# SurFACTS in Biomaterials

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## Drug-Eluting Stents Show Promise for Leg Arteries

*By Tate Gunnerson*

Treating peripheral arterial disease with drug-eluting stents may save lives and limbs in people with severely obstructed arteries, Greek researchers have found.

Peripheral arterial disease is common in the lower extremities and sometimes leads to severe obstructions, known as critical limb ischemia (CLI), a condition in which the decreased blood flow causes pain and skin ulcers.

"CLI is today a major health problem, especially in Western societies, and is associated with high morbidity and mortality rates," said Dimitris Karnabatidis, the lead researcher and an assistant professor of interventional radiology at Patras University Hospital in Rion, Greece. "More specifically, an estimated 1 percent of the worldwide population over 50 years old suffers from CLI."

Karnabatidis' study involved 103 people, three-fourths of them diabetics. A normal stent — a wire mesh tube used to prop open an artery — was placed in an artery in 41 participants, and 62 were given drug-eluting stents, which were stents coated with sirolimus, an immunosuppressant.

After three years, the researchers found that people with drug-eluting stents had more open arteries (higher primary patency) and less renarrowing (binary restenosis), and they were less likely to need a repeat procedure. People with

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## From the Editor

### On My Microscopic Soapbox – the SBIR Re-authorization Bill

I am using this editorial as a Call for Action for U.S. members to contact their elected Washington representatives in support of the reauthorization of the Small Business Innovation Research (SBIR) program. For those who are not familiar with SBIR, let me explain. The SBIR program requires all US government agencies that provide research funding (e.g. NIH, NSF, DoD, EPA, and others) to set aside a small percentage of their total extramural research budgets for contracts or grants to small businesses to support innovative research. The SBIR program was created, as stated by Roland Tibbets, the program founder, "to provide funding for some of the best early-stage innovation ideas – ideas that, however promising, are still too high risk for private investors, including venture capital firms." An extension to this program, the Small Business Technology Transfer Program (STTR) supports technology transfer from academia to small business, such as where the principal investigator may be a Professor. The percentage of grant funding that is set aside for the SBIR and STTR programs is currently 2.5 percent and 0.3 percent, respectively, of each agency's extramural grant support. The program was initially authorized in 1982, and then reauthorized in 1986, 1992, and 2000. The current reauthorization will end July

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*By Steven L. Goodman, Ph.D., 10H Technology Corporation*

31, 2009, and this is only due to two continuing resolutions that have temporarily maintained the program. So why should you care?

The SBIR/STTR program has been one of the most successful programs for the creation of innovative new technologies and high technology jobs in this nation's history. This has been a major "Fountain of Youth" for our industry, as well as all other high-technology industries in the U.S. Some statistics presented by the Small Business Technology Council illustrate the general importance of this program. Further on, I will show examples in our own chosen field:

"U.S. small businesses employ more scientists and engineers than large businesses (32 percent vs. 27 percent), and more than universities and federal labs combined (32 percent vs. 29 percent). Yet, high-tech small firms receive only 4.3 percent of Federal R&D funds, while larger firms receive 50.3 percent and universities and colleges receive 35.3 percent." Thus, small business—even with the SBIR program— is receiving proportionally less federal funding than other sectors.

"The high-tech small businesses generate 5 times more patents per R&D dollar than large businesses. With access to only 3 percent of the total dollars that large corporations can devote to R&D, small companies are still able to produce 15 percent of all business-owned patents. SBIR companies are about 20 times more productive than universities in generating patents per Federal dollar. [While] SBIR companies received only 2.5 percent of the Federal extramural R&D funds they generated over 1.5 times as many patents as universities which received over 30 percent of the funds."

In the time of our current economic woes, technology development funds to create small businesses that will grow and improve productivity, is certainly a noble goal. So, what about our industry?

To see the impact on our industry we need look no further than Surfaces in Biomaterials' member companies and attendees at the 2008 meeting. Some notable examples include SurModics, which received over $6 million in SBIR grants when it was known as BSI Corporation. Genzyme received about $850,000, as well as Focal, a company that was later acquired by Genzyme, which received about $100,000. The Polymer Technology Group is another member company that received about $3.5 million in SBIR funding, and is now part of DSM Biomedical. From my own experience I can cite Imago Scientific Instruments (not a member, alas). Imago was my employer from 2000-2004, and received about $1.2M that helped it to develop a new analytical instrument from crude prototype to world-wide sales, and then to a distribution relationship with FEI, one of the leading Electron Microscope firms. Other Foundation Member companies include AST Products (~$2 million), Hystitron ($1.7 million), Affinerty ($4.6 million), and Nerites ($200K).

As a small business entrepreneur, I can't emphasize enough how important the SBIR/STTR program is to our industry's innovation. My consulting firm works with many early stage companies with the development of their technology and their business. For each and every one of these, even a small $100,000 grant is critical to the engineer/scientist/entrepreneur who is trying to develop their idea that may be the next drug coated stent, controlled release device, or a personalized medicine diagnostic wonder. This is especially so right now with the decrease in Venture Capital and Angel investment. If in doubt about the importance, ask the member companies listed above how important these SBIR fund have been for them to develop their technologies. Or ask the big firms, such as Genzyme, Boston Scientific, Johnson and Johnson DePuy, and others how many of the companies they have acquired technology from were once SBIR funded.

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*SurFACTS in Biomaterials* is the official publication of the foundation and is dedicated to serving industrial engineers, research scientists, and academicians working in the field of biomaterials, biomedical devices, or diagnostic research.

# Dr. Daniel Ammon Elected Fellow, American Institute for Medical and Biological Engineering

Daniel M. Ammon, Jr., Ph.D., Research & Development, has been elected a Fellow of the American Institute for Medical and Biological Engineering.

Dan has been active in the Surfaces in Biomaterials Foundation since 2005.

Dan was nominated and elected by The College of Fellows for outstanding achievements in medical and biological engineering. A formal ceremony was held during the Institute's Annual Event in Washington, D.C., on February 12 to induct the 108 new members.

The College of Fellows leads the way in technological advancement, advocating for public policies that facilitate further progress and preparing young scientists and engineers to build on that progress in the decades to come. Over the years, AIMBE Fellows have helped to revolutionize medicine, engineering and related fields that enhance and extend the lives of people all over the world. Counting several Nobel Prize winners among them, their work also helps protect the environment, leads to new national security safeguards and contributes to a better society in many other ways.

Dan joined Bausch & Lomb in 1992 and is the fourth R&D employee who has been selected for this honor. The other B&L employees that have been selected for this honor were Jay Kunzler, Joseph Salamone and George Grobe. Dan has devoted most of his career to researching and developing innovative materials for applications in contact, contact lens solutions and intraocular lenses. He has 40 U.S. patents and patent applications and has also written and contributed to several technical papers.

The AIMBE fellowship is the most recent honor that Dan has received over his career, including Bausch & Lomb's Chief Scientific Officer Award in 2005 and Recognition for Leadership for the Surfaces in Biomaterials Foundation Award in 2006. He holds a Ph.D. in Analytical Chemistry and a Bachelor's degree in Chemistry from the State University of New York at Buffalo.

# Dr. Bruce S. Lamb Joins Affinergy as Senior VP of Research & Development

Affinergy, Inc., a Duke University spinout with a proprietary site-specific biological delivery system, announced that Dr. Bruce S. Lamb joined its executive team as Senior Vice President for Research & Development. Dr. Lamb has 23 years of leadership experience in development of multiple surgical products such as biologic hernia meshes, wound care products, and other biosurgical products. Most recently, Dr. Lamb served as Senior VP of Development and Regulatory Affairs at LifeCell, Inc., which was acquired in 2008 for $1.7 billion in cash.

"Bruce is a highly accomplished leader with a proven record of developing medical products that help large numbers of patients," said Peyton Anderson, Affinergy's CEO. "I believe Bruce will be a transformative leader for Affinergy as we develop our own products and assess other technologies and companies to acquire. It is a great testament to our existing employees, partners, and investors that we can recruit a leader like Bruce to join Affinergy. We're delighted to welcome Bruce and his family to RTP as we continue building Affinergy into a product based company."

"Affinergy is uniquely positioned to develop exceptional products for a wide variety of patients and I find that personally exciting," said Dr. Lamb. "It is rare to find a young company with such talented people, a robust technology, excellent infrastructure, and a strong financial position. I share Affinergy's high expectations to become a large and profitable product company that directly benefits patients, employees, and shareholders. Our greatest challenge will be prioritizing the multiple opportunities."

Prior to Dr. Lamb's leadership role at LifeCell, Inc., he spent 6 years at Johnson & Johnson's Ethicon Division where he was VP, Worldwide Research & Development for Biosurgicals. Previously, he worked for Convatec for 7 years in increasing roles of responsibility within product development. Dr. Lamb began his career with 6 years at Pfizer's Hospital Products Group. He earned his Ph.D. in Polymer Chemistry at SUNY College of ESF, Syracuse. He earned his M.S. in Chemistry at the University of Wisconsin, Milwaukee and his B.S. in Chemistry at Bradley University.

# The Wide World of Biomedical Applications of Raman Spectroscopy

*By Klaus Wormuth*

As quoted from one of my grad school professors, Raman spectroscopy and microscopy yield "rich juicy data" on the chemical nature of biomaterials and tissues. Long considered an expensive and difficult basic research tool, Raman spectroscopy has recently become a relatively inexpensive and easy product development and quality control tool, enabled by the advent of tiny powerful lasers and fast sensitive detectors.

In our lab at SurModics (www.surmodics.com), using a tabletop Raman imaging system we routinely apply Raman microscopy to determine the coating thickness, degree of mixing between drug and polymer, and the polymorphic form of the drug within drug eluting coatings on stents and other medical devices. Raman microscopy also finds use in the troubleshooting of product scale up and manufacturing. Since Raman microscopy allows fine focusing; the chemical composition of micron-sized small foreign particles and impurities in biomaterials can be distinguished from background materials, aiding in "CSI" types of manufacturing investigations.

Currently, biomedical applications of Raman spectroscopy for ex vivo histological and in vivo disease detection are expanding at a rapid pace. Raman microscopy applied to the characterization of skin diseases, eye diseases, coronary artery disease, and bone disease yields spectral signatures which can distinguish healthy tissue from diseased tissue. For example, in the study of bone disease, Raman spectroscopy determines changes in protein secondary structure and the nature of crystalline materials (for example, see the research of Prof. Michael Morris: www.umich.edu/~morgroup/).

Catheter-based Raman spectroscopy probably presents the greatest potential to quantify the chemical composition of vulnerable plaques in coronary artery disease, in that Raman spectroscopy identifies the relative amounts of cholesterol, triglycerides, phospholipids, elastin, and calcium salts in plaque. While proven ex vivo, the Raman method awaits further development to become a practical in vivo analytical tool. Recently however, Prescient Medical (www.prescient-medical.com) presented data at the TCT 2008 conference on the vPredict™ catheter Raman system for in vivo detection of vulnerable plaque.

In addition, robust hand-held Raman spectroscopy devices (for example: www.ahurascientific.com) or online Raman detectors (for example: www.controldevelopment.com) allow rapid identification of raw materials (often without removing the packaging) for monitoring of production processes, aiding in the quality control of biomaterials and pharmaceuticals. Thus, the "rich juicy data" provided by Raman spectroscopy aids many aspects of biomaterials research, development and production.

# Medical Device Sector Ripe for Deal-Making

Large medical device makers armed with cash hoards and seeking ways to grow are stepping up acquisitions of young companies with promising technology pipelines but scarce capital.

The past few weeks have seen a burst of deals, most recently the announcement by Medtronic Inc that it plans to buy two privately held, replacement heart valve developers for more than $1 billion.

And analysts expect more deals this year amid the urgency on the part of maturing medical device makers to find new engines for long-term growth.

"There are opportunities out there, and we're going to see this continue throughout 2009," said BMO Capital Markets analyst Joanne Wuensch, who expects Medtronic, with $1.75 billion in cash and short-term investments on its balance sheet, to continue shopping. "Medtech stocks have outperformed, so these companies still have a currency," Wuensch said. "A lot are in hunker-down mode, but they are not in crisis mode."

Meanwhile, small development-stage companies are running up against the challenge of raising capital at a time when credit markets have seized up.

"You've got receptive buyers and receptive sellers, and deals are getting done," said Thomas Weisel Partners

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# Medtronic Buys Heart-Valve Makers for $1.03 Billion

*By Alex Nussbaum*

Medtronic Inc., the world's second-biggest maker of medical devices, agreed to pay at least $1.03 billion for two closely held makers of heart valves that can be installed without chest-splitting surgery.

Medtronic will buy CoreValve Inc. for $700 million, and additional payments if its technology meets development goals, and Ventor Technologies Ltd. for $325 million, the Minneapolis-based device maker said in two statements.

The deals boost Medtronic's presence in the market for heart valves installed on the tip of flexible tubes threaded through blood vessels. The devices may help as many as 300,000 patients too frail for open-heart surgery, Medtronic said. CoreValve and Edwards Lifesciences Corp., both of Irvine, California, are the only sellers of the valves, though Johnson & Johnson and St. Jude Medical Inc. have said they plan to compete as well.

Minimally invasive valves "are the future of the market," Venkat Rajan, an analyst at Frost & Sullivan in San Antonio, said in an interview. For Medtronic, today's deals are "both an offensive and defensive move, giving them access to more technologies that they can leverage, a more robust pipeline."

The acquisitions keep the technology out of the hands of New Brunswick, New Jersey-based J&J, the world's largest medical device maker, at least temporarily, Rajan said.

## 'Lifesaving Technology'

"Our manufacturing and global distribution strengths will accelerate the use of this lifesaving technology," Medtronic Chief Executive Officer Bill Hawkins said in the statement about CoreValve.

Ventor Technologies, based in Netanya, Israel, is testing its valve technology in Europe, Medtronic said in the statement.

So-called transcatheter valves generated about $100 million in sales last year, a figure that could grow to $1.5 billion by 2015, said Larry Biegelsen, a Wachovia Capital Markets analyst in New York, in a note to clients.

Edwards, which sells its $30,000 Sapien valve in Europe, is the only company with a minimally invasive valve in human trials in the U.S. The company has said it expects U.S. Food and Drug Administration approval as soon as 2011.

## 2014 Approval

CoreValve's alternate system held 54 percent of the European market last year and may be approved in the U.S. as soon as 2014, Biegelsen said. Medtronic's purchases will have little impact on Edwards, the world's largest maker of all heart valves, because it has a two-year head start in the U.S., he said.

Edwards generated $18.5 million in revenue from Sapien in last year's fourth quarter and expects sales of $75 million to $95 million this year, the company said in its Feb. 3 earnings report.

## Potential Targets

With CoreValve spoken for, would-be entrants such as J&J may turn to smaller, closely held companies still developing transcatheter valves, said Rajan, the Frost & Sullivan analyst.

Possible targets include Evalve Inc. of Menlo Park, California, JennaValve Technology of Munich, and Sadra Medical Inc. of Campbell, California, he said. They make more sense than the larger Edwards, with its market capitalization of $3.22 billion, Rajan said.

Still, Medtronic's acquisitions could make Edwards more enticing, said Michael Weinstein, a JPMorgan Chase & Co. analyst in New York, in a note to clients.

"Its Sapien platform now represents the only late-stage asset available for other players eyeing entry into the space," Weinstein said. An acquisition of Edwards, if it comes, is unlikely until after results of U.S. clinical trials of Sapien, due in mid-2010, Weinstein said.



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atherosclerotic disease, or narrowing of the arteries, often must undergo multiple surgical procedures to repair renarrowed arteries at the site of angioplasty or stenting, the researchers said.

"After having such a good experience with drug-eluting stents in the coronary system, there's been enthusiasm about using them in legs," said Dr. Kirk Garratt, director of clinical research at Lenox Hill Heart and Vascular Institute of New York. "We've traditionally used balloons to get these vessels open, but because the vessels get pretty small as you get down below the thigh, the long-term patency rates are not everything you'd dream of."

Because vessels in the leg are either much larger or much smaller than those in the coronary system, the researchers said they were concerned that drug-eluting stents might prove less beneficial as a treatment, but recent studies had shown encouraging results.

"Our main finding was that in the below-the-knee region, sirolimus-eluting have better results than simple stents for CLI treatment in the long term," Karnabatidis said. "Specifically, drug-eluting demonstrated encouraging three-year results compared to simple stents regarding all the predefined angiographic endpoints and the reintervention-free survival clinical endpoint."

The findings were expected to be presented at the Society of Interventional Radiology's annual scientific meeting in San Diego.

Also at that meeting, researchers from the John Hopkins School of Medicine were to present a study theorizing that, in the future, adult stem cells can be extracted from a healthy donor's bone marrow and injected into the legs of someone with peripheral arterial disease to grow new blood vessels.

Recent success using luciferase, a bioluminescence imaging agent produced by fireflies, enabled researchers to locate and track stem cells in the body and move this treatment one step closer to reality, they said.

Further research will attempt to verify the feasibility of stem cell therapy for peripheral artery disease and verify the effectiveness of existing therapies using drug-eluting stents.

"Multicenter randomized trials are necessary to support these promising results and build on the level of clinical evidence supporting the integral value of below-the-knee drug-eluting stents in critical limb ischemia treatment," Karnabatidis said.

Garratt added that "the real value of the work being done now is that we're finally getting some experience with stents that are both suited for lower extremity application and can elute drug."

But he added a caution: "Whenever you have a small sample in a single center, you never really know if the findings are going to play out in a bigger trial."

# FDA Clears Serica's Silk Tissue Repair Tech

Serica Technologies Inc., a maker of biomaterials, has received U.S. Food and Drug Administration 510(k) clearance for its SeriScaffold soft tissue repair technology.

The company makes ligament grafts, surgical meshes and gels made from a protein produced by B. mori silkworms. SeriScaffold is a natural silk biomaterial that acts like a scaffold in supporting weak or damaged tissue. The technology could be used in breast cancer patients recovering from reconstructive surgery, as well as plastic surgery procedures in general. The scaffold will use silk for restructuring, rather than synthetic materials or cadaver tissue from humans or animals. Additionally, the scaffold could find use in rotator cuff and hernia repair surgeries, the company said.

Pre-clinical studies show more time for healing ligaments due to a slow biosorption rate for silk. Serica officials said the company seeks a partner for aesthetic and reconstructive surgery.

Serica, formerly Tissue Regeneration Inc., was founded in 1998 by Gregory Altman. Altman, CEO of the company, developed the firm's technology after he ruptured his anterior cruciate ligament, or ACL, while playing varsity football at Tufts University.

# Chameleon Scientific

*By Dan Storey*

Medical companies use chemistry or mechanics to produce the vast majority of surfaces for implanted or inserted medical devices. In stark contrast, Chameleon Scientific harnesses high-energy, physics-based processes to create surfaces with radically new performance and characteristics not seen in the native device.

Chameleon Scientific currently employs three separate and distinct technologies. While all three are based on the use of plasma physics and how the plasma can be controlled to modify the surfaces of devices, they each serve a very unique purpose and surface modification capability. The first of the technologies utilizes a high current (>300A) low voltage (<20v) regime. This technology allows for the gross surface topology modification in the range of 200 nm to 20 microns. The next technology uses a very high voltage (> 50,000 V) and low current (<10mA). This technology allows for the direct deposition of biomolecules and is the subject of our first issued patent. Finally the third technology uses a low voltage (>200 V), low current (>1 A), high pressure plasma to get true nano-texture surfaces in the range of 1 to 100 nm.

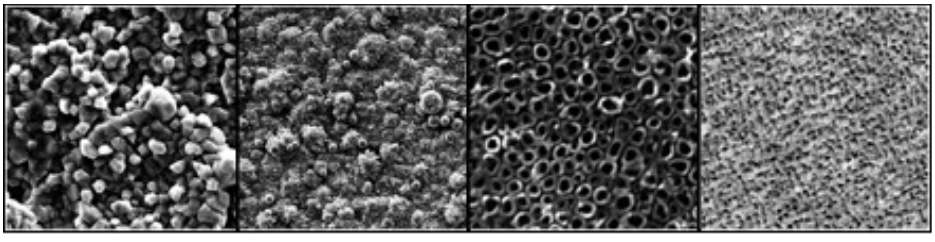
By working at a more basic level – manipulating the physics of a surface's interaction properties – Chameleon Scientific can direct chemical and biological action within the body to create new surface performance.

Chameleon's work focuses in several critical areas: high-activity antimicrobial surfaces that generate 6 log reductions in bacteria; drug and biomolecule elution surfaces without polymers or linkers; and surfaces to encourage or discourage the attachment of osteoblasts, endothelial cells, fibroblasts, gingival and other cells. Chameleon is also applying its technologies to create specialty conductors for enhanced sensing, and for production of super-durable generator leads, down to 2Fr., for pacing, left-heart CRT, neuro and spinal applications.

Chameleon's technologies apply high levels of energy to rearrange atomic and molecular structure, change surface energy, and alter surface charge, contact angle and nano-topology to control in vivo performance. Chameleon builds nano surface structures to hold and elute drugs and changes the atomic bond between surfaces and attached materials, drugs and biologicals.

"New applications arise every week. It's very exciting." says Chameleon's CTO, Dan Storey. Chameleon is developing surfaces for major medical devices companies. Its technologies are being applied to cardiac stents, orthopedic implants, dental implants, wound care products, sensing leads and generator leads, among others.

*Examples: SEM images of Chameleon surfaces from left to right: Cubic, spiky or spinulose, tubular, porous. Each produces vastly different surface performance, both singly and in combination.*

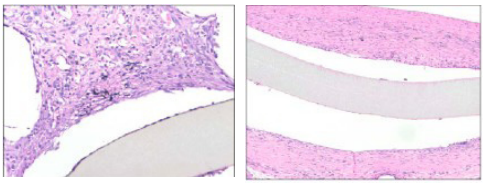


## Silver Antimicrobial

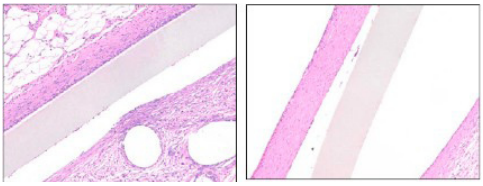
Chameleon's first commercial surface on an implanted device will be one of its high-activity silver antimicrobial coatings. Chameleon is scheduled to begin commercial production of this surface within the next month. The antimicrobial surface is a proprietary construction of silver, silver oxide and other elements. Results in serial dilution tests show an 8-log reduction in bacteria count during the first week and a 5-log reduction past 14 days (see graph). Antimicrobial efficacy can be "tuned" to achieve 3, 7, 14, and 21-day performance depending upon the requirements of the device and application.

In in vivo testing, antimicrobial silver/silver oxide coated polypropylene prevented the formation of bacteria, bacteria colonies and biofilms for 28 days (subcutaneous rabbit model). In an intramuscular rabbit healing study, there was no necrosis observed at 9 days and tissue in-growth at 28 days was equal to the control (uncoated) sample. The lesions were consistent with a benign foreign body reaction in the muscle, and with a more acute inflammatory reaction in the subcutaneous tissue (See histology photos below).

*Coated polypropylene at 9 and 28 days*



*Uncoated polypropylene at 9 and 28 days*



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# U.S. Health Reform Casts Shadow on Device Sector

*By Susan Kelly and Debra Sherman*

Economic reforms proposed in President Barack Obama's 2010 budget may put pressure on prices for medical devices, but a massive overhaul of how much the government pays through Medicare is seen as unlikely.

The Obama administration's efforts to reform the healthcare system include incentives for hospitals to spur Medicare/Medicaid cost reductions, expansion of competitive bidding programs for suppliers and more research to compare treatments.

Investors are concerned that hospital reimbursement rates will face pressure from Medicare payment cuts through the government's system of codes known as diagnosis related groups, or DRGS, set annually each spring, analysts said. Hospitals would in turn press device makers on pricing.

Uncertainty about what healthcare reform means for the medtech sector has pressured those stocks, historically a safe haven in rough economic times.

"The uncertain impact of health reform on demand, pricing and regulation, and the uncertain time frame for figuring it all out is certainly hurting the stocks," said Leerink Swann analyst Rick Wise.

"It's clear that with a constrained budget there is going to be pressure on all participants to avoid waste, to optimize pricing and utilization. But I haven't heard anything that makes me think there is going to be some new profound way to single out devices," Wise said.

Medicare reimbursement rates to hospitals have been rising incrementally each year for the past decade, and nothing in the budget indicates that will change this year, said Jeff Johnson, analyst with Robert W. Baird and Co.

"What we've received in the Obama budget doesn't seem to suggest that there will be a sizable, across-the-board cut in DRGs. The details are so vague," Johnson said. "But you have to have it on your radar screen for the intermediate to longer term."

Medical therapies, technologies and diagnostics that can demonstrate a clear benefit in extending and improving the quality of patients' lives will always have pricing power, industry analysts said. Marginal improvements to products will not.

True breakthrough products such as drug-eluting stents, transcatheter replacement heart valves and cancer screening for the human papilloma virus will be paid for, said Jefferies & Co analyst Peter Bye.

"Both pharma and medtech are going to have to accelerate new platform technologies, and it is going to increase the risk on the R&D front," Bye said.

## Medtech Not Targeted

Capital Alpha Partners healthcare analyst Kim Monk noted that the medtech sector is one part of healthcare that is not being directly targeted.

Reforms, she said, "are certainly directed at the providers, who don't have much price sensibility. They're looking at comparative effectiveness research and pay-for-performance. They'll crack down on hospital readmissions, and reimburse for quality, not quantity. They want providers to have some financial skin in the game ... but this is long-term reform," she added.

David Nexon, an executive with Advamed, the trade association representing medical technology companies, said he does not see medical device prices as a significant driver of rising healthcare costs overall. While advances in medical technology have been blamed as a major factor in rising medical costs, medical devices, he said, "are a relatively small and constant share of healthcare costs."

Two specific initiatives, quality incentive payments to healthcare providers and the bundling of payments for hospitalizations and 30 days of post-discharge care, are unlikely to pose a significant risk to medical device manufacturers, analysts said.

And some suggested it could take three to five years for the government to begin collecting data for comparative effectiveness research to determine whether certain drugs, devices and treatments are better than others for specific health problems. The recent stimulus bill provides $1.1 billion for such studies.

The Obama budget also calls for greater funding to strengthen the U.S. Food and Drug Administration's oversight of food and medical products, which could lead to heightened inspection and compliance costs and more recalls, something device makers are already facing.

# Regulatory Corner

*By Phil Triolo*

## Recent Obama Appointments

Barack Obama has promised a much-needed overhaul of America's health care system. While the details of the overhaul have yet to be officially announced, several appointments have been made and actions taken that have a direct effect on the regulation of medical products in the United States.

After Tom Daschle asked to be withdrawn from consideration as Secretary of the Department of Health and Human Services (HHS) because of tax irregularities, the President appointed Kathleen Sebelius to this post. Sebelius is a two-term Democratic governor from Kansas who served previously as a state insurance commissioner and oversaw Kansas' Medicaid program. She has been credited with boosting health care assistance for the poor during her tenure.

Sebelius appeals to members of both parties, having been commended by Republican governors such as Arnold Schwarzenegger of California and Jon Huntsman of Utah. Republicans from Sebelius' home state of Kansas also voiced their support of her appointment. She will most probably focus her efforts on health care reform, and leave the control of FDA to its new Obama appointee, Dr. Margaret A. Hamburg.

Hamburg is a former New York City Health Commissioner. In that capacity, she developed a tuberculosis control program that sharply reduced the incidences of the disease and led efforts that resulted in increased child immunization rates. In 1997 she left NYC to become HHS Assistant Secretary for Planning & Evaluation. At HHS she initiated a bioterrorism program and led planning efforts for a pandemic flu response. She is currently a senior scientist at the Nuclear Threat Initiative and Associate Director of the National Institute of Health's National Institute for Allergy & Infectious Diseases. Thus, she has a great depth and breadth of knowledge of public health issues and infrastructure as well as security issues.

Hamburg replaces FDA Acting Commissioner Dr. Frank Torti, who had been touted as an exemplar of a re-emphasis of a science-based approach by the Agency. Torti, himself, replaced Dr. Andrew von Eschenbach. Appointed to the Commissioner post in 2005, von Eschenbach was at the helm of the agency during a period when it lost the confidence of both the American public and Congress. Dr. von Eschenbach stepped down on January 20, 2009, the day Mr. Obama was inaugurated as the 44th U.S. president.

Commissioner Hamburg has her work cut out for her, as the issues facing the Agency are many and include:

- Restoring the public's confidence in the ability of the FDA to safely regulate foods and medical products after the concern caused by the recent peanut butter and heparin recalls;
- Distancing the agency from a perception that it is too close to the pharmaceutical and medical device industries it regulates;
- Redressing concerns of FDA reviewers who have accused their superiors of ignoring their technical concerns and bowing to political and industry pressures, thus restoring morale to Agency employees;
- Crafting a pathway for the approval of follow-on biologics;
- Improving the quality and timeliness of drug and device reviews while faced with resource shortfalls;
- Emphasizing a science-based approach to regulatory efforts at a time when keeping pace with scientific developments can be a challenge for even a well-staffed and fully funded agency.

Baltimore Health Commissioner Dr. Joshua Sharfstein, who led the Obama administration's transition team for the FDA, has been selected to be Dr. Hamburg's Chief Deputy. Sharfstein has focused his efforts on drug safety issues, most recently as the proponent of a March 2007 citizen petition that requested a FDA review of pediatric doses of cough and cold products. As a result of the petition, manufacturers voluntarily recalled those products. He also served for over four years on the congressional staff of Rep. Henry Waxman (D- California) as an investigator on his staff on the House Oversight & Government Reform Committee. He has a history as an investigator and monitor of the drug industry.

It appears as if their appointments are a bit of a political compromise, as Sharfstein is closely associated with Rep. Henry Waxman (D-California), while Hamburg was championed by Sen. Edward Kennedy (D-Mass.).

Based on their backgrounds and talents, there is reason to believe that Hamburg will concentrate her efforts on tobacco regulation and food safety while Sharfstein will devote his efforts to regulating the safety and efficacy of medical products. What will occur with respect to any split in responsibilities is anyone's guess at this point. Some

*Regulatory Corner Continued on Page 12*

# CorNova Looks to Improve Stent Devices

*By Marc Songini*

Burlington-based medical device startup CorNova Inc. is taking existing stent-related devices and processes and combining them with cutting-edge technologies, such as fiber optics, to get better patient outcomes.

The company is at work on a set of balloon catheters designed to help eliminate cases of stent restenosis, or thrombosis, by helping with stent selection and optimizing the process of implanting the stent, explained Eric Ryan, the company CEO. Its FiberHalo catheters carry a hair-thin fiber wire that provides blood vessel measurement from inside the balloon itself to assist in stent procedures, without a corresponding increase in time, risk or cost.

CorNova claims fiber-optic capability in the stent itself will provide a marked improvement over current procedures, which are done under fluoroscopy, which has low resolution, or by using the more cumbersome intravascular ultrasound medical imaging technology. The addressable market is in the billions of dollars, Ryan estimated. Founded in 2003, the company, so far, has been funded by angels and institutional investors, but Ryan declined to say by how much.

"CorNova is constantly evaluating partnership opportunities," he said.

The FiberHalo stent deployment catheter uses fiber optics to make measurements that allow physicians to tell if a stent is adequately deployed. If there is an under-expanded portion of the stent, the FiberHalo catheter is capable of locating it. To fix an under-expanded stent, doctors would be able to insert Cornova's FiberHalo post-dilation catheter, which is also equipped with fiber optics. It identifies the under-expanded area, allowing doctors to inflate the balloon to correct it.

CorNova is also at work on a predilatation FiberHalo catheter, which will be able to detect arterial plaque composition. Relying on known data, this will allow doctors to select the best stent treatment, said Ryan. The company plans to start pre-clinical studies for FiberHalo in 2009, but there are no specific deadlines for when the FiberHalo might hit the market, said Ryan.

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*Deal-Making Continued from Page 4*

analyst Raj Denhoy. "Technological innovation and clinical advancement haven't stopped just because the capital markets aren't acknowledging it." But a start-up medical device maker can no longer count on plans to pay back its private investors with capital raised through an initial public offering, Denhoy said.

"Everybody's asking themselves how do we shore up our finances, how do we get to profitability?" said Leerink Swann analyst Rick Wise.

Besides cash flow, the big diversified healthcare companies have the regulatory and legal muscle and huge global infrastructures needed to bring new medical devices to market, and the patience to await a return on their investment.

"The small guy is just the opposite – they have the idea but need the capital," said Wise, who expects Johnson & Johnson, St. Jude Medical Inc., Abbott Laboratories and Stryker Corp to be active acquirers.

Last month, J&J completed the acquisition of breast implant maker Mentor Corp for $1.07 billion. Abbott is in the process of buying Advanced Medical Optics EYE.N, the leader in Lasik laser vision correction, for almost $1.4 billion, plus another $1.4 billion in debt.

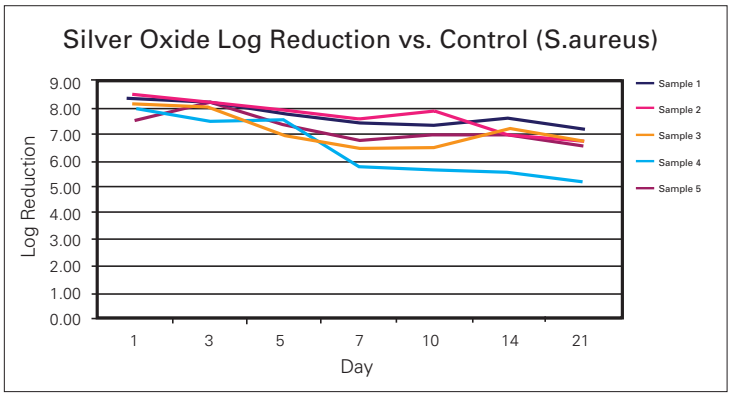
Analysts say there are not a lot of distressed assets in the medical technology sector. Still, stock prices are somewhat depressed, making valuations attractive to device makers that are looking for ways to supplement their growth.

"The device companies don't have the pressure the drug companies have (to expand their product pipelines), but they have seen their growth slow," said JPMorgan analyst Michael Weinstein. Most analysts aren't expecting blockbuster deals along the lines of Boston Scientific Corp's $27 billion acquisition of Guidant in 2006.

Despite the merger-readiness of small and large companies, deals in the sector have their own inherent challenges. The device sector actually consists of many subsectors, each with its own target customers and insurance reimbursement practices.

"It makes deals challenging," said a healthcare investment banker who requested anonymity, "but the cost benefits outweigh those risks."

*Chameleon Continued from Page 7*

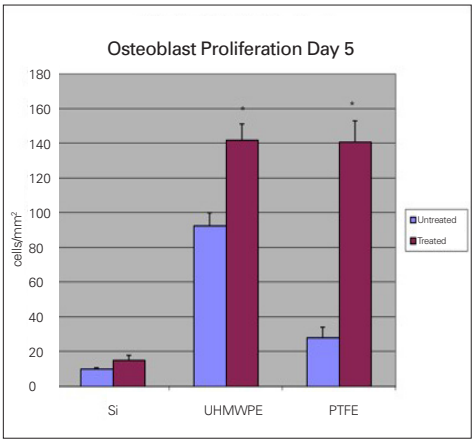



*Example of a 21 day serial dilution test and associated log reduction versus control. Silver oxide coating was tested 5 times for statistical purposes. Silver oxide coating was applied to polypropylene.*

## Osteoblast Attachment

Orthopedic and spinal in vivo implant device materials are usually surface modified in attempts to promote or improve cell attachment. Unfortunately, even when there is some minor cell attachment or extensive tissue in-growth, there are no long-term implanted devices that adequately promote actual tissue growth. Some protocols employ growth factors on the surface of a device to aid in tissue attachment, but results are not always satisfactory and growth factors are not routinely used. Few successful attempts have been made to modify implant surfaces (typically alloys, ceramics and selected polymers) so that new tissue cells readily attach and grow, and current technology has failed to develop surfaces that significantly enhance tissue attachment.

This being said, in in vitro tests, Chameleon modified surface topologies have exhibited enhanced attachment and proliferation on numerous metals, alloys, ceramics and several different types of polymer. Surfaces exhibited an increase in cell attachment of 1.5 X to 4X over the untreated controls (see graph) after a five-day, in vitro proliferation test.




**p<0.01 (compared to respective uncoated sample.)*

## Drug-elution Surfaces

Chameleon's high-energy processes, along with its capability to create nano surface structures, provides the ability to attach and control the delivery of a broad range of drugs and biomolecules without the challenges faced with carrier or degradable polymers or linker molecules. The company can attach molecules directly to a metallic, polymer or ceramic surface and control the rate of delivery of those molecules over time periods that range from hours to weeks.

Chameleon's development work with dental implants, cardiac stents and other implanted devices shows that even fragile biologicals such as RGD, BMP2 and heparin can be attached and delivered without compromising integrity and activity. Its technologies also allow attachment only where needed, avoiding the all-over application common in dip coating.

Chameleon is taking the first steps into an entirely new area of surface design and creation by employing proprietary, high-energy processes to control the interaction between materials and the human body.

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*From the Editor Continued from Page 2*

I have been in touch with my Senator (Senator Russ Feingold), who is the sponsor of 2009 S. 177, an amendment to the reauthorization which proposes to substantially boost the percentage of funds to small business (details at http://feingold.senate.gov/e4/rls_e4_010609.html). Certainly some may not agree on the level of expansion that is proposed in this bill, but as a regular panel reviewer of NIH SBIR proposals, I do see a great many highly meritorious proposals that do not receive funding.

Please contact your elected official in support of the reauthorization of the SBIR/STTR program, whether it is "as is" or 2009 S. 177 that will increase the set-asides. Let your representatives know how important the SBIR program is to the medical device industry, and to your State. Let them know how important this is to jobs creation. Let them know how many life-saving and cost-lowering technologies had their roots in small businesses.

*Regulatory Corner Continued from Page 9*

predict the eventual breakup of the FDA into separate Food Safety and Medical Product agencies, a scenario denied by the administration. Others predict that Hamburg will retain traditional control of the Agency and Sharfstein a lesser, well-defined role, while others foresee the agency as a "two-headed monster" with a potential for conflict between the two appointees as well as with their boss, recently appointed HHS director Sebelius, who selected neither of them.

One thing is rather certain. Sharfstein's history as a drug safety advocate suggests that there will be increased scrutiny of drug applications and post-market drug safety issues and a departure from what many perceived as a cozy relationship between the FDA and pharmaceutical companies during the past administration. This increased scrutiny of drugs will most probably spill over to device and nutraceutical regulatory issues.

## Government Accounting Office Report on the 510(k) Process

The GAO recently issued a document entitled *Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process* which can be found at http://www.gao.gov/new.items/d09190.pdf.

The authors studied a group of devices that, at the time the Medical Device Amendments were enacted in 1976, was assigned the FDA's highest risk Class III designation—yet has been allowed to be marketed in the U.S. after undergoing the 510(k) premarket notification process rather than the more stringent premarket approval (PMA) process. The full text version of the document describes the differences between the 510(k) and PMA processes in great detail and is a good resource in this respect. Briefly, the FDA clears devices, typically categorized into the medium-risk Class II category, after finding them "substantially equivalent" to [non PMA-approved] devices already legally marketed in the U.S. under the 510(k) process. It approves the highest-risk Class III devices that it finds to be "reasonably safe and effective" under the PMA process. The latter process is more burdensome to both the FDA and industry and usually requires a clinical investigation, whereas 510(k) clearance is usually issued on the basis of the results of comparative bench tests. According to a summary of the report published by the GAO:

"GAO found that in fiscal years 2003 through 2007 FDA cleared submissions for 24 types of Class III devices through the 510(k) process. As of October 2008, 4 of these device types had been reclassified to class II [requiring 510(k) premarket notification], but 20 [Class III] device types could still be cleared through the 510(k) process. FDA officials said that the agency is committed to issuing regulations either reclassifying or requiring PMAs for the Class III devices currently allowed to receive clearance for marketing via the 510(k) process, but did not provide a time frame for doing so…

"**Recommendation**: The Secretary of Health and Human Services should direct the FDA Commissioner to expeditiously take steps to issue regulations for each Class III device type currently allowed to enter the market through the 510(k) process. These steps should include issuing regulations to (1) reclassify each device type into Class I or Class II, or requiring it to remain in Class III, and (2) for those device types remaining in Class III, require approval for marketing through the PMA process."

Only a few devices fall into the category of Class III devices that can be cleared under the 510(k) process. These Class III devices that the FDA has identified as being "high risk" and requiring either reclassification into Class I or II or that PMAs be approved before they can be marketed in the U.S. include Iontophoresis Devices, Metal/ Metal Hip Joints, and Shortwave Diathermy Devices. A complete list of the subject devices and their current status (Class III requiring 510(k)s or reclassification into Class I or II) appears in the report.

Unless you happen to be developing one of the Class III devices that is in a bit of a regulatory limbo, the report has little relevance. The report doesn't criticize or comment on either the 510(k) process or the PMA process. However, there are some grumblings about the 510(k) process, as assuring that a device to be marketed in the U.S. in 2009 is substantially equivalent to a device marketed prior to 1976 may not be the soundest way to assess its suitability. But that is a topic for another discussion.

*The next* Regulatory Corner *will address the new Comparative Effectiveness Research (CER) initiative and its potential impacts on the medical product industries.*

## Meeting/Conference/Trade Show Calendar

| Meeting/Conference/Trade Show | Dates | Place | Web Address |
|---|---|---|---|
| Design of Medical Devices Conference | Apr 14-16 | Minneapolis, MN | dmdconf.org/ |
| BayBio2009 I Life Sciences – Branching Out | Apr 16 | Palo Alto, CA | baybio.org/wt/home/BayBio2009 |
| BIOMEDevice Boston | Apr 22-23 | Boston, MA | devicelink.com/expo/bioboston09/ |
| Society for Biomaterials Annual Meeting | Apr 22-25 | San Antonio, TX | biomaterials.org/Meetings/09AnnualMeeting/ |
| American Academy of Neurology (AAN) - Annual Meeting | Apr 25 - May 2 | Seattle, WA | am.aan.com/ |
| Advanced Wound Care & Wound Healing Society (SAWC & WHS) - Annual Symposium | Apr 26-29 | Dallas, TX | sawc.net |
| American Pain Society (APS) - Annual Scientific Meeting | May 7-9 | San Diego, CA | ampainsoc.org/meeting/ |
| Heart Rhythm Society (HRS, formerly NASPE) | May 13-16 | Boston, MA | hrsonline.org/Sessions |
| American Society for Microbiology (ASM) - 109th General Meeting | May 17-21 | Philadelphia, PA | gm.asm.org |
| BIO International Convention | May 18-21 | Atlanta, GA | bio2009.org |
| European Association of Percutaneous Cardiovascular Interventions (Euro PCR) | May 19-22 | Barcelona, Spain | europcr.com/ |
| American Society for Artificial Internal Organs (ASAIO) | May 28-30 | Dallas, TX | asaio.com |
| Medical Design & Manufacturing East (MD&M) | June 9-11 | New York, NY | devicelink.com/expo/east08/index.html |
| American Orthopaedic Assoc.(AOA) - Annual Meeting | June 10-13 | Bonita Springs, FL | aoassn.org/AnnualMeetings.asp |
| AAPS National Biotechnology Conference | June 21-24 | Seattle, WA | aapspharmaceutica.com/meetings/biotec/bt09/index.asp |
| Controlled Release Society (CRS) - 36th Annual Meeting & Exhibition | July 18-22 | Copenhagen, Denmark | controlledreleasesociety.org/meeting/default.cfm |
| International Conference of the IEEE Engineering in Medicine and Biology Society | Sept 2-6 | Minneapolis, MN | embc09.org/ |
| 22nd European Conference on Biomaterials | Sept 7-11 | Lausanne, Switzerland | esb2009.org |
| MEDTEC China | Sept 8-10 | Shanghai, China | devicelink.com/expo/shanghai08/ |
| Transcatheter Cardiovascular Therapeutics (TCT) | Sept 21-26 | San Francisco, CA | tctmd.com |
| Orthopedic Design & Technology (2nd annual) | Oct 6-8 | Fort Wayne, IN | odtexpo.com/ |
| American Neurological Assoc (ANA) | Oct 11-14 | Baltimore, MD | aneuroa.org/index.php?src=gendocs&ref=2008SLC__Home |
| VIVA (Vascular Interventional Advances) | Oct 19-23 | Las Vegas, NV | vivapvd.com/index.cfm |
| Medical Device & Manufacturing Minneapolis | Oct 21-22 | Minneapolis, MN | devicelink.com/expo/minn08/ |
| **BioInterface 2009** | **Oct 26-28** | **San Mateo, CA** | **surfaces.org** |
| American Association of Pharmaceutical Scientists (AAPS) | Nov 8-12 | Los Angeles, CA | aapspharmaceutica.com/meetings/futuremeetings/index.asp |
| American Heart Association (AHA) | Nov 14-18 | Orlando, FL | scientificsessions.americanheart.org/portal/scientificsessions/ss/seeyounextyear2009 |
| Medica | Nov 18-21 | Dusseldorf, Germany | medica.de |
| BIOMEDevice 2009 | Dec 9-10 | San Jose, CA | devicelink.com/expo/biomed08/ |

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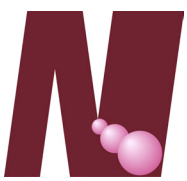

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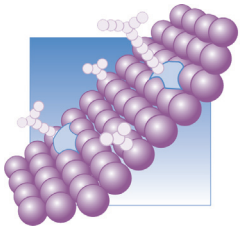

Surfaces in ***Biomaterials*** Foundation