Medical Device Daily™
The Daily Medical Technology News Source
Thursday, October 4, 2012 Vol. 16, No. 192 Page 1 of 10

AdvaMed 2012 Conference

Industry wants more detail for unsolicited off-label inquiries

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

BOSTON — The second day of AdvaMed 2012, hosted by the **Advanced Medical Technology Association** (AdvaMed; Washington), included a session dealing with the recent guidance for responding to unsolicited inquiries into off-label indications, and many in attendance may have hoped for a promise from FDA that it would fill in the blanks in the December 2011 guidance on this subject. Despite promises to provide more detail, a senior manager at the agency's device branch said it is unlikely the agency will be able to draw a line that addresses every conceivable scenario, leaving doctors and representatives of device makers with a legal high-wire act to pull off when a patient urgently needs care and a doctor has no satisfactory

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Trautman: IMDRF following other efforts on single audits

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

BOSTON — One of the sessions held on the last day of AdvaMed 2012 dealt with regulatory harmonization – or regulatory convergence as the realists like to say – but the FDA representative to the International Medical Device Regulators Forum (IMDRF) indicated that IMDRF is behind the curve on inspectional harmonization and hence is piggybacking on existing efforts. Kim Trautman, FDA's liaison to IMDRF also said, however, that the organization is working on standards that might help IMDRF leapfrog other inspection accreditation programs, but that those efforts are still in the early stages.

FDA said earlier this year it would roll out a pilot program by June that would allow the agency to accept inspections by

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The MDD Interview

Broadened role ahead for Indiana Health Information Exchange

2nd of 2 parts

By JIM STOMMEN, *MDD* Contributing Writer

Harold Apple is CEO and president of the Indiana Health Information Exchange (IHIE), the nation's largest health information exchange organization. IHIE connects the state's hospitals, physicians, long-term care facilities and other healthcare providers, enabling medical information to follow patients regardless of treatment location to improve care coordination and patient outcomes. Physicians in the IHIE network provide care to more than 10 million patients.

Apple was formerly the majority owner, CEO and president of Vector Technologies, a business process outsourcer, consulting and software development company in the life insurance sector. He also was one of the founders

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ConforMIS launches iTotal G2 knee replacement system

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

According to recent studies, nearly one in five patients with a total knee replacement system are not satisfied with the results of their surgery. Issues that plague patients are often implant overhang; errors in component placement; and off-the-shelf implant shapes that don't match the patient's native anatomy. These complications can lead to residual pain for the patient.

A recently launched implant by **ConforMIS** (Burlington, Massachusetts) is said to effectively deal with many of these issues. The company reported launch of its iTotal G2 knee replacement system. The device is the next generation version of iTotal, which was cleared by the FDA in January of 2011.

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Don't miss today's MDD Extra: Orthopedics

INSIDE:

AHC Media

Report from Europe

Study shows alternative route for Medtronic's CoreValve

A *Medical Device Daily* Staff Report

New data presented at PCR London Valves 2012 reinforced **Medtronic**'s (Minneapolis) clinical case for an alternative route to the heart for transcatheter aortic valve implantation (TAVI) using its CoreValve stent.

Data from 151 patients showed 97% procedural success for the direct aortic approach with an overall 30-day mortality rate of 8.6%, an incidence of stroke at 3.9%.

Transfermoral access is the predominant access route in TAVI procedures where the prosthesis traverses the body using a catheter delivery device to arrive in the aortic arch and descend to be seated within the native valve.

For patients who have torturous and heavily calicified vessels the alternative route until recently has been transapical where the catheter passes through an incision between two ribs and after puncturing the ventricle ascends to place the valve.

Only **Edwards Lifesciences** (Irvine, California) offers a device approved for transapical procedures.

While Medtronic is continuing a clinical trial to win approval for a similar approach, the smaller size and flexibility of the CoreVale and its delivery system have encouraged interventional cardiologists to explore other route for transfemorally-challenged patients.

Notable, CoreValve pioneered the subclavian approach that maintains a more minimally invasive profile.

Like transapical, direct aortic access is more invasive, also requiring an incision between two ribs in 62% of cases or with a minimal puncture of the sternum.

The advantage of direct aortic access is that the catheter punctures the aortic artery and descends as with other CoreValve procedures to seat the self-expanding nitinol stent.

The pioneer of this technique is Giuseppe Bruschi, MD, cardiac surgeon at **Niguarda Ca' Granda Hospital** (Milan, Italy), who is co-primary investigator in Medtronic's ADVANCE Direct Aortic Study.

The data was collected from interventions performed at 15 centers across Europe and Israel.

Opko launches 4Kscore with IHT

Opko Health (Miami) reported its strategic partner, **International Health Technology** (IHT; Cambridge, UK) launched the Opko 4Kscore in Europe as part of IHT's ProstateCheck program being offered as an early detection service.

Earlier this year, Opko executed a sublicensing deal with IHT to commercialize Opko's novel panel of kallikrein biomarkers and associated algorithm (4Kscore) for the early detection of prostate cancer in a laboratory setting in the UK, Ireland, Sweden and Denmark.

The Opko panel represents the culmination of a decade of research by scientists in Europe and the U.S. and has been demonstrated in over 10,000 patients to predict the probability of cancer-positive biopsies in men suspected of having prostate cancer. Extensive studies have shown that the use of the panel could eliminate a significant number of unnecessary prostate biopsies, a possible reduction of over 50%, along with a high frequency of associated pain, bleeding and infection, sometimes requiring hospitalization.

IHT, through close cooperation with some of the largest private hospitals chains in the UK and abroad, has access to world class private facilities and specialists to provide testing services for corporate clients in the private sector.

IHT specializes in launching new diagnostic technology in the private sector as part of a clinical service and as a distribution partner. Opko is a diagnostics company that seeks to establish industry-leading positions in large and rapidly growing medical markets by leveraging its

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Agreements/contracts

NeoChord wins exclusive rights to new imaging tech

A *Medical Device Daily* Staff Report

NeoChord (Eden Prairie, Minnesota), a device company focused on minimally invasive mitral valve repair, said it has obtained the exclusive rights to 'augmented reality' imaging technology from the Robarts Research Institute (RRI) at **Western University** (London, Ontario).

Financial terms of the licensing agreement were not disclosed. Minimizing invasiveness associated with cardiac procedures has led to limited visual access of the targeted cardiac structures, the company noted. To address vision limitations, RRI developed an imaging technology that integrates transesophageal echo (TEE) with a magnetic tracking system along with geometric models of the pertinent anatomy and the NeoChord mitral repair device.

"We believe the NeoNav system complements our minimally invasive mitral valve repair technology perfectly," said John Zentgraf, VP of R&D at NeoChord. "As presented by Michael Chu, MD, cardiac surgeon at Western University, the early research findings on the NeoNav system won the 'young investigators' award at the 2012 ISMICS (International Society for Minimally Invasive Cardiothoracic Surgery) conference recently held in Los Angeles. Dr. Chu's research team demonstrated faster and more accurate navigation to the target anatomy than that provided by TEE alone."

The advanced imaging technology licensed to NeoChord was invented and developed in the laboratory of Terry Peters, PhD, a preeminent scientist with the Imaging Research Laboratories at the Robarts Research Institute (RRI), and a professor in the departments of medical imaging and medical biophysics at Western, as well as a member of the graduate programs in Neurosciences and Biomedical Engineering.

In other agreements/contracts news:

• **ICF International** (Fairfax, Virginia), a provider of consulting services and technology solutions to government and commercial clients, has been awarded a re-compete contract by the National Eye Institute (NEI) to provide communication services to the National Eye Health Education Program (NEHEP). The contract has a value of $15 million and a term of one base year and four option years.

ICF will support NEHEP with all communication services, including strategic planning, program development, implementation and evaluation, partnership development, formative research, earned media placements, social media, and community-based training and capacity building. The company will provide creative and multi-media services, assist with writing articles for peer-reviewed journals, and develop abstracts and present at national conferences on behalf of the NEI, as well as provide logistical and database support.

• **Humanetics** (Minneapolis), a specialty pharmaceutical company, said it was recently awarded a small business innovation research (SBIR) Fast Track contract from the National Cancer Institute (NCI) to work with **Henry Ford Hospital** (Detroit) to study and develop BIO 300 as a radiation modulator for use during radiotherapy of lung cancer.

The SBIR Fast Track award includes two phases. The Phase I award is for nine months, totaling $197,224 and includes preclinical proof of concept experiments. Phase II, if approved by NCI, will advance the drug into a human efficacy trial in lung cancer patients. The Phase II award is $1,499,181. The preclinical and clinical trials will be conducted at Henry Ford Hospital.

The goal of the research is to demonstrate the ability of BIO 300 to improve outcomes in lung cancer patients who receive traditional radiation treatment. BIO 300 will be evaluated for its ability to sensitize lung cancer cells, making radiation more effective at reducing tumor size, while also protecting normal tissues from the negative side effects of radiation. ■

Deals roundup

LeMaitre Vascular to acquire XenoSure rights for $4.6M

A *Medical Device Daily* Staff Report

LeMaitre Vascular (Burlington, Massachusetts), a provider of peripheral vascular devices and implants, has signed an agreement to acquire the manufacturing and distribution rights to XenoSure from **Neovasc** (Vancouver, British Columbia), for $4.6 million. XenoSure is a bovine pericardium patch used primarily for carotid and vascular reconstructions.

The two companies have also signed a back-up supply agreement to assure product availability during the manufacturing transfer. LeMaitre Vascular recorded XenoSure revenues of $4.5 million in the 12 months ending Sept. 30, a 61% increase over the prior 12-month period.

In January 2009, the company became the exclusive U.S. vascular distributor of XenoSure, inheriting sales of roughly $600,000 a year. Since then, the company has secured exclusive worldwide distribution rights and is now selling the implant through its direct sales force in the U.S., Europe and Canada. The original distribution agreement was to have expired in January 2016, while the exclusive acquisition option period was to have begun in January 2014.

Neovasc retains the right to process and distribute bovine pericardium for all other applications that do not compete directly with the Xenosure vascular surgical patch business. ■

HIT roundup

UnitedHealthcare gives $20M to rural hospitals for EHRs

A *Medical Device Daily* Staff Report

UnitedHealthcare (Minnetonka, Minnesota) said that it has provided $20 million in financing to help 11 Critical Access Hospitals in rural communities throughout California improve health information technology (IT) systems, including the adoption of electronic health records.

The announcement was made during a statewide rural health conference in Lake Tahoe (Rural Health Conference 2012: Rural Medicine in the 21st Century) where health care leaders and medical professionals from throughout California gathered to discuss rural health issues including clinical best practices, use of technology to improve delivery of care in rural areas, wellness promotion strategies and electronic medical records.

The 11 hospitals selected for funding comprise California's Critical Access Hospitals, which are located in remote areas of the state. These health facilities have a maximum of 25 beds and are located at least 35 miles from another hospital, or 15 miles from another facility and in mountainous terrain or areas with only secondary roads.

UnitedHealthcare purchased the 11 hospitals' private placement bonds worth $19.4 million with a flexible repayment plan that includes a rebate of up to 10% for early repayment. UnitedHealthcare also provided $577,000 in grants to pay for additional financing costs. Earlier, UnitedHealthcare provided $200,000 in grants to the California State Rural Health Association to assess IT needs at California's Critical Access Hospitals, for a total financial support of $20 million.

In other HIT news, **St. Luke's University Health Network** (Campbell, California) reported a partnership with SCI Solutions, a provider of cloud-based community connectivity and rules-based scheduling services, to connect its hospitals to the referring physicians within its community and improve patient satisfaction through access management innovations. Through this partnership, SCI's solutions will be implemented for St. Luke's employed physician network of nearly 380 providers in six hospital facilities in the Lehigh Valley, Pennsylvania and Phillipsburg, New Jersey.

"St. Luke's has always been very committed to providing our community with innovative solutions in healthcare," said Chad Brisendine, CIO of St. Luke's University Health Network.

The services offered to St. Luke's physicians through the partnership include Order Facilitator, SCI's electronic order solution, which will integrate with SLHN's health information exchange and electronic medical records, streamlining order submission to the health system, maximizing the conversion of orders into appointments and minimizing network leakage. ■

Grants roundup

Scripps Health nets $3.75M from Qualcomm Foundation

A *Medical Device Daily* Staff Report

Scripps Health (San Diego) reported that it has been awarded a $3.75 million grant from the **Qualcomm Foundation** (San Diego) to be used for the Scripps Translational Science Institute, which was established by Scripps Health in collaboration with various parties to support the development of breakthrough digital technologies designed to revolutionize the practice of medicine.

The funding will advance clinical trials of cutting-edge wireless biosensor systems, the creation of rapid pharmacogenomic diagnostic tests that can be administered in retail stores, and the development of apps and embedded sensors for tracking and predicting heart attacks, Type 1 diabetes and certain types of cancer.

"The combination of wireless technologies, sensors, diagnostics and DNA sequencing tools offers unparalleled opportunities to dramatically impact health care. The Qualcomm Foundation is proud to support this endeavor – bringing breakthrough technologies to the field of medicine to improve patient care," said Dr. Paul E. Jacobs, Qualcomm Incorporated's chairman/CEO and Qualcomm Foundation chair.

STSI is a National Institutes of Health-supported consortium led by Scripps Health in collaboration with The Scripps Research Institute and several other scientific partners.

In other grants news, **AIDS Healthcare Foundation** (AHF; Los Angeles) is reported that it has received a generous grant in the amount of $12,415 from the S.L. Gimbel Foundation Advised Fund at The Community Foundation Serving the Counties of Riverside and San Bernardino. This grant is funding expansion of AHF's HIV Educational Support Group Program and HIV 101 Course, a unique program that motivates clients through providing in-depth HIV information and education, self-efficacy skill building, peer support and medication adherence.

Many clients attending the weekly meetings are concurrently enrolled in AHF's Success Through Anti Retroviral Therapy (START) program, an intensive counseling program for clients struggling with medication adherence in medical outpatient settings. START represents the only intensive education and counseling program for treatment adherence within the context of specialized HIV medical care in Los Angeles.

In addition to weekly support group meetings and the START program, AHF facilitates HIV 101 Courses designed to inform and provide detailed information overview on understanding the history of HIV/AIDS, the virus' effect on the body, how to correctly take HIV medication, and how to remain adherent to treatment. ■

Europe

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discovery, development and commercialization expertise and novel and proprietary technologies.

Brainlab releases Buzz Digital OR

Brainlab (Munich, Germany) reported the release of Buzz Digital OR, what it calls a major step forward in information integration for the surgical suite. Buzz encompasses a vast spectrum, from pure DICOM viewing to complete digital OR functionality, including video management and documentation – at the touch of a finger, or two.

The Buzz is IP-centric, software-centric, workflow-centric, and patient-centric, and bundles hardware and software. Buzz Digital OR effectively manages advanced OR workflow – facilitating planning, navigation and intraoperative imaging connectivity. The newly designed control concept for Buzz enables intuitive management of data sources and displays with drag and drop functionality, the company said.

Buzz Digital OR is available in either 'on-wall' or 'in-wall' configurations. Brainlab makes software-driven medical technology that supports targeted, less-invasive treatment.

Cardiac Dimensions markets Carillon

Cardiac Dimensions (Kirkland, Washington) has initiated its commercial efforts in Europe, treating the first patients with its Carillon mitral contour system under its CE mark approval. The Carillon system is a minimally invasive therapy for treating heart patients suffering from functional mitral regurgitation (FMR). An estimated 70% of the 20 million people worldwide with heart failure also suffer from FMR.

Cardiac Dimensions' Carillon system combines an implantable device with a percutaneous catheter delivery system. The implantable device consists of a proximal anchor and a distal anchor connected by a shaping ribbon. Utilizing the heart's natural structures, the device is intended to reduce mitral annulus dilatation upon deployment, thereby significantly reducing FMR. Rapidly delivered via the venous vasculature, Carillon has the potential to treat most heart failure patients in a minimally invasive fashion, the company said.

Mauna Kea brings Cellvizio to Turkish market

Mauna Kea Technologies (Paris) received clearance from the Turkish Ministry of Health to sell both its Cellvizio 100 Series endomicroscopic imaging system and AQ Flex 19 miniprobe in Turkey. The company said it has secured **Cordamed** (Istanbul)as its distributor.

According to medical markets specialist **Infomedix** (Viterbo, Italy), spending on medical devices in Turkey is expected to triple in the next three years from $1.1 billion in annual import and export sales today to $3.12 billion in 2015.

ClearCanvas gets CE mark for RIS/PACS software

ClearCanvas (Toronto), a medical imaging informatics company, reported the receipt of the CE mark for its RIS/PACS software.

"We are very excited about the potential the CE mark has created for ClearCanvas to build on its 25,000 strong user base," said Norman Young, CEO.

The commercial version of the popular open source RIS/PACS solution is designed to give each practice a flexible, easy to use software solution, independent of practice size and workflow complexities. "Efficient workflow is critical to the operational effectiveness of any clinical practice, so it's important to provide a flexible, intuitive solution," said Young.

The ClearCanvas RIS/PACS solution includes key features like customizable worklists, hanging protocols and roaming user profiles while also offering more advanced functionality to empower practices all over the world.

ClearCanvas is a provider of medical imaging solutions designed for radiology, specialty clinics, community hospitals and research facilities. ■

Patent watch

Bovie granted fifth patent for J-Plasma technology

A *Medical Device Daily* Staff Report

Bovie Medical (Melville, New York), a maker of electrosurgical products, reported it has received initial orders for J-Plasma and has been granted its fifth patent for the product. The company says it has five additional patents pending based on the J-Plasma technology.

J-Plasma is formed by passing helium over Bovie's proprietary electrode, which is held at high voltage and high frequency, producing a luminous discharge beam. The electrode can also be in the form of a retractable surgical blade, providing multiple modes of operation in a single instrument. The extended surgical blade can be used for incisions and other cutting procedures, and when retracted, the blade is used to form the J-Plasma beam for coagulation. Bovie noted that the extended blade can also be used in combination with the J-Plasma beam, providing an enhanced cutting capability with minimal impact on surrounding tissue. ■

Off-label

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approved options to use.

FDA unveiled the draft guidance to some speculation that the guidance was principally about the use of social media for off-label indications (*Medical Device Daily*, March 15, 2012), but the sheer number of potential scenarios seems certain to keep regulator and regulated alike on edge until a few cases have made their way into warning letters and/or lawsuits. Steve Silverman, director of the office of compliance at the Center for Devices and Radiological Health, acknowledged that the draft guidance as written is short of ideal, but said the agency can go only so far in efforts to fill in the blanks.

"I don't think we're striking the right balance" at present, Silverman conceded, but he asserted that the subject is inherently complex and as yet largely undefined. He said industry's interest in "specific factual scenarios" was logical, but nonetheless claimed, "speaking to the myriad scenarios is death by a thousand cuts" for FDA because it is impractical to attempt to address each possible scenario. The draft guidance is a case of "cutting with a broad sword," he shrugged, pleading the case that the agency "will never be able to anticipate and speak with specificity about every exchange" that goes on between doctors and sales reps, or between the general public and a device maker.

"We engage in line drawing," Silverman observed of FDA's attempts at rulemaking and guidance development, stating that a doctor whose patient needs a quick decision will not always be able to get the information needed about off-label use without running the risk of crossing a legal Rubicon.

Susan Alpert, MD, formerly an employee of both FDA and **Medtronic** (Minneapolis), said her background gave her a fractured perspective on the matter. "I suffer from schizophrenia, particularly on this issue," she quipped, explaining that as a practicing pediatrician, "most of what I used was off-label," largely because of a dearth of products developed specifically with the child or adolescent in mind.

The current regulatory scenario for unsolicited off-label inquiries "sets up a complicated situation for physicians," Alpert said. Pediatricians are "sometimes encouraged to use things off label, but at the same time, we're expected to understand the complexities of the regulatory environment," which prohibits manufacturers "from having these conversation with us."

"Clinicians do not understand these distinctions," Alpert continued, asserting "it is incumbent upon us as an industry" and on FDA "to educate and make it understandable what can be obtained" in terms of information so that the practicing physician can obtain "the information they need and not put the company's employees at risk."

Alpert also argued there should be more clarity "about what is scientific exchange" and when a conversation is scientific in nature rather than a case of solicitation. "Every conversation a clinician has is as a scientist," she observed, even if the company representative is in sales mode. Alpert also indirectly pointed out that more and more commonly, the hospital or clinic is the purchaser rather than the physician, a fact she indicated should be factored into the agency's understanding of the nature of some conversations.

When a doctor needs an answer regarding off-label use, "I'm going to ask a person I know," Alpert said, which is generally a salesperson who represents the manufacturer to the hospital. This, she said, calls for some sort of guidance that will "make sure we're not creating a false sense of promotion and marketing when it's about a patient sitting in front of us."

DTC guidance withdrawn as admin matter

The matter of FDA's withdrawal of a 2004 guidance dealing with direct-to-consumer ads for medical devices gained a little clarity during the session dealing with unsolicited inquiries into off-label device usage (*see story above*), thanks to the fact that Steve Silverman, director of the Office of Compliance, was on hand.

Silverman said the withdrawal of the 2004 document "was not part of a policy decision," but was "an administrative decision." He said the guidance had been in draft form and never finalized. "Were we to return to the subject, it would be more appropriate to initiate the process from the beginning" rather than resume work on a product with eight years of regulatory dust on board.

FDA did nothing to publicize the withdrawal of the guidance other than to simply note the withdrawal on the guidance web page at the agency's site (*Medical Device Daily*, Oct. 2, 2012). *Medical Device Daily* has had little luck obtaining a copy of the now-defunct draft guidance, and an agency spokeswoman told *MDD* that FDA "has no current plans to re-issue draft guidance on DTC." She referred those interested in the requirements on advertising of restricted devices to sections 502(q) and 502(r) of the Federal Food, Drug, and Cosmetic Act.

Silverman said he could not address the question of whether the agency intends to take another crack at the guidance, although the agency's 2009 guidance dealing with presentations of risk and benefit information in advertisements for drugs and devices may cover some of the same ground (*MDD*, May 28, 2009). FDA also held a two-day meeting in November 2009 addressing the use of social media for devices and pharmaceuticals, but there is as yet no indication that a social media guidance is forthcoming from CDRH. ■

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IMDRF

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other national authorities when conducted under ISO 13485 (*Medical Device Daily*, March 26, 2012), a program that follows a mutual recognition agreement between Health Canada and FDA. The latest device user fee agreement, MDUFA III, reauthorizes the third-party inspection program at FDA, but industry has not always embraced such inspections partly because of the difficulty of getting a third party auditor to simultaneously conduct FDA and ISO audits.

Trautman said IMDRF's medical device single-audit working group has commenced work on a "common set of requirements for third parties and regulators," and the working group is "looking at base materials, such as ISO17021." She made reference to a 2011 annex to 17021, which generally is a standard for assessment of conformity for audits and certification of management systems. Annex 2011 addresses consistency of audits and the impartiality of auditors.

Trautman said, "we decided we would make 17021 a normative reference" in the IMDRF approach, although she acknowledged there are other sources of standards in the works, including a preliminary draft of EU legislation. Health Canada has a provision for outside party inspections as does Japan's Ministry of Health, Labor and Welfare, Trautman observed, but she also mentioned the UK's IAF MD9, which draws on ISO 13485 and went into effect in July. Trautman reminded the audience that IMDRF had met recently in Sydney, Australia, and the audit working group had come up with substantially more material to use for crafting a standard for inspections. She also said IMDRF is not particularly interested in being particularly prescriptive, even where a code of conduct for inspectional entities is concerned. "We are not going to dictate a code of conduct to the third parties," she said, but she indicated that IMDRF is interested in a set of minimum requirements. European notified bodies are also working on a code of conduct, Trautman said.

On the question of special audits, Trautman said "there's a movement afoot to lay out specific criteria when unannounced audits should take place," but she acknowledged that while IMDRF is working on a multi-lateral single audit program, "not everyone at IMDRF is on the multilateral effort." She pointed out that some of the nation-to-nation efforts are "going on at a much faster pace and at a bigger scope" than anything IMDRF has cobbled together to date, so whatever can be grafted from multi-lateral efforts, "that's what we're trying to do."

Trautman promised that while "we have to ensure there is appropriate oversight of the inspecting group" to guarantee competency, IMDRF is nonetheless keenly aware of a need "to minimize the burden" to industry.

Trautman briefly revisited the emergence of IMDRF from the Global Harmonization Task Force, stating that GHTF "was a wonderful foundation. It brought us a long way in 20 years," but the participating regulators felt that the regulator-plus-industry forum had begun to feel its inherent limitations. Regulators "feel we need to step up and adopt" standards toward convergence, Trautman said, hence the formation of the regulators-only forum.

"We feel like in 20 years, we have harmonized general principals" via GHTF, Trautman stated, but she remarked that regulatory convergence is now the operating terminology. "There is a true commitment . . . to actually take affirmative steps toward converging [regulatory] practices" she claimed, stating that the governments involved in IMDRF are "all trying to get on the same sheet of paper," but "now it's a little more work because we actually have to adopt" standards.

Trautman said the recent IMDRF meeting in Sydney did not include any change to the membership of the management committee. China is still on board as an observer only, and "Russia did send regrets" for failing to attend, Trautman said, explaining that Moscow claimed its staff had encountered issues with their visas. "India has been a bit of a question mark," she observed, stating that IMDRF is "still having difficulties getting any kind of firm commitment" from New Delhi. Regulators from New Zealand and Singapore sat in on the management committee meeting, however, and Argentina expressed interest in observing meetings as well.

Trautman frankly acknowledged that a common regulated products submission document format is "a very difficult topic," which is drawing the interest of two working groups. One addresses an HL7 standard for messaging/packaging to convey regulatory data, and IMDRF is "working on making that an ISO standard." She said this began as an ICH standard, which complicates matters somewhat because the International Conference on Harmonization is a pharmaceutical standards organization with the obvious orientation. Despite that, "we'd rather be part of this earlier than later," Trautman mused, so IMDRF will participate in beta testing for this system.

The second working group for regulatory filings, the table of contents (ToC) group, is working in something of a void. "Nobody has said absolutely this where their jurisdictions are going" Trautman stated, but she explained that the GHTF version of a ToC, the summary technical document (STeD), was "too high level, and we needed to delve into details" of a device application to make the standard useful to multiple regulatory bodies. The ToC working group is "trying to develop more specificity," Trautman related, adding, "they want to do a pilot just on the ToC" for two submissions, one of which would be an *in vitro* diagnostic. She remarked that different regulators would want different amounts of data, but that the idea is to develop a series of data sets for the various parts of a regulatory filing so that sponsors can add and subtract informational packages without having to draft filings from scratch. "As long as there are certain core packages," Trautman said, sponsors could work from these packages to more readily assemble regulatory filings. ■

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Apple

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of the Indiana Software Association and the Indiana Information Technology Association.

MDD: I keep reading about HIEs in many other states having difficulty developing sustainable business models. How are you different from those who may be struggling in that regard?

Apple: Constant attention, and while we believe we are self-sustainable without grant money right now, I would admit that it's marginally so and one of the reasons that have been reasonably successful in that regard is the fact that we had close relationships with our major hospitals here in Indianapolis and they were willing to pay us fees for service, which is really what our service has been built on.

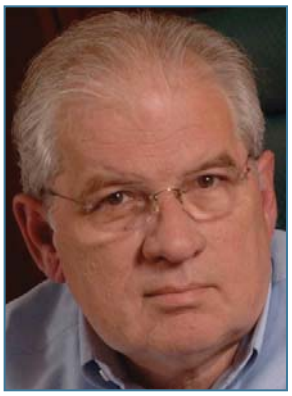
We absolutely had grant money in the early stages and continue to have some, but the organization and its founders, meaning those five hospitals, decided a couple of years ago that it was important for this to be a self-sustaining entity so that it would not have to live based on various grant programs, whatever the source. As a result of that, I was engaged about a year and a half ago to be the CEO of IHIE, with the primary goal of extending the mission of being sustainable and operate as a business so that we could develop and invest and grow this organization.

One of the significant things that I believe other HIEs are probably learning to operate under now is the investment required to exchange this data from a technology point of view and then to be able to use that data in a productive way requires a pretty extraordinary investment in technology and smart people. Consequently, in my opinion, they can't function in small geographic areas. In spite of our success, we're still a fairly small geography in the context of operating in Indiana.

It's my belief that over the next five to 10 years, we'll see fewer HIEs but much larger entities, and, quite frankly, we intend to be one of those larger entities. I believe we will mirror our primary customers in terms of their behavior. In order to function economically, you have to have enough scale to lower overall unit costs, and just as you see hospitals continuing to consolidate through mergers and acquisitions, I think the same thing will happen to the HIE market.

The big difference is that there aren't many HIEs that have much critical mass, so it will be more of a greenfield type of development in the sector across the country rather than mergers and acquisitions, because there are only a few that approach our size, and I know what our economics are, so it doesn't make sense from a business point of view for some of these local exchanges to be able to get to the point where they can be sustainable on a continuing basis.

I'm sure that perspective isn't shared by all, but if you really step back and look at the marketplace, which is what we've done over the last couple of years, some of these exchanges are existing only because the federal government has put so much money out there for them to get started. But it took us 10 years to get to the point we are,



HAROLD APPLE
Cites Path for Growth

and it's not an easy place to play. It's a very complex business, and I think fundamentally that's how we'll see things start to change as the sector begins to mature over the next several years.

MDD: IHIE is a federally-designated Beacon Community tasked with sharing your knowledge with other similar organizations nationwide. How do you see yourself influencing the development of the national model for HIEs?

Apple: I think the Beacon program helped us focus primarily on the quality part of the services we provide as one objective. The other objective that really helped was to hook up more hospitals to our existing model, which is why we've had significant growth over the past couple of years, growth that was difficult to execute on, which was part of the challenges we've had. With the kind of resources we already had, I believe others will find it difficult to use that money as well as we did. It really helped us develop more maturity in the organization.

The end result is that we are in a better position to be a better model and a larger organization in the future, more so than creating an entity that was in a mode where it was going to help others. It's more leading by example initially than really having a significant focus on sharing.

Part of the Beacon money will go toward developing the statewide network we were talking about earlier, but that's a pretty unique situation and across the country, save for some of the very large population areas, it's going to be difficult to spread this thing to the four winds, so to speak, and reach many of the less-populous areas until there are a few HIEs that really have significant size. I think that's what Beacon did for us.

Another thing Beacon did is raise this as a significant issue, and it has stimulated private investment because people are starting to recognize that the challenge is significant enough that it makes sense to invest in it. And investors want sustainability, right? They want payback. So the Beacon program really spotlighted health IT in such a way that showed that the healthcare industry had not taken advantage of IT like other industry segments, so opportunities existed. It's really important that the private community get involved and invest in it so we can start pushing this stuff down the hill.

MDD: IHIE seems to have quite a product development process in place. Could you describe some of the new services you've launched this year, and discuss the importance of having a well-defined pipeline in place?

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ConforMIS

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"The implant is specifically designed to address these concerns," Philipp Lang, chairman/CEO of ConforMIS told *Medical Device Daily*. "You have no more overhang of the implants. [The implant] recreates the shape the patient had prior to the surgery, corrected for deformity. It recreates the normal natural shape of each patient corrected for any orthopedic deformity."

The iTotal G2 was developed on the foundation of the company's patented iFit technology for designing patient-specific implants and jigs. Each iTotal G2 is made to fit an individual patient precisely based on their CT scan. Since each implant is made to fit just one patient, surgeons avoid the sizing and fit trade-offs that are a traditional part of standard knee surgery. The implant shape and geometry also closely matches the patient's natural joint anatomy and curvatures, providing the potential for more natural knee motion. Finally, the pre-navigated disposable instruments help place the implants accurately and reproducibly.

"The focus for us in this evolution of the device is to perfect the instrumentation," Lang told *MDD*. "We're very happy with the implant and our clinical feedback exceeds all expectations. The key aspect for us was that we wanted to perfect the surgical technique so that every surgeon; regardless of their practice; regardless of the volume of surgeries they're doing; could get a very reproducible result [with the implant]."

The iTotal G2 system comes packaged in a small sterile kit that includes the implant components and all of the disposable instruments for the procedure. In contrast to an off-the-shelf total knee system which may require between six to eight trays of instrumentation, only one reusable instrument tray is required at the hospital for the iTotal G2. This provides a highly efficient system that reduces the hospital inventory management, transport and sterilization costs. It also reduces the instrument set up and reprocessing required in the operating room.

"For the patient population that requires a total knee replacement, the physician's ultimate goal is to give patients a long lasting, more natural feeling knee," said Gregory Martin MD, medical director of the Orthopedic Institute at JFK Medical Center in Florida and a member of the surgeon design team for the iTotal G2. "With the ConforMIS iTotal Knee System, I'm seeing in my early patient data that I'm resecting less bone, measuring less blood loss and that patients are having a quicker return to activities they enjoy. The patient response is noticeably different than what I'm used to seeing in my standard total knee patients."

As the iTotal G2 is introduced into broad commercial release, the company has updated the implant design to address a greater range of anatomies, introduced a more efficient and simplified surgical technique and instrumentation system, and updated the patient-specific iView with more detailed surgical planning information.

The company said that the device also has the CE mark.

Concerns on past news that the market for elective surgeries has shown signs of a slowdown were not a major concern for the company. Lang said that studies point to a greater increase in the use of implants in the future, citing an aging and more active population. While he noted that there did seem to be a slowdown of these elective procedures, he said current data shows an uptick in the market.

"What we've seen since the beginning of the economic crisis in 2008 is that a lot of patients postpone their surgery elective procedures," Lang said. "The big orthopedic companies all showed a significant slow down in procedural volume. [ConforMIS] hasn't really seen that. What we're seeing today– starting late 2011 through 2012 – is that there's clearly recovery in the market if you look at the procedures that are being reported by the larger orthopedic companies." ■

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Product Briefs

• **Boston Scientific** (Natick, Massachusetts) has received FDA approval for its S-ICD system, the subcutaneous implantable defibrillator, or S-ICD, for the treatment of patients at risk for sudden cardiac arrest, or SCA. According to the company, the S-ICD system sits entirely just below the skin without the need for thin, insulated wires – known as electrodes or 'leads' – to be placed into the heart. This leaves the heart and blood vessels untouched, offering patients an alternative to transvenous implantable cardioverter defibrillators, or ICDs, which require leads to be placed in the heart itself. The study results support that the S-ICD system is an important new treatment option for a wide range of primary and secondary prevention patients. The S-ICD system is designed to provide the same protection from sudden cardiac arrest as transvenous ICDs. The S-ICD system is intended to provide defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing.

• **Echometrix** (Madison, Wisconsin) has received FDA clearance to market its EchoSoft ultrasound technology. EchoSoft is a powerful software package that is used with diagnostic ultrasound to assist with the diagnosis and monitoring of musculoskeletal conditions. EchoSoft's technology generates color maps to help trained clinicians visualize structural characteristics that are unique to tendons and ligaments. This information is not available through the use of diagnostic ultrasound equipment or conventional software packages. Echometrix makes ultrasound technology devices.

Apple

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Apple: We have initiated one program that's especially important. Like many others, we have a bandwidth problem in terms of the number of people we can put on. What we have tried to do is stimulate interest in services that are directly related to our primary service, and one of those is what we call ImageZone, a cloud-based image sharing service. We have collaborated with another entity to provide that service, and it's just getting under way, so we can in fact expedite viewing of MRIs, X-rays, etc., primarily for care.

For example, the hospitals in Indianapolis are still the primary treatment centers in the state for trauma, so there are two Level I trauma centers here and many trauma patients from out of state get transported by helicopter to Indianapolis. In order to expedite the delivery of that care, because time is critical, we need a service that can take advantage of diagnostics that were performed at the point of origin on a quick basis rather than just putting it on a CD and taping it to the stretcher. So we felt an image-sharing service had a lot of potential, both from expediting the care that is offered at the trauma center, but secondly so that you don't replicate images that have already been made and hopefully impact costs in a positive way.

We have just over the last year started what we call a traditional product management function in the organization. Historically, new services came out of a research orientation because of the Regenstrief Institute's participation in the organization, but that needed to be formalized in a way that new services could be identified and hardened in a commercial way rather than just being an extension of what's created in a research entity.

We are just in the early stages of identifying the kinds of things that we have that provide commercial value to the customers that we have now and hope to have in the future. If the organization is going to be sustainable, then every product we sell has to be sustainable. It's a traditional business discipline that is not always shared by start-ups or entrepreneurial enterprises or not-for-profit organizations just because they haven't had the resources or the experience to do those kinds of things. It's a part of our maturing as a business and is very key.

MDD: When it comes to patient information in healthcare, privacy and security are key questions, often the basis for public rejection of such efforts. With all the changes that occur so rapidly on the technology side, how are you assuring that privacy and security issues remain front and center?

Apple: One of the keys to success has been a very sophisticated governance activity that started early on in terms of managing both the privacy and the security of this data so that patients, physicians and healthcare institutions would not be concerned about abuse. That remains one of our primary missions to ensure that we maintain appropriate management over the data that we hold.

I'll always underscore governance in terms of being the "Big Daddy" in terms of how we treat this data. If a small business person were to look at this, he'd look at is as an inhibitor because you can't move as fast as you'd like to because there are a lot of people who have some say over the data that we hold. So in some cases that would be viewed as a negative, but in our case, we view it as a positive because it is the reason we exist.

This business is based on trust, so privacy and security in terms of how we behave in holding that data and using that data for the common good is strategically important. We believe that process, which has been developed over many years and is reasonably mature, is the reason we've been successful and therefore has to be part of the thread of our whole existence. Privacy and security is a key thing, so we spend a lot of money in terms of making sure that's bulletproof.

MDD: What does the future look like for IHIE and other health information exchanges?

Apple: As you start to think about the expansion of these databases and where things are headed, the important point is that it's going to take a lot of investment nationally. The commercial side of the market needs to exist, not just the government, because that's our model from a philosophical point of view as Americans. So we've got to tie those two trains together and be willing to operate in that world.

The cost of dealing with regulation and privacy and security is significant, and that's another reason why I believe these organizations will have to get bigger. Because that's a key cost component and is strategically important to the survival of the sector, it's going to require larger entities to be able to amortize all of those costs, all the way from technology to security, across a much larger population. ■

People in the News

• **Air Techniques** (Melville, New York) has named Janet Liebert as their new sales & marketing analyst. Most recently, Liebert's experience has been in banking and finance. Air Techniques makes dental equipment.

• **NanoString Technologies** (Seattle) has named James Johnson as the company's new chief financial officer. Johnson previously was CFO at Relypsa. NanoString Technologies is a provider of life science tools for translational research and developer of molecular diagnostics.

• **Parallon Business Solutions** (Franklin, Tennessee) has named Chris Taylor to the position of executive VP and chief financial officer. Taylor previously was CFO at HCA's TriStar Health. Parallon Business Solutions provides healthcare business solutions.

• **Reach Health** (Alpharetta, Georgia) said Gene Guertin was named chief technology officer. For the past 11 years, Guertin was with HealthPort Technologies, having served as both chief technology officer and chief information officer. Reach Health is a provider of telemedicine technology solutions.

MDD's Ortho Extra

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

Thursday, October 4, 2012

Keeping you up to date in recent developments in orthopedics

Odds of successful grafts improved by new method of resurfacing bone . . .

Coating a bone graft with an inorganic compound found in bones and teeth may significantly increase the likelihood of a successful implant, according to Penn State researchers. Natural bone grafts need to be sterilized and processed with chemicals and radiation before implantation into the body to ensure that disease is not transmitted by the graft. Human bones have a rough surface. However, once a graft is sterilized the surface changes and is not optimal for stimulating bone formation in the body. "We created a method for resurfacing bone that had been processed, and resurfacing that bone so that it is now nearly as osteogenic as unprocessed bone – meaning it works nearly as well as bone that hadn't been processed at all," said Henry J. Donahue, Michael and Myrtle Baker Professor of Orthopaedics and Rehabilitation, **Penn State College of Medicine** (Hershey, Pennsylvania). "That's the bottom line." Donahue, who is also a faculty member of the Huck Institutes of the Life Sciences, and Alayna Loiselle, postdoctoral fellow in orthopedics and rehabilitation, Penn State College of Medicine, teamed up with Akhlesh Lakhtakia, Charles Godfrey Binder Professor of Engineering Science and Mechanics. They developed a way to create a rough surface on bone grafts that is similar in texture to the surface of an untreated bone. This similarity promotes healing in the bone. The researchers found that by coating a bone with the inorganic compound hydroxyapatite, using physical vapor deposition, they could closely mimic the rough surface of an untreated bone. To find the optimum thickness of hydroxyapatite, Donahue and Loiselle sterilized the graft samples in their lab at **Penn State Hershey Medical Center**. After sterilization, the samples went to the University Park campus, where physical vapor deposition layered different amounts of hydroxyapatite on the grafts. Then the samples were returned to Hershey for Donahue and Loiselle to test. The researchers saw that the optimum thickness of hydroxyapatite was in the middle of what they tested. If the hydroxyapatite coating was not thick enough – or there was none – the graft implant worked, but did not integrate as well as if there were a few nanometers more layered onto the surface. If the hydroxyapatite was too thick, the graft implant again worked, but did not integrate as well as the researchers had seen was possible. "I thought we wouldn't need to coat the bone more than a couple of hundred nanometers. As it turns out, it was much less than that," said Lakhtakia. A hundred nanometers is about the size of a single virus. Fifteen years ago Lakhtakia started an area called sculptured thin films. He thought these might be used to heal broken bones, but wasn't sure how. He suggested that for two bones to be joined, coating the two opposing faces with sculptured thin film might bring them together. Bone is living tissue, so bone would grow through the sculptured thin film and fuse together and create some sort of adhesive bond. "When [Dr. Donahue] said he had this particular problem and asked if I could do something about it, I thought about that," said Lakhtakia. "In 15 years or so, my understanding had considerably evolved, and the one thing that I thought was that whatever needs to be done on the bone should not take too much time and should be little in size. If it is little, there is a better chance of integration inside the body – less foreign material inside the human body." The researchers also believe this method could be used for soft musculoskeletal tissue implants and orthopedic device implants. The researchers have filed a provisional patent for this work.

Unnecessary knee arthroscopies still being performed? . . .

Arthroscopy is still commonly being performed on people with osteoarthritis (OA) of the knee despite evidence against the effectiveness of the surgical procedure for this condition, according to research published in the October 1 issue of the *Medical Journal of Australia*. Although the number of knee arthroscopies had declined overall, rates had remained steady in those with osteoarthritis in the 9 years to 30 June 2009, according to Dr Megan Bohensky from the **Center of Research Excellence in Patient Safety** and coauthors, who studied usage patterns in Victorian hospitals. According to the authors, research published 10 years ago and backed by subsequent studies questions the benefit of knee arthroscopy in patients with osteoarthritis. "Because arthroscopic procedures can be associated with complications, it is important that they are

used only when they are likely to have measurable positive outcomes", the authors wrote. "Given the uncertain evidence of effectiveness, general practitioners should encourage patients with OA of the knee who have no evidence of major mechanical derangement to try non-surgical treatments in the first instance", they wrote. In an accompanying editorial, Professor Rachelle Buchbinder, director of Monash Department of Clinical Epidemiology, Cabrini Health and Professor Ian Harris from the South Western Sydney Clinical School, University of New South Wales wrote that it was difficult to "shift the convictions of many surgeons." They wrote that in contrast to new drugs, promising new surgical interventions continued to be introduced into practice before their proper evaluation. "The use of arthroscopy for knee osteoarthritis has been allowed to continue, exposing patients to an intervention that is at best ineffective, and at worst, harmful", they wrote.

The effects of aging on muscles may be explained by inadequate cellular rest . . . Is aging inevitable? What factors make older tissues in the human body less able to maintain and repair themselves, as in the weakening and shrinkage of aging muscles in humans? A new study from **Massachusetts General Hospital** (MGH; Boston) investigators and collaborators at **King's College London** describes the mechanism behind impaired muscle repair during aging and a strategy that may help rejuvenate aging tissue by manipulating the environment in which muscle stem cells reside. The report will appear in the journal *Nature* and has received advance online release. Rare muscle stem cells are located inside each skeletal muscle of the body. Also called satellite cells, due to their position on the surface of the muscle fibers they serve and protect, these cells are essential to maintaining the capacity of muscles to regenerate. Satellite cells are able to generate new, differentiated muscle cells while keeping their identity as stem cells, retaining the ability to maintain and repair muscle tissue. Normally in a resting or dormant state, satellite cells respond rapidly to repair injured tissues. The current study finds that aging muscle stem cells lose their ability to maintain a dormant state, so that when called upon to repair injured muscle, they are unable to mount an adequate response. Andrew Brack, PhD, of the MGH Center for Regenerative Medicine, senior and corresponding author of the *Nature* paper, says, "Just as it is important for athletes to build recovery time into their training schedules, stem cells also need time to recuperate, but we found that aged stem cells recuperate less often. We were surprised to find that the events prior to muscle regeneration had a major influence on regenerative potential. That makes sense to us as humans, in terms of the need to sleep and to eat a healthy diet, but that the need to rest also plays out at the level of stem cells is quite remarkable." An assistant professor of Medicine at **Harvard Medical School** (Boston), Brack is also a principal faculty member at the Harvard Stem Cell Institute. In a series of experiments in mice, the authors found that a developmental protein called fibroblast growth factor-2 (FGF2) is elevated in the aging muscle stem cell microenvironment and drives stem cells out of the dormant state. Satellite cells that are forced to replicate lose the ability to maintain their identity as stem cells, reducing the stem cell population. The authors also found that blocking the age-related increase in FGF signaling both in aged satellite cells or in the cellular microenvironment protected against stem cell loss, maintained stem cell renewal during aging and dramatically improved the ability of aged muscle tissue to repair itself. Lead author Joe Chakkalakal, PhD, a research fellow in Brack's lab, says, "This work highlights the usefulness of targeting the aged stem cell or its environment to protect stem cells and the tissues they serve from the effects of aging." Noting that FGF2 is known for laying the foundation for muscle development, Brack adds, "At present we don't know why this developmental factor is re-expressed in the aged stem cell environment. It appears that what was beneficial for the development of muscle becomes detrimental during aging. After this proof-of-principle study, we are beginning to ask whether the lessons we have learned can be translated to improving the health of the ever-growing aged human population."

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