that it always has a single source of the truth for measuring and forecasting the performance of its business.

"We were looking for a scalable solution that could help us improve our margins, forecast our business, leverage our resources and manage our entire project lifecycle better. After evaluating multiple solutions, we truly feel that Deltek First is an ideal and very powerful application, especially because it unites resource management, project accounting, finance accounting, scenario forecasting and dashboard reporting in one integrated multi-dimensional solution. It has been very reassuring working with Deltek throughout the selection process, because the company understands the project-centric nature of our business which is at its heart about people based service delivery. We look forward to working with Deltek as a key business partner in the years to come as we transform our financial and commercial management processes with Deltek First," said Graham Yeatman, finance director of Retroscreen. ■

Deals roundup

TeamHealth Holdings in plan to acquire Mobile Emergency Group

A *Medical Device Daily* Staff Report

TeamHealth Holdings (Knoxville, Tennessee) reported on the continued growth in its Alabama operations through an acquisition of the practice of **Mobile Emergency Group** (MEG; Mobile, Alabama), the physician group that currently provides services to the emergency departments of **Mobile Infirmary Medical Center** (Mobile, Alabama), and **North Baldwin Infirmary** (Bay Minette, Alabama).

Both hospitals are part of Mobile-based Infirmary Health System (IHS). On Dec. 15, TeamHealth commenced staffing and administrative services for these emergency departments that care for roughly 57,000 patients annually.

"We share TeamHealth's commitment to quality, efficiency and exceptional patient care," said William Admire, CEO. "The organization's infrastructure and administrative support provides the necessary resources to improve our efforts to recruit and sustain emergency physicians and enhance clinical care for the patients we serve."

In other dealmaking activity, **Allergan** (Irvine, California) said it has completed the acquisition of **SkinMedica** (Carlsbad, California).

Allergan paid about $350 million for the business, which includes a variety of "physician dispensed" non-prescription aesthetic skin care products and prescription products (*Medical Device Daily*, Nov. 19, 2012). In connection with the closing of the transaction, SkinMedica spun out its Colorescience aesthetic make-up business. Allergan plans to operate SkinMedica as a separate global business based out of SkinMedica's current headquarters in Carlsbad.

"The acquisition of SkinMedica reinforces our commitment to fueling growth through a combination of internal investment in research and development and leveraging external opportunities," said David E.I. Pyott, chairman and president/CEO, Allergan. "Today marks a significant achievement for Allergan, as our acquisition of SkinMedica will enable us to assume a leadership position in the 'physician dispensed' topical aesthetics category and will further strengthen our leadership position in the facial aesthetics market by expanding our product portfolio to better meet the needs of physicians and their patients." ■

Dubreuil

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project management processes within their organizations, so they've become more discriminating when they're looking for a development partner. They want to know not only that you can create award-winning designs, but that you have a process and the talent to meet whatever needs they might have.

That's generally been the biggest change and challenge for design firms. The larger ones have learned to adapt and have survived while the smaller firms still have a livelihood, but not so much in medical devices.

MDD: How do you expect the pending imposition of the medical device tax to impact the business of medical product developers such as yourselves?

Dubreuil: We have already seen a number of large medical OEMs reorganize in an effort to address this. It's already having an impact on our business, with potentially fewer new products being developed in favor of refreshing existing product lines in order to maximize their investment and minimize their R&D spending.

One of the folks I follow in this business is Michael Matson, an equity research analyst at Mizuho Securities who does a lot of research on this area, and one of his points is that the earnings per share threshold that these large companies have to meet in order to make shareholders happy is really critical. He's suggesting that the large-cap and mid-cap companies are going to see EPS growth reduced by an average of 4% and that the small-cap companies are going to see their EPS growth reduce by an average of 12%. That's a huge hit to the bottom line, and I think it's going to have a pretty significant effect on our business opportunities in general.

The flip side of that is there may be fewer projects that get funded for R&D, but there may also be cuts in staff, and we've seen that happening at some of the larger medical OEMs like Medtronic and Stryker, so it could have a balancing effect on our business. We could potentially see fewer projects that occur, but may see an increase in the need for outsourcing based on the fact that these OEMs don't have sufficient staff to execute whatever projects are still in their development pipelines.

MDD: How does the process of going from idea to product work at Farm? Start with the philosophy, then a glimpse at how the project evolves.

Dubreuil: The process is pretty structured. Because we're ISO-13485 certified and involved primarily with medical-device design, we're required to have a structured process to satisfy regulatory compliance, but it's that same process that has made us successful. Our process is very oriented towards usability and towards full product development, so we employ a very broad-based process that begins with research into user needs and then typically moves from defining those needs into specification development. We then develop product

MARC DUBREUIL
Cultivates Medical Products

requirements and product specifications so that we clearly know what it is we're going to be designing and developing.

We then move into concept development phases where we create numerous concepts for evaluation by our clients, by our own internal teams, and often by end-users who represent the target market. We then down-select the concepts to a single solution, and begin to do engineering, analysis and design iteration in order to arrive at a solution that meets the product requirements.

What is unique about Farm's process is that we incorporate usability insights and user feedback into the concepts, prototypes, engineering samples and models that we create in order to ensure that what comes out at the end meets the needs of the end user, the usability requirements and the product requirements as stated by the client.

Once we've finished with engineering, we move into design transfer and into the verification and validation processes, so that we're verifying the design to the product requirements and validating the product to the user needs. Then, because we're not a manufacturer, we typically employ a robust design transfer process that allows us to transfer the design and engineering information to manufacturers that assures that the product will be built correctly.

It's a very structured, step-by-step process that applies to all elements of design. It applies to the industrial design, the engineering components, the graphical user interface and all of the usability components. Each one of those areas of development has its own user research, design, development, verification and transfer to manufacturing component, but these are completely integrated at Farm. Mechanical engineering, industrial design, software, systems integration, and manufacturability are all part of what we provide.

MDD: Tell me about the communications process between you and a client. How important is that to the overall project?

Dubreuil: Beyond regulatory or ISO or other requirements such as risk analysis and usability, in which you have to be really robust, project management tools are really important. We've seen the large OEMs move to

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Washington

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cleared in July 1995, when the device was owned by **Bioflex** (Columbus, Ohio). The warning letter says that the cleared indications, in addition to the muscle spasm and disuse atrophy indications, included use of the device to increase in local blood circulation, muscle re-education, and immediate post-surgical stimulation of calf muscles as a prophylactic to thrombosis. The warning letter states that instruction manuals and brochures for Axiobionics' wearable therapy system for the upper extremities promoted the devices for claims such as spinal cord and traumatic brain injury in addition to the cerebral palsy and stroke claims.

The company evidently engaged a graphic designer without documenting discussions of how the designer's recommendations worked into the design of several items, including the Plexus device for arms and the Biobelt for lumbar spinal application. FDA says that Axiobionics "and the graphic designer would discuss projects verbally without documenting design plans" in a citation for documentation of design and development plans.

This situation migrated to another citation, one for procedures for transfer of design changes into product specifications. A citation that may be related to these consultations stated that Axiobionics replaced double-sided silver lycra fabric used in the Plexus and Biobelt "with coated flexible wires as the conducting component." FDA stated that these activities "were not adequately documented before their implementation." This change was noted later in the warning letter as not having been updated in the 510(k) filing for the devices, but both devices were also cited later in the warning letter for lack of procedures governing manufacturing procedures.

Axiobionics did not respond to contacts for comment.

GAO; CMS has overlapping programs

If there's one thing that drives deficit hawks crazy, it's redundant programs at the federal level, and a Government Accountabilty Office (GAO) report says that the Centers for Medicare & Medicaid Services suffers from precisely that problem with the programs in play at the agency's healthcare delivery innovation office. The report was addressed to three Republican members of the U.S. Senate and will no doubt be addressed in hearings under the 113th Congress, yet another angle for congressional oversight of the agency. However, CMS indicated it finds GAO's concerns overblown.

GAO says in the report's summary that the Center for Medicare and Medicaid Innovation has focused on 17 model programs since its inception in 2010, but that the center is "still relatively early in the process of implementing these models." The item sure to capture attention in congressional hearings is the statement that the Innovation Center "projects that a total of $3.7 billion will be required to fund testing and evaluation of the 17 models," with funding for individual models ranging as high as $931 million. According to GAO, the innovation office had awarded contracts for evaluation of 10 of the 17 models as of Aug. 1, and the innovation office is said to have "taken steps to monitor its progress in implementing the 17 models through biweekly reviews of standard milestones and related data."

GAO said it had pegged "three key examples of overlap between the 17" models and ongoing efforts from other areas at CMS, explaining that the overlaps are in similar goals, similar activities, and/or the targeting of similar populations. The summary notes that the overlapping programs "also have differences," and CMS officials are said to have explained that the innovation programs in question are intended to be complementary" to other programs underway at the agency.

The summary claims that GAO's evaluation prompted CMS officials to establish that it is not paying for a given set of services under more than one contract, but CMS is said to be working to ferret out any such redundancies.

The full report states that the Medicare Payment Advisory Commission determined that spending on demonstration projects at CMS ran "less than $1 billion for the period of fiscal years 2000 through 2010." That figure, GAO says, has ballooned to $10 billion for fiscal years 2011-2019, and a projected $10 billion for subsequent decades, numbers that are sure to draw interest in a fiscally difficult climate.

Another reason for tighter congressional scrutiny is spelled out in the passage stating that unlike demonstrations in times gone by – which could be expanded across Medicare and Medicaid only by statute – the Affordable Care Act allows CMS to expand the use of demonstration program characteristics into the agency's administration of Medicare and Medicaid via rulemaking so long as such a program did not boost spending and would not result in denial or limitation of coverage.

GAO says that the innovation center is also immune to several other provisions typically governing demonstration projects, including the absence of a mandate that models be budget neutral. The Affordable Care Act is also said to have made the testing and roll-out of care models immune to judicial review as well as to the requirements of the Paperwork Reduction Act.

Jim Esquea, assistant secretary for legislation at the Department of Health and Human Services, indicated in a response to the GAO report that CMS is intent on eliminating duplication of effort in the programs, but argued "that only one of the three examples cited poses a genuine risk of duplicative effort."

Esquea asserted that the accountable care programs do not overlap with Medicare shared savings programs because the Pioneer ACO program does not permit dual participation, while the advanced payment ACO model is designed to augment the shared savings programs.

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Elixir

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a challenge in the industry because it required a level of strength and support that only permanent metallic stents had been able to provide, the safe and gradual bioresorption of the scaffold once the blood vessel healed, and for excellent clinical outcomes. The DESolve novolimus eluting bioresorbable coronary scaffold holds the promise to overcome these challenges, Elixir noted.

"We have the lowest drug dose on our DES platform, the thinnest polymer load, and the thinnest stent struts," Sirhan told *MDD*. He added that these qualities of the device have led to "exceptional clinical outcomes at six to nine months, but also sustainable outcomes . . . those differentiate us from comparable available technology today."

In late October Elixir reported enrollment completion of its 120-patient, pivotal clinical trial evaluating the safety and efficacy of the DESolve novolimus eluting bioresorbable coronary scaffold system. Patient follow-ups are expected to be completed by the end of this year, the company noted.

The primary safety endpoint of the DESolve Nx trial is the composite of major adverse cardiac events (MACE) comprised of cardiac death, target vessel myocardial infarction (MI) and clinically-indicated target vessel revascularization (TLR). The primary angiographic endpoint of the trial is in-stent late lumen loss at six months as assessed by quantitative coronary angiography (QCA). In a sub-set of patients, additional QCA assessment will be conducted at 24 months; stent and vessel assessment using intravascular ultrasound (IVUS), optical coherent tomography (OCT) will be conducted at baseline, six and 24 months; and multi slice CT (MSCT) at 12 months thus providing long-term assessment of the scaffold and surrounding vessel.

"Bioresorbable drug eluting scaffolds that effectively treat the coronary artery obstruction without leaving a permanent metallic implant behind in the long term are undoubtedly the next frontier for interventional cardiology," said Stefan Verheye, MD, PhD, **ZNA Middleheim Hospital** (Antwerp, Belgium), and principal investigator of the DESolve Nx study. "Having used the DESolve bioresorbable scaffold system in two clinical studies, and observed its impressive performance, I am confident that Elixir's DESolve scaffold system can achieve and maintain excellent long-term clinical outcomes."

The DESolve scaffold made from a proprietary poly-L Lactide (PLLA)-based polymer provides optimal strength and support to the artery while delivering the novel anti-proliferative drug, novolimus. Some unique features of the DESolve scaffold design as demonstrated in preclinical testing include (a) the ability to self-appose to the vessel wall in cases of malapposition; (b) the ability to maintain radial strength and vessel support for the critical period of vessel healing while bioresorbing within 12-24 months; and (c) a wide margin of scaffold expansion without strut fracture.

The multi-center, prospective DESolve Nx trial was designed to enrolled 120 patients at 15 centers in Germany, Belgium, Poland, Brazil and New Zealand. Enrollment completion of the trial follows "outstanding results" of Elixir's DESolve first-in-man study wherein at six months, the DESolve demonstrated excellent late lumen loss of 0.19 ± 0.19 mm, no artery blockage (0.0% binary restenosis), no late malapposition (0.0%), low acute recoil (6.4% ± 4.3), no cases of blood clots (0.0% stent thrombosis), and a single MACE event due to a stenosis in the segment 5 mm proximal to the scaffold, which itself was widely patent, the company reported.

In late October, Alexandre Abizaid, MD, PhD, from the **Instituto Dante Pazzanese de Cardiologia** (Brazil), conducted a live case from Sao Paulo of a patient enrolled in the DESolve Nx trial undergoing six-month follow-up. The angiographic, IVUS, OCT, and MSCT imaging of the coronary vessels treated with the fully bioresorbable DESolve scaffold was projected live in the main arena at the annual Transcatheter Cardiovascular Therapeutics (TCT) meeting in Miami. The coronary vessels of the patient were widely patent, and these results were well received by an expert panel of cardiologists at TCT.

The device's ability to self-appose to the vessel wall, or self-correct, is one of the key differentiating features of the DESolve scaffold system, Sirhan said. He also noted that the device's ability to fully resorb in the body within one to two years makes its resorbable rate about half the time of competing devices. Finally, he said the scaffold comes in a full range of sizes without limitations in manufacturing ability.

"The feedback that we're getting [from physicians in the field] is that they're recognizing that we have the deepest and broadest portfolio of any company in the industry," Sirhan said. He noted that the case presented at TCT was a very difficult case and its successful outcome reinforces the technology's performance ability.

"We look [to be] the future of resorbable scaffolds," Sirhan said. "We feel our technology to be the most advanced, faster resorbable times by about half the time, self-directing scaffold properties to allow it to have a user-friendly deployment . . . puts us into a position of really getting this technology into" the mainstream marketplace.

Elixir also recently reported excellent long-term results of its CE mark-approved DESyne novolimus eluting coronary stent system compared to the control Endeavor zotarolimus eluting coronary stent system in the EXCELLA II randomized clinical trial at the three-year endpoint (*Medical Device Daily*, Oct. 26, 2012).

At three years, device-oriented composite endpoints (DoCE), a measure of major adverse events, for Elixir's DESyne were exceptionally low and essentially unchanged through one, two and three years (4.3%, 4.3% and 5.0%) while the control Endeavor increased yearly (7.0%, 9.9% and 12.7%) with a trend towards statistical significance (p=0.057). TLR

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Dubreuil

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fairly large, robust and integrated program management systems, and a lot of the big companies have directors or VPs of program management.

In the service business you're basically left to develop your own system for program management, but it is a really strong component of success. Within the program management tools are the communication tools that you're asking about. They're all tied together, beginning with defining with your clients how you're going to communicate, what you're going to communicate, how often you'll communicate.

The tools go well beyond face-to-face meetings to embrace how we communicate in online design meetings, perhaps featuring larger teams at both ends, and in general just being much more flexible in being able to connect across the country or across international borders. We now can share much richer information about the designs, and we also have communication tools that provide our clients insight into the financial side of the project such as how we are doing relative to budget. We also can give them better information on how we're doing relative to schedule, we give them information and requirements to respond to challenging or difficult areas, priorities, option items.

So we use a number of tools to help us with communication and program management that are really critical to keeping our team on track, keeping our clients' teams on track, and keeping everybody informed about the key aspects of budget, timing, critical action items, and any quality issues that arise.

Along with that is this big component of manufacturing. How do we as designers make sure that what we're designing is manufacturable and make sure that in the design transfer process, it's a smooth process and not a "hand it over the wall" type of thing. That typically means that we are looking to get manufacturers identified and involved as early in the process as we can.

We are hoping that they are available to be working with us during the design process so that we have their input about manufacturing methods and materials and new technologies that might apply to the product that they can provide to us. We like to give them a seat at the table and responsibility to bring more information, more feedback, more engineering support when it comes to manufacturing engineering. We like them to be involved in helping to meet process capability requirements – that's really critical to a successful program.

(In Part 2 of the MDD Interview next week, Marc Dubreuil discusses the importance of usability in product design, the emphasis on product safety, measurement of outcomes for new products, use of virtual prototyping and other new tools in design, and working on optimization of existing products as they move to second-generation form.) ■

Elixir

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rates at three years were significantly lower in favor of the DESyne stent as compared to the control (l4% vs. 9.9%; p=0.008), the company noted.

Elixir's DESyne stent elutes the m-tor inhibitor compound novolimus. According to Elixir, it is the first drug eluting stent to successfully combine the thinnest durable polymer coating, the lowest drug dose, and thin stent struts to achieve excellent clinical outcomes as compared to other commercially available DES systems, the company said. The EXCELLA II trial had previously demonstrated both non-inferiority and superiority of DESyne compared to Endeavor for the primary endpoint of in-stent late lumen loss at nine months.

"We look forward to completing follow-up phase for DESolve and filing for CE mark approval and then looking for getting our IDE submission and approval completed in 2013 for DESyne and looking at demonstrating more of the clinical trial benefits of our scaffold," Sirhan told *MDD* when asked about the company's goals for the new year. ■

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Esquea said the innovation office's Partnership for Patients program is somewhat duplicative with respect to work done by the Center for Clinical Standards and Quality, but said that CMS has already begun work to eliminate those duplications. ■

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Product Briefs

• **PhysioSonics** (Bellevue, Washington) received FDA clearance for the Presto 1000 Flow Monitor system for cranial blood flow monitoring. The Presto 1000 Flow Monitor is designed to allow any clinician to perform mid cerebral cranial blood flow monitoring, freeing institutions to more efficiently deploy sonographers who are required less often for the system. It is also designed to replace periodic measurement with continuous monitoring. PhysioSonics uses its "Flash" Doppler for the monitoring functions. The addition of Flash, with the transducers attached to headset, assists in locating and maintaining the flow of information from mid cerebral arteries.

• **Roche** (Basel, Switzerland) said the FDA has accepted the use of its PCR based mycoplasma detection test MycoTOOL for release testing of one of Roche's biological products. It is the first available mycoplasma PCR test accepted by the FDA for release testing of a biopharmaceutical product that can replace conventional and time-consuming mycoplasma detection assays based on culture methods. Mycoplasms are frequent causes of contamination in biopharmaceutical production, cell therapy, tissue engineering and vaccine manufacturing. The MycoTOOL PCR Mycoplasma Detection Kit provides all critical reagents for performing an easy to use sample preparation and PCR. It offers a high sensitivity (<1 CFU/ml for most isolates) and is compatible with a diverse spectrum of sample types as cellular matrices (Human cells, primary and continuous), canine cells, nonhuman primate cells, many different rodent cell types and cell-free matrices (culture supernatants of CHO or human stem cells, egg derived samples). The test also minimizes the risk of false negative and false positive test results: lysis controls of the matrix eliminate the risk of undetected intracellular Mycoplasma and positive controls verify potential PCR inhibition.

People in the News

• **Air Techniques** (Melville, New York) said Robert Olivero as their new product manager. Olivero previously held the position of technical business manager/field application engineer with Avnet Electronics Marketing in the semiconductor industry. Air Techniques specializes in dental equipment.

• **Harris** (Melbourne, Florida) has named Vishal Agrawal, MD, president of the company's healthcare solutions business. Agrawal joins Harris from McKinsey and Company, where he was a partner and leader in the firm's North American Healthcare Systems and Services practice. Harris is a communications and information technology company.

• **IGI Laboratories** (Buena, New Jersey) said Kenneth Miller has been named senior VP of R&D. Prior to joining IGI Laboratories, Miller held various leadership positions at Mylan Technologies eventually rising to senior director in 2008. IGI Laboratories is a topical generic drug development and manufacturing company.

• **Third Rock Ventures** (Boston) said that Mark Perry and Uday Kumar, MD, have joined Third Rock as entrepreneurs-in-residence in the firm's West Coast office. Perry is chairman of the board of Pathway Therapeutics and is a board member of Nvidia. Kumar, a cardiologist and cardiac electrophysiologist, is the founder of iRhythm Technologies. Third Rock Ventures was founded in 2007 with the mission to launch transforming companies.

Med-Tech Notes

Ohio hospital uses Cook's Zilver PTX stent

OhioHealth Riverside Methodist Hospital in Columbus, Ohio, has treated the first patient with the **Cook Medical** (Bloomington, Indiana) Zilver PTX drug-eluting peripheral stent. device as part of Cook's U.S. commercial launch.

"It was a great honor for my institution to be first to implant Cook Medical's Zilver PTX as part of the stent's commercial roll-out," said Gary Ansel, MD, system medical chief, vascular, for OhioHealth. "This technology is so advanced and offers such prolonged patient benefit, I believe it will very quickly challenge older PAD treatments such as balloon angioplasty and bare metal stenting in the U.S. as the standard of PAD care."

Zilver PTX, approved for use in the above-the-knee femoropopliteal artery, is the only drug-eluting stent approved for use in a peripheral artery in the U.S, Cook says. The device has a proven drug effect that reduces by more than 50% the need for followup procedures to reopen the artery. These followup procedures can be expensive, which places extra burdens on patients, physicians and facilities.

The disease Zilver PTX targets, peripheral arterial disease (PAD) affects an estimated 8-12 million Americans each year.

MDD's Ortho Extra

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

Thursday, December 20, 2012

Keeping you up to date on recent developments in orthopedics

Engineering researchers pinpoint the origin of bone fractures . . .

A new study from engineering researchers at **Rensselaer Polytechnic Institute** (Troy, New York) shows, for the first time, how the little-understood protein osteocalcin plays a significant role in the strength of our bones. The findings could lead to new strategies and therapeutics for fighting osteoporosis and lowering the risk of bone fracture. Funded by the U.S. National Institutes of Health, the study details how fractures in healthy bones begin with the creation of incredibly tiny holes, each measuring only about 500 atoms in diameter, within the bone's mineral structure. In the case of a slip, trip, or fall, the force of the impact on a bone physically deforms a pair of joined proteins, osteopontin and osteocalcin, and results in the formation of nanoscale holes. These holes, called dilatational bands, function as a natural defense mechanism, and help to prevent further damage to the surrounding bone. However, if the force of the impact is too great - or if the bone is lacking osteopontin, osteocalcin, or both - the bone will crack and fracture. The multi-university study, led by Deepak Vashishth, head of the Department of Biomedical Engineering at Rensselaer, is the first to give evidence of fracture at the level of bone's nanostructure. Partnering with Rensselaer on the study were **Villanova University** (Villanova, Pennsylvania), the **Hospital for Special Surgery in New York**, and **Yale University** (New Haven, Connecticut). "This study is important because it implicates, for the first time, the role of osteocalcin in giving bone the ability to resist fracture," Vashishth said. "Since osteocalcin is always the point of fracture, we believe that strengthening it could lead to a strengthening of the overall bone." Long known but little understood, the protein osteocalin has been produced by and present in animal bones since before the dawn of humanity. Recently, abnormalities in ostoecalcin production have been associated with Type 2 diabetes as well as problems in reproductive health. Vashishth's new study, however, is the first to explain the structural and mechanical importance of osteocalcin in bone. Now that osteocalcin is known to participate in bone fracture, new strategies for strengthening the bond between osteocalin and osteopontin can be investigated, Vashishth said. Augmenting the body's natural supply of osteocalcin, for example, could be one possible strategy for treating osteoporosis and other conditions leading to increased fracture risk, he said. Osteocalin must be in its carboxylated form to get absorbed into bone, and the protein is carboxylated by vitamin K. Vashishth said future studies could investigate the relation between vitamin K intake, osteocalcin, and bone strength. "Currently, all of the advice for treating osteoporosis is related to calcium. We believe there's more to the story than just calcium, and the results of this new study raise an important question about vitamin K. Leafy green vegetables are the best source of vitamin K - wouldn't it be great if eating spinach and broccoli was not only healthy, but also good for your bones? We plan to investigate this link in future," Vashisth said.

Evidence insufficient to recommend routine antibiotics for joint replacement patients who undergo dental procedures . . .

The **American Academy of Orthopaedic Surgeons** (AAOS; Rosemont, Illinois), and the **American Dental Association** (ADA; Chicago) found that there is insufficient evidence to recommend the routine use of antibiotics for patients with orthopaedic implants to prevent infections prior to having dental procedures because there is no direct evidence that routine dental procedures cause prosthetic joint infections. The AAOS and ADA's recommendations are based on a collaborative evidence-based clinical practice guideline that focuses on the possible linkage between orthopaedic implant infection and patients undergoing dental procedures. "As clinicians, we want what is in the best interest of our patients, so this clinical practice guideline is not meant to be a stand-alone document. Instead it should be used as an educational tool to guide clinicians through treatment decisions with their patients in an effort to improve quality and effectiveness of care," said David Jevsevar, MD, MBA, chair of the AAOS Evidence Based Practice Committee which oversees the development of clinical practice guidelines. "It has been long debated that patients with orthopaedic implants, primarily hip and knee replacements, are prone to implant infections from routine dental procedures," added Dr. Jevsevar who also is an orthopaedic surgeon in St. George, Utah.

"What we found in this analysis is that there is no conclusive evidence that demonstrates a need to routinely administer antibiotics to patients with an orthopaedic implant, who undergo dental procedures. Elliot Abt, DDS, MS, MSc, who served as member of the AAOS-ADA work group on behalf of the ADA, pointed out that the review committee conducted a thorough review of existing clinical research published in the peer-reviewed literature. "This guideline was based primarily on clinical research which examined a large group of patients, all having a prosthetic hip or knee and half with an infected prosthetic joint," said Dr. Abt, a general dentist in Skokie, Illinois, and a member of the ADA Council on Scientific Affairs. "The research showed that invasive dental procedures, with or without antibiotics, did not increase the odds of developing a prosthetic joint infection." This clinical practice guideline, with three recommendations, is based on a systematic review of the correlation between dental procedures and prosthetic joint infection (PJI). Recommendation one, which is based on limited evidence, supports that practitioners consider changing their longstanding practice of prescribing prophylactic antibiotics for patients who undergo dental procedures. Limited evidence shows that dental procedures are unrelated to PJI. Recommendation two addresses the use of oral topical antimicrobials (topical antibiotic administered by a dentist) in the prevention of PJI in patients undergoing dental procedures. There is no direct evidence that the use of oral topical antimicrobials before dental procedures will prevent PJI. Recommendation three is the only consensus recommendation in the guideline, and it supports the maintenance of good oral hygiene. "Research is always changing and we need to work to improve clinical research databases, so in the future any type of prospective research done in this area will help shed light on prophylaxis and orthopaedic infection rates," Jevsevar said. The "Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures" guideline replaces the previous AAOS Information Statement, "Antibiotic Prophylaxis for Bacteremia in Patients with Joint Replacement." The full guideline along with all supporting documentation and workgroup disclosures is available on the AAOS website.

Patients with severe back pain who quit smoking report less pain than patients who continue to smoke . . . For years, research has shown a link between smoking and an increased risk for low back pain, intervertebral (spine) disc disease, and inferior patient outcomes following surgery. A new study, published in the December 2012 *Journal of Bone and Joint Surgery*(JBJS), also found that smokers suffering from spinal disorders and related back pain, reported greater discomfort than spinal disorder patients who stopped smoking during an eight-month treatment period. Nearly all adults will be seen at some time by a physician for back pain or other painful spinal disorders. As smoking has been identified as a modifiable risk factor for chronic pain disorders, researchers reviewed the smoking history and monitored the reported pain of more than 5,300 patients with axial (back) or radicular (leg) pain from a spinal disorder, treated surgically or non-surgically, over an eight-month period. At the time of entry into care, patients who had never smoked and prior smokers reported significantly less back pain than current smokers and those who had quit smoking during the study period. Current smokers reported significantly greater pain in all visual analog scale (VAS) pain ratings worst, current and average weekly pain when compared with patients who had never smoked. Those who quit smoking during the course of care reported greater improvement in reported back pain than those who continued to smoke. The mean improvement in VAS pain ratings was clinically significant in nonsmokers.The group that continued smoking during treatment had no clinically significant improvement in reported pain. Using the Oswestry Disability Index (the most commonly used outcome measure for low back pain assessment), greater mean improvement was observed in patients who had never smoked when compared to current smokers. "We know that nicotine increases pain," said study author Glenn R. Rechtine, MD, University of Rochester Department of Orthopaedics. "In this study, if you quit smoking during treatment, you got better. If you continued to smoke, there was statistically no improvement, regardless of the treatment you had. Smoking is bad for you. Basically, the likelihood to improve your care surgical or non-surgical was dramatically decreased if you are a smoker. "This study supports the need for smoking cessation programs for patients with a painful spinal disorder given a strong association between improved patient reported pain and smoking cessation," said Rechtine.

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