

# BIOMEDICAL BUSINESS & TECHNOLOGY

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## The *BB&T* interview:

### *Mark DuVal*

*His law firm focuses on FDA-related matters  
Dealing with the issues facing a regulated industry*

#### Interview by JIM STOMMEN, Contributing Editor

Mark DuVal, JD, is president of DuVal & Associates, a Minneapolis-based firm dedicated to counseling companies in the medical device, pharmaceutical, biotech, food and nutritional supplement industries. His practice includes providing strategic regulatory advice, developing compliance programs, designing and implementing sophisticated marketing programs, counseling on reimbursement matters, conducting sales training and interfacing extensively on behalf of companies with the FDA with relation to product approvals and clearances, clinical trial negotiations, approvals, policy arguments, appeals, etc.

Prior to founding the firm, Mark was general counsel for 3M Pharmaceuticals and Drug Delivery Systems, working both domestically and internationally. He also worked at Medtronic as an expert on FDA matters and in corporate compliance. Mark is a frequent national speaker and writer on a variety of issues relating to product approvals/clearances and other regulatory/reimbursement issues.

## The Inside Story

- ❑ **Advanced laparoscopic surgery: A blended mix of new technologies.** SAGES conference 2010, Page 6.
- ❑ **Healthcare reform still a key topic at ACC 2010 meeting.** Story on page 9.
- ❑ **Sunrise Medical completes \$120 million refinancing, spins off DeVilbiss division.** *International Report*, page 13.
- ❑ **CancerGuide Diagnostics enters into research collaboration with Duke University.** *Acquisitions & Agreements*, page 17.
- ❑ **CMS to cover NaF-18 PET for metastatic bone cancer under CED.** *Market Developments*, page 18.
- ❑ **FDA clears ECG, blood pressure combo system.** *Product Briefs*, page 21.

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**BB&T:** *Those involved with the med-tech industry – as operators of companies, providers of services to those companies or investors – are alarmed over possible changes in the FDA’s 510(k) program, the primary route to market approval for most companies in the space. Could you outline where it appears the agency is headed on this issue?*

DuVal: Therein lies the problem. While the FDA has been very public about the fact that it is addressing the 510(k) program, and it has outlined categorically some of the areas that it will be reviewing, they haven’t been forthcoming with a lot of detail. That is very problematic, because, for example, when FDA holds these town hall meetings where everyone gets their five minutes at the microphone, all you can do is speak your peace as to what you think they might be doing.

FDA has created “working groups” to revisit the 510(k) program and look for improvements. First, they have talked about re-examining the 510(k) program in the definitional or interpretational areas of what are the new indications and new intended use, they have also talked about when does a new featured benefit or new technological characteristic raise a “new” type of question about safety and effectiveness. So they are going to be digging into that.

The second thing they’re going to be looking at is what is the quantum of evidence necessary to clear a 510(k) and when is it appropriate to request human clinical data? In addition, they’re talking about the issue of multiple predicates and predicate creep, and a variety of other issues. We in industry have broadly provided FDA input on those issues, but it’s not the same as if you’re sitting at the table.

The FDA has asked an independent group, the Institute of Medicine (IOM), to take a look at the 510(k) program as well. The FDA, and IOM, have deemed industry a “conflict of interest.” Our position is that we are one of the main interests, in the sense that we are the primary stakeholder that uses the system and has input into it. We can provide them with meaningful input about what is working at FDA and what isn’t, and how might the 510(k) program be changed. The IOM has a number of members with heavy academic backgrounds and seemingly little experience interfacing with FDA as industry does. That doesn’t mean they won’t have something to contribute – they will. Public Citizen is a member too, and they are one of the biggest critics of the medical device industry on the planet.

It’s unfortunate that they really don’t round out the membership to get industry’s active input. I don’t mind that there are industry/510(k) critics and non-industry people at the table, there should be, but why would they



MARK DuVAL  
Tilts at FDA Windmills

not include people from industry – from the start-up community, from medium-sized companies, from the large companies – just to provide them meaningful input about the 510(k) program from another perspective. So it’s concerning. The biggest issue I have is that we would like to have participation. It’s sort of a black box; we see input going in, but we don’t know what’s going to come out.

**BB&T:** *One phrase that caught my attention in particular, because there has been a lot said about it lately, is “predicate creep.” It kind of looks to me like FDA is pretty much looking to stomp out predicate creep completely.*

DuVal: Yes, that’s concerning to me and industry as well. We view predicate creep as a positive attribute of the process. The whole 510(k) process was designed to accommodate technological change, and embrace it. But the way FDA tends to use the term predicate creep is as a perjorative – that there is something wrong with the system when we make incremental advances to technology. That’s a good thing, not a bad thing. I understand FDA’s issue is how do we keep up with all this technological change, but that is their charge—always has been—and the 510(k) program gives FDA enough flexibility to ask for the information they need, within reason and limits, to examine new technology.

**BB&T:** *Do you have a sense of what is the reasoning behind this push to re-do the 510(k) program overall?*

DuVal: In fairness to the FDA, they are increasingly being confronted, or faced with new and more complex technologies, so at base the products are very similar to some of the existing predicates, but they have some level of change. And it is that change which introduces the complexities to FDA’s review, because if it’s a new technological characteristic, it often will raise unanswered questions of safety and effectiveness. And the agency is trying to get its arms around the question of what kind and amount of evidence are we going to require to grant a “substantial equivalent” determination? When we feel we fall short, when we feel that the change is too great, and the product is too different from the existing predicate, what should FDA do? Well the FDA and industry have a nice outlet in the *de novo* program, which can be used when FDA finds there is not an existing predicate. Remember, when a company gets a “not substantially equivalent” letter, meaning they are not getting a 510(k) clearance, the device is then automatically classified as a class III high risk device – even if the device does not

deserve that risk classification. With a *de novo* request for reclassification, the company can request FDA to review a device as a class II moderate-risk device. If FDA agrees and proceeds down the *de novo* path, FDA is not limited by the substantial equivalence standard or review; it can ask for information that establishes “reasonable assurance of safety and effectiveness,” the PMA standard of review. This is more than what is needed for a 510(k). Because the device is now considered in class II, a moderate, not high-risk class, FDA should not require the company to submit the same amount of information required of a high-risk class III device. The data request is risk-adjusted.

So they’re grappling with all of that in a world of more complex devices – how do you ask for enough information without asking for more than is truly needed, which affects speed of innovation to the market? I understand it’s a struggle for them – it’s a struggle for industry as well. But there are reasonable ways out of this. My view is that the 510(k) program is sufficiently flexible as it currently stands to accommodate this kind of dialogue and debate, and we just need to put some parameters around it. Maybe you have tier one 510(k) devices that really are “me too” devices, and tier two, which present a little more of a challenge for the agency, and then what are the requirements for those tier two-type 510(k) devices? And the *de novo* program is a way out for devices that don’t quite meet the 510(k) criteria, but do not belong in a class III high risk category.

**BB&T:** *I think it’s interesting that when this subject has come in conversation in recent months, one of the things that they almost always bring up, especially those in the investor community, is that the system is pretty good – it may need some tweaking, but it’s pretty good. And if big-time change is coming, that’s one of those ‘throw out the baby with the bathwater’ things.”*

DuVal: The folks I deal with, and I probably am working with 100 medical-device companies at any given time, really believe that the framework is good – it’s still very viable. We need to upgrade it a bit, to figure out how to interpret certain provisions and how to make it work as new technologies come into the marketplace, but to consider replacing it entirely is really a nightmare consideration for industry. We have a familiarity with this program, and it’s fundamentally sound and workable with some improvements. Between FDA and industry, we can come up with those improvements.

**BB&T:** *Are any short-term “fixes” being considered while awaiting the Institute of Medicine’s supposedly definitive report on the 510(k) program?*

DuVal: They have a number of internal working groups at FDA – I think it’s nine or 10 such groups – that have been assigned discrete and insular kinds of proj-

ects to examine the 510(k) program. I know they include things such as, when does another indication constitute a new intended use, and when does it constitute the same intended use? Another is the issue of new technological characteristics – when is a new type of question of safety and effectiveness question raised by that new feature? There’s a group working on that. There is one working on the amount of performance and clinical data needed to clear a 510(k). I think there is one that is about predicate creep and the use of multiple predicates. There is a working group on *de novo*. So all of those issues that I outlined before, there are working groups assigned to them.

I give CDRH Acting Director Jeffrey Shuren great credit, and Donna Bea Tillman before him, for wanting to re-examine all these things. The industry is just asking for more certainty, more predictability, and if that’s the outcome of all this work, great. If the outcome is that they propose an entirely new system to be thrust upon industry without us really having any input, that’s very troublesome.

I’m not sure FDA is really too focused on the second half of its mission. It’s a twofold mission, right? One is protecting patients, and the other is speeding innovations to market. If the industry has one concern with the agency today, it is that there is not a whole lot of concern with speeding innovations to market anymore. They have become so risk-averse, the emphasis has become entirely on protecting patients to the nth degree, and we will never have a perfect device or drug that gets through the FDA, no matter how much study we do. So we deprive patients of the benefits of products that get on the market in Europe two to eight years before they get on in the U.S., and that’s a travesty. I think Dr. Shuren is trying to bring a better balance to FDA’s analysis.

**BB&T:** *Is the basic thrust of the FDA’s plans for 510(k)s that devices approved under the program demonstrate superiority to the predicate device, rather than non-inferiority, the existing standard?*

DuVal: In operation, some of FDA’s review teams use a lot of inappropriate standards for “substantial equivalence.” I have had this dialogue with many FDA folks – I take a lot of companies on appeal to the FDA. I am frequently debating the agency that one, you are asking for information you want, but don’t need in order to establish substantial equivalency. Secondly, you often are asking for comparison to standard of care, and that’s not the role of the FDA. Thirdly, they’re also frequently asking the sponsor to establish the clinical utility or clinical benefit of the device when it already has been established by the predicate. In asking for that type of information, FDA is essentially practicing medicine, which is an inappropriate request for FDA. FDA should allow devices that have established substantial equivalence to come to the

market and allow the medical community to determine if they like the device or not. The device should simply go through FDA and substantiate its labeled claim.

All of these are issues that I debate on a weekly basis with the agency. You will find these issues discussed in the internal FDA report released on the ReGen review discussed by FDA's own lawyers, by the Office of Chief Counsel (OCC). In that report, the OCC cited the review staff for asking all those inappropriate questions that were outside the scope of the statute. They should not be asking them, but they are – throughout much of CDRH.

**BB&T: So then, is FDA following the legal standard for review of a 510(k)?**

DuVal: In my view, sometimes yes, many times no, and I think they get away with it because they can. Most of the time all you buy yourself by arguing with FDA on these issues this is endless appeals, unless you get to someone who knows the statute at the top from management. As someone who works intimately with the agency day in and day out, I really feel the loss of Donna Bea Tillman and Dan Schultz, because they were very fair-minded and were a breath of fresh air. I mean, they would sometimes overturn staff when they were outside the scope of their authority or jurisdiction. Dr. Shuren, I have great hope for him as well. I did the first industry appeal to him last week, the first one he has heard, on a PMA, and I found him to be a good listener, very intelligent and asked really good questions. The jury is out to see what kind of a decision-maker he'll be. I think he'll be fair-minded as well and, I think, decisive.

**BB&T: What is your view of the amount of data the FDA is asking for today – reasonable or unreasonable?**

DuVal: Both. There are times when I have taken clients to the agency and I feel my clients haven't done enough. There are times when I think they've provided more than enough. But the data requirements are escalating so rapidly within the FDA, and the FDA has become fairly academic. They are continually populating themselves with people who have come over from the drug side of FDA and they have sort of a drug view of performance data and human clinical study requirements, so we are getting some unbelievable requirements. And the other thing that is very concerning is that they don't do a good job in the pre-IDE setting of agreeing upon things that would actually result in the clearance of the product. They give feedback that suggests "Yeah, you can do that study ethically, and you're covering the patient and what-not," but what we really want to know as an industry is, if and when we do that study would it be likely to result in a clearance if the data turn out well? They fall down a lot in giving guidance there. When you do the study that

they've agreed to with you, they later backtrack and say, "Well, we really need more data," or "You should have done a more valid comparator," or whatever. So industry winds up wanting to pull its hair out, because in any normal interface between a regulator and a regulated company, we want certainty and predictability, and we don't always get that out of the agency today. It's quite the contrary. When we do it's a breath of fresh air.

**BB&T: What would be the impact on the device industry if the kind of changes being discussed actually are implemented?**

DuVal: It's hard to calculate, but I can tell you this: I am one of the founders of the Minnesota Medical Device Alliance, which invited 125 CEOs and venture capitalists to a meeting here in Minneapolis a couple of months ago. The sole purpose of this group – I call it an organism, not an organization, because we're really a single-issue organism – is to provide input to the FDA, the Institute of Medicine and Congress on the 510(k) program. The reason the venture capital community and CEOs are involved is that they are extraordinarily fearful that if the FDA's data requirements continue to escalate, they continue to be unpredictable in how they operate, and they continue to cause tremendous delays and attendant expense for industry, that investment is going to go away.

I moderated a panel at which the two venture capitalists and two CEOs on the panel basically said, "We have to report to our investors as well, and the medical-device sector is not nearly as attractive as it used to be. If it continues on this current trend line, we will not be investing in medical devices – we will be investing in other industry segments. It will just not be worth it when you consider that you not only have to get through the gauntlet of FDA, but you then have to consider the prospect of not being reimbursed by CMS."

**BB&T: Plus, now you have to pay a device tax – or you will, beginning in 2013.**

DuVal: Exactly.

**BB&T: Many industry watchers and participants say the relationship between FDA and the industry has never been more strained than it is at present. They say that in addition to potentially dramatic changes in the 510(k) program, so-called "normal" operations at the agency are at a snail's pace. Has aversion to risk been taken to new levels in today's FDA?**

DuVal: Are you talking about the pace, or the quality of decisions, or both?

**BB&T: Both. First the pace, but also the inability to**

*get a decision. The agency seems to show a remarkable affinity for not wanting to touch anything unless the answer is obvious.*

DuVal: About the pace, our group has looked at some data from MassMEDIC, the Massachusetts medical device organization, which has put out some interesting statistics that say that as the FDA has gotten more money and more people and they have cleared fewer devices with fewer 510(k) applications to review. It's somewhat analogous to the situation we find in education: the more you spend per pupil, usually the results go down, not up. So we're concerned that we're spending more, but not seeing the results.

We are supporters of the agency; we want the FDA to do well. We want to see it well-staffed, well-funded, etc. But here's the dynamic that I think is in play. As they hire more people, these people are increasingly better educated and they have discrete areas of expertise – I call them silos of expertise. And each member of a review team drills down into his or her area of expertise and regurgitates all the conceivable questions that they can come up with. If you multiply that by all the members of a review team, you get a lot of questions. And some of them really are not very important; others are not relevant, while others are quite important and they should be the main focus of the inquiry, of the exchange with the company. But the bottom line is the review. The indians are running the chiefs nowadays – the review staff comes up with all these questions, and there is nobody at the managerial level of FDA who feels they can overturn a staff decision, because of all the whistleblower activity that has gone on. A manager feels unable to say, "No, that's a great question but I think it's irrelevant" or to say "No, I think we have factored your scientific views into our decision and I'm going to clear this product despite there being some remaining concerns."

*BB&T: One of the things the FDA seems to be just sweeping under the rug is third-party review. It seems like they're taking the fact that there hasn't been a real rush to third-party review and now seems to be leaning in the direction of pulling the plug on that program.*

DuVal: When you compare ourselves to the European model, which is entirely third party, it is unfortunate that the FDA's mindset is one of thinking about getting rid of third-party review at a time when I think they should be expanding it. But again, FDA is getting increasingly academic in its approach. If the third-party reviewers out there in the hinterlands are viewed as being scientifically on par with those inside FDA, when the review gets in-house at the agency, the third-party reviewer is getting so beat up that the FDA ends up delaying the submission with questions. They just seem to have an inability to let

go, and to me it equates to an inability to accept even a modicum of risk in exchange for the reward or the benefit we get by getting good devices to the market sooner rather than later. But they want so much data today – an inordinate amount of data in some cases – that we're really killing the goose that laid the golden egg.

*BB&T: That's a good lead-in to the next question. It is not uncommon for firms to have had products approved in Europe for years, with perhaps thousands of patient uses of those products, but to not even be able to get FDA approval to start a U.S. trial. Is the U.S.'s role as the leader in bringing new medical technology to the marketplace in danger of being permanently eclipsed?*

DuVal: Yes, absolutely. I have heard that over and over from the venture community. I took a client on appeal to the FDA last week in a PMA application. Their device has been on the market in Europe for eight years, over 3,000 uses for the main device and another 7,000 for a very similar device with an almost identical technology. So you have about 10,000 uses in Europe, and we have a "non-approvable" letter here in the U.S. I have other clients in the *in vitro* diagnostics segment, for example, and the FDA in some therapeutic segments is three and four generations of diagnostics behind Europe and the rest of the world. It's sad to think about that, That U.S. citizens don't have the benefit of diagnostics that are on the market years before they are available in the U.S. because of onerous FDA requirements. Personnel at the Office of In Vitro Diagnostics (OIVD) are very conservative and sometimes operate outside the scope of the statute. I have told OIVD management that they are really practicing medicine – they are looking for clinical or operational truth and are substituting their judgment instead of allowing a device that meets its labeled claim and allowing it to come to the marketplace so physicians can determine its utility. The device will either succeed because the physicians will find a place for it, or it will fail because they don't believe in it and won't accept it; it won't have commercial uptake. Let the medical community decide the utility of these diagnostics on the market. FDA is trying to establish clinical utility, clinical benefit. That's a really pivotal point that we need to discuss as a society: What is FDA's role? ❖

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# Advanced laparoscopic surgery: A blended mix of new technologies

By DIANA TUCKER

*BB&T* contributing writer

WASHINGTON – Like other healthcare issues in Washington, over the past few years there has been a heated debate on whether surgery would go the direction of NOTES (natural orifice trans-endoluminal surgery) or single port surgery; and at this year's annual meeting of the **Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)** (Los Angeles) both sides (unlike the Republicans and Democrats) have come to the conclusion that it will be both. To keep the information gained from this 2nd largest surgical association in perspective, it is important to note that only about 30% of all surgeries in the U.S. are performed laparoscopically; albeit the attendees here perform the majority of their surgeries using laparoscopy, of which about 5%-10% are single port.

**BB&T at  
SAGES  
2010**

High on the list of enthusiasm at the exhibits, were new products that support all of the advanced procedures: NOTES, single port, robotics, microlaparoscopy, and a myriad of other innovative approaches designed to treat in a more minimally invasive way the variety of procedures that fall under the heading of general surgery.

Since single port surgery instruments are available and used today, they took the headline spot at most of the exhibits. Although NOTES maintains a strong following, it remains in the background of most exhibit booths since there are yet any FDA-cleared, NOTES-specific products that can produce revenues.

The stand out in the crowd of single port exhibitors was **Covidien** (Norwalk, Connecticut) whose SILS (single incision laparoscopic surgery) platform includes the

**Table 1**  
**Comparison Between Procedures**

Transluminal	Endoluminal
Focused on replacing surgery	Focused on a standard laparoscopic procedure
Makes a hole in an organ	Less of a paradigm shift
Appropriate procedures: organ retrieval, staging	Appropriate procedures: esophagus, stomach colon
Revolutionary	Evolutionary

broadest offering (see **Table 5**). One of the 14 new products launched at this meeting was their SILS Stitch, the only automatic endoscopic suturing device with articulating features and rotating tip that should save valuable time in the OR. Covidien's endomechanical & energy products contribute about 35% of sales and even more in operating profit. To expand even further in these areas, they added more "SILS" single port instruments (shears, dissectors, clinch, suturing device), a new stapling technology (Tristaple), and a new Ligasure line.

**Ethicon Endo-Surgery (EES; Cincinnati)**, a **Johnson & Johnson** (New Brunswick, New Jersey) company, had 7 new products, which will be officially available within the next few months. EES developed a novel percutaneous instrument platform that utilizes a full sized instrument head on a 3 mm shaft that can be introduced percutaneously thus offering "the best of both worlds: performance and cosmesis." These new products represent the company's commitment to transforming patient care by enabling innovation through collaboration across the continuum of surgical techniques—from advanced minimally-invasive to open procedures. This blending of product mixes to meet the needs of specific surgeons and procedures appeared to be the theme throughout the meeting.

"To achieve the best possible patient outcomes, surgeons need technology solutions that are as diverse as the procedures they perform and the techniques they use," said Kevin Lobo, worldwide president, Ethicon Endo-Surgery.

Although an early strong proponent in NOTES research and product development, EES has now opted to present a blended approach to serving the NOTES, single port, microlaparoscopy and robotic markets. Brian Dunkin, MD, of the **Methodist Institute of Technology Innovation and Education** (Houston) presented a pre-clinical study that used a percutaneous retraction device and a magnetic anchoring and guidance system (MAGS) that consists of an internal surgical device coupled across the ab-

**Table 2**  
**Human NOTES Procedures Performed in U.S.**  
**(Top 4 institutions according to number of procedures)**

Institution	Number of Procedures in Humans
Ohio State	80
University of California San Diego	41
Legacy Health	13
Northwestern University	10

Source: Eric Hungness, MD, Northwestern University (Chicago, IL)

**Table 3****Potential for cost savings with single port surgery**

- Elimination of extra person in OR (platform or anchor system)
- Reduce number of ports required (trocar, port, closure devices)
- Decrease OR time (eventually) due to fewer closures
- Reduce infections
- Lower amount of analgesics required post-op
- Trend toward reusables to lower cost

dominal wall and manipulated using an external hand-held magnet. MAGS is being co-developed by EES with the **University of Texas Southwestern Medical Center** (Dallas) for application in all types of next generation surgery including NOTES, single and reduced port. In his presentation, Dunkin demonstrated how the integration of the percutaneous instrument platform and MAGS may help overcome some critical limitations of single port laparoscopic surgery by improving the surgeons' dexterity. He concluded "devices that enable surgeons to perform single site surgery more like traditional laparoscopy may improve adoption of this type of surgery."

To get started in this patient-driven market, the shout-out to surgeons that have yet to start training in any of the advanced techniques was to begin by using "reduced" port operations. This can mean either reduce the number of ports that would normally be used in a procedure, or reduce the size of each port, or both. Interestingly, when the size of the port is reduced from 5-10 mm down to 2-3 mm, it is referred to as microlaparoscopy, whereas 20 years ago when 2 mm ports were first introduced, it was called needleoscopic surgery. Call it what you want, the reduction in size not only means a virtually scarless outcome, but also the potential to eliminate a port for each needleoscopic instrument used, resulting in cost savings. Original needleoscopic instruments fell out of favor largely due to their lack of rigidity that led to inefficiencies in surgery. The newer micro instruments that employ advanced technology materials are strong enough to get the job done sufficiently. **Stryker Endoscopy's** (San Jose, California) microlaparoscopy instruments have a trocar like tip, eliminating the time and cost of making a small incision using a trocar prior to insertion. In addition to Stryker, **Karl Storz** (El Segundo, California), also has microendoscopy, or minilaparoscopy, instruments

available. As yet, there are no 3 mm stapling devices or energy devices and only 2 cameras at that size.

In a plenary session on NOTES, Jeffrey Marks, MD Associate Professor Case Medical Center, Director of Surgical Endoscopy, **University Hospital** (Cleveland) remarked, "Has the air gone out of the balloon with NOTES? Two years ago this huge ballroom would have had people spilling out into the halls. Today, we have some empty seats." Adding to that comment, another panel member, Paul Curcillo, MD Director, Robotics and Minimally Invasive Surgery **Drexel University** (Philadelphia) said that the seemingly lower interest in NOTES was because the early market and product development was exciting. "Although we have hit milestones with NOTES, we are now entering clinical trials which are long and hard."

Marks discussed similarities and differences between endolumenal and translumenal (NOTES) procedures, while Curcillo shared his feelings that there will eventually be a blended mix between NOTES and Single Port surgery.

According to Marks, "Some of the tools that were developed for NOTES will work well with endolumenal approaches as well; no procedure is always going to be done one way or the other" While American surgeons have approached NOTES as a research-based science, Marks cited a study done in Germany with 125 patients that underwent a NOTES laparoscopic cholecystectomy. They had a 1% major complication rate and a 6% morbidity rate, which is considered unacceptable in the U.S. He noted that two probable causes for this was that they did not use a platform for anchoring and stability, nor did they use flexible instruments but rather off-the-shelf standard laparoscopic instruments. "If studies like this continue, NOTES will die," he said. "It is up to us to determine the best products and procedures that make the risk-benefit ratio acceptable."

Marks concluded by noting that surgery is in a state of evolution with many approaches available and although one might argue that NOTES might not survive in the robust way it was once believed it would, we would not have the single port approaches we have today if NOTES never existed. Or, "Was NOTES a means to an end?"

**Low Adoption Due to Lack of Training**

Embedded in many of the presentations at this

**Table 4**

*For the second year in a row, SAGES utilized the interactive Google Moderator to solicit both questions and audience responses during the plenary sessions. With about 400 surgeon respondents in the audience, below are some of the results:*

**Key Questions and Responses Posed to the Audience**

- In the next 10 years, most surgical practices will have a robotic system: 24% Yes; 74% No
- A primary, single, symptomatic, uncomplicated inguinal hernia should have a laparoscopic repair: 60% Yes; 40% No
- There is an ethical responsibility to make minimally invasive surgery available to all patients: 75% Yes; 25% No

**Table 5**  
**Companies with Single Port Products**

Company	Brand	Camera/Scope	Port	Disposable/ Reuseable	Articulating Instruments	2-3 mm
Applied Medical	GelPort	No	Yes	D	No	No
Cambridge Endo	Autonomy	No	No	D	Yes	No
Covidien	SILS	No	Yes	D	Yes	N/A
Ethicon-Endo-surgery	SSL	No	Yes	D	Yes	N/A
Intuitive Surgical	Products pending FDA Approval	Yes	N/A	N/A	N/A	N/A
Novare	Real Hand	No	No	D	Yes	No
Olympus	LESS	EndoEye	TriPort	R	Pre-bent	No
Microline/ Starion	N/A	No	No	R	Yes	No
Storz	N/A	Cameleon	Endocone	R	S-shape	Yes
Stryker	N/A	Ideal Eyes	No	R	No	Yes
Surgiquest	Airseal	No	Anchor	D	No	No

*Source: Biomedical Business & Technology and Industry Sources*

meeting was the question “why are 70% of all surgical procedures still performed as an open procedure?” Originally, when laparoscopy was a nascent entity, a key barrier for adoption was the possibility of cancer recurrence. Since then many studies have proven that there is no difference in cancer recurrence. So why, with a proven shorter length of stay, less pain, better wound management, improved cosmesis, would there still be a resistance to laparoscopy? Of the roughly 500,000 cholecystectomies performed in the U.S. annually, only 40% are done laparoscopically. Many of the more advanced surgeons attending this meeting feel that the hurdle to adoption is that the operation is much more difficult to perform, thus requiring additional training.

This is also true with the conversion from multiple port to single port surgery. And although potential cancer recurrence was often cited as the reason not to perform laparoscopic surgery, oftentimes, benign surgeries are more difficult to perform than cancer surgeries. Many feel that such a low level of adoption after 20 years is due to lack of training. In an effort to train more surgeons on advanced laparoscopic procedures, notably single port, Covidien has taken their show on the road. Literally. They have fully equipped a semi-truck with all their SILS equipment and are offering mobile training services at local Medical Centers. “Delivered Tour” features a state-of-the-art operating room-style facility housed in an 85-foot, nearly 80,000-pound tractor-trailer that will travel

around the country to bring these advanced laparoscopic surgery tools directly to surgeons and hospitals. When parked, the truck expands to a 1,200-square-foot facility with a conference room, clinical training area with advanced audio-visual tools and five operating room stations that will accommodate 10 surgeons simultaneously. The truck’s inaugural route is scheduled to commence this week beginning in Raleigh, North Carolina, traveling through parts of Florida, then to Atlanta and finally returning to Raleigh. This test route will help determine the feasibility of such an undertaking. Surgeons sign up in advance of the arrival of the mobile center and then partake in an hour of didactic training, followed by another hour of hands on lab using tissue blocks. Talk about “taking it to the road.” Now that’s a road show!

#### ***Search for cost savings in addition to cosmesis***

The initial objective of reducing the number and size of ports was to improve upon laparoscopic surgery in terms of less pain, quicker recovery, and with a more cosmetically appealing result; but recently it is also to be able to decrease cost by reducing ports, trocars, disposables, and even eliminating an extra body in the OR.

Patient demand for scarless surgery is the key driving force for adoption regardless of the approximate incremental cost of performing the same procedure using standard laparoscopic technique of about \$425 for single port and \$2000 for robotic. The Holy Grail is to be able to

decrease the total cost of care, regardless of the price of individual instruments.

But with Obama healthcare at our doorstep, should the incremental cost of developing advanced technologies with modest incremental patient benefit be better spent at finding a lower cost to perform the same tasks? To this point, at one of the plenary sessions, a speaker pointed out that in India (it was later corrected that it was in Germany) mosquito netting has been used to replace the very costly mesh that is used in hernia repair. With the change in economy and healthcare delivery, there could very well follow a movement towards cost savings rather than technology advancement if in fact the advancement is only cosmetic. To that end, it is expected that the next round of product developments and clinical trials may center on forms of cost savings. Besides trending away from costly disposables, another form of cost savings will be found in eliminating additional personnel in the OR. Several products have been designed to be anchored to a fixed platform, eliminating the need for another hand to hold the instrument or camera. Stryker offers the Wingman camera clamp, **ProSurgics** (Cupertino, California) offers FreeHand robotic camera holder, **Virtual Ports** (Richmond, Virginia) offers a self-retractor, and Dennis Fowler, MD Professor of Clinical Surgery, **Columbia University** (New York) demonstrated a new technology being developed called Insertable Robotic Effector Platform (IREP) that eliminates the need of an extra hand. It is anticipated that more products that reduce the amount of time or people in the OR will enter the market. ♦

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# Healthcare reform still a key topic at ACC meeting

By OMAR FORD  
BB&T Staff Writer

ATLANTA — In December when members of the **American College of Cardiology** (ACC, Washington) were planning for this year's healthcare reform forum, the focus was going to be geared toward implementation of a new bill that was already signed into law. Little did ACC members know that lawmakers would still not have settled on a plan.

### BB&T at the American College of Cardiology

For about an hour and thirty minutes at this year's annual ACC meeting held here in Atlanta, Congressman Paul Ryan (R-Wisconsin) hashed it out with Chris Jennings, who serves as president of Jennings Policy Strategies (JPS), a nationally-respected health policy and advocacy consulting firm in Washington, D.C.

The session turned into a full-fledged debate and for several moments during the discussion the two went back and forth sharply divided over the upcoming healthcare bill.

"[This plan] federalizes the regulation of healthcare, Ryan told the audience. "This is the creation of a new open entitlement program that will rival the cost of Medicare and Medicaid."

Ryan, who comes from a family of cardiologists as well as his uncle serving as past ACC President, added that Medicare and Medicaid already have an under filled promise of \$76 trillion.

"This is not a path to go down," he said. "We believe that the healthcare system should hook the patient back up with the doctor. We want to fix what's broken in healthcare and not break what's working in healthcare."

Ryan, who is also the House Budget Committee Ranking Republican, said that the bill in its form gives the government way too much control in the healthcare market.

"What smart 22-year-old wanting to go into the field of medicine would say that they wanted to rack up \$300,000 in student loans just so they could be a de facto employee of the federal government."

Instead Ryan is proposing a plan that would:

- Provide a refundable tax credit — \$2,300 for individuals and \$5,700 for families — to purchase coverage in any state, and keep it with them if they move or change jobs.
- Allow Medicaid recipients to take part in the same variety of options by using the tax credit to purchase

high-quality care;

- and establish and fully fund Medical Savings Accounts (MSA) for low-income beneficiaries to cover out-of-pocket costs, while continuing to allow all beneficiaries, regardless of income, to set up tax-free MSAs.

Jennings, who said that he highly disagreed with Ryan's stance and parts of his plan instead said that rhetoric and fear were the two leading causes of opposition to President Obama's healthcare plan.

"Healthcare reform is far too often fought over fear," he told the audience. "The language of socialism, rationing, one size fits all . . . "This is the language we hear all the time, as if our current system is nirvana. We need to step back and say we need to stop the rhetoric and role up our sleeves."

He said that many organizations were at the table because they see the inadequacies in healthcare. Jennings then made a volley to gain support for President Obama's healthcare bill.

"They know the current trendline is unsustainable and we need a change. The mistake is not to take the opportunity to shake the system up."

But there still remains the question if the bill under consideration – which was already passed in the House, will be signed into law. There has been some opposition from Democrats who say that parts of the bill need to be fixed and that a plan to address those sketchy parts after passage would be too difficult and complicated.

According to the Associated Press The House contains 253 Democrats, but a number of those lawmakers are certain to vote against the bill. In a recent survey 34 Democrats are judged to be a "firm no," "leaning no," or "likely no." An additional 73 Democrats are categorized as "undecided."

Ryan told the group that his best guess was that Democrats were down seven to 10 votes in order for passage, but he cautioned the audience against counting out House Speaker Nancy Pelosi (D-California) and said she could easily gain those votes.

"We can't turn this safety net into a hammock," Ryan told the audience. "But the problem is that our safety net has gaping holes in it."

As it stands a vote on healthcare could come late in the week. One thing that both sides agree with is that healthcare does need some type of reform measure.

"We do have problems in healthcare that need to be fixed," Ryan said. "Costs are going through the roof."

### ***Bare-Metal stents better than DES?***

Drug-eluting stents have been a source of controversy for years. Many question their safety or their efficacy, while others say that these popular devices are being implanted far too often. But one of the greatest questions

surrounding the device: is it safer than a bare metal stent (BMS)?

According to two research studies that were released at the ACC meeting, the answer is maybe . . . perhaps . . . but more research is needed to know for sure.

In the first study presented at the meeting Danish researchers looked at 626 patients examining the effectiveness and risks of the two types of stents implanted right after a major heart attack for a three-year-period.

The group discovered patients who received BMS systems were far more likely to have complications – such as requiring more intervention for blockages, while patients who had drug-eluting stent (DES) systems implanted were more likely to die from heart-related problems.

A little more than 6% of patients in the study who received DES treatment died, compared with the 2% who got the BMS, according to Peter Clemmensen, MD, of **Copenhagen University**, a lead researcher for the study.

"It could have been a play of chance, that we had sicker patients in the DES arm," Clemmensen said during a media press conference. "We have seen a signal here. But before doctors stop using these devices perhaps they could wait for longer term studies for a larger trial."

During the press conference Clemmensen said that an ideal number of patients would be 18,000 for this type of trial and would be a more useful number to determine if the "deaths" were a direct side effect of treatment with the DES.

But the chances of doing an 18,000 patient trial tracking mortality rates in DES usage would be difficult and extremely time consuming, according to David Holmes Jr. MD, a moderator for the press conference.

In the PASSION study, a separate trial, five-year findings from it suggest that safety and benefits of DES compared with BMS in acute heart attack show there is no statistically significant difference in either the safety or efficacy between the two groups.

The findings of this study contrast with researchers' belief that the paclitaxel-eluting stent would perform significantly better for cardiac death, recurrent heart attack, and target lesion revascularization. The results also failed to show a statistically significant difference between the two stent types in preventing very late stent thrombosis.

Research also pointed out a two-fold increase in the occurrence of definite stent thrombosis in the DES group compared with the BMS group – at 3.6 % and 1.7%, respectively – the occurrence of both definite and probable stent thrombosis, was comparable, at 3.9% and 3.4%, respectively.

The five-year data follow in line with both PASSION's one-year data and two-year data – which also found no statistically significant safety or benefit differences between the two stents – but the study shows that the five-year results are especially important to examine in light of data in

clinical registries that associate DES use with very late stent thrombosis.

"This is a difficult choice to make," said Maarten Vink, MD, of the **Onze Lieve Vrouwe Gasthuis Hospital** (Amsterdam, the Netherlands). "There is no difference between DES and BMS - but there is a chance of stent thrombosis with DES." He added that based on the results of the PASSION trial, "there was no reason to implant older generation DES in patients."

PASSION was undertaken between March 2003 and December 2004 and randomized 619 patients with acute heart attack received either treatment with a BMS or DES.

But the elephant in the room for the PASSION trial is the same as for Clemmensen's study - there were just not enough patients to take part to come to a more solid conclusion.

It's a sticking point that Vink acknowledges.

"Right now, the clinical guidelines are not conclusive concerning the use of drug-eluting stents in angioplasty for acute heart attack, as the European Society of Cardiology does not define if they should be used, while the American College of Cardiology provides an indication for them," Vink said. "Because the guidelines are not uniform, I think their use will remain an issue—one without a definite answer—until we have data from more large, randomized, long-term studies."

Another issue is the fact that the PASSION study tested older generation DES and does not account for the recent breakthroughs with the stents.

Vink was asked if he thought it would be feasible to have a study testing more current generation devices.

"The way technology is evolving you're always going to be a step behind," he told reporters during the conference.

"Already later generation devices have shown better results than the stents we've used in [PASSION]."

So what is the answer? Which is better?

At this point researchers point out that larger studies must be done.

### *Next generation DES safer than previous iterations*

While the jury is still out on drug-eluting stents being safer and more effective than bare metal stents, there is one question about the popular devices that can be conclusively answered. That is that the latest generation of DES seem to be much safer than their predecessors, according to a panel at the 59th Annual Scientific Session of the ACC.

As many crowded their way into the early morning session, which provided an update on DES, as well as key long-term data on several clinical studies regarding the devices, it seemed as if this particular part of the device's efficacy debate was at long last put to rest.

"The benefits of drug-eluting stents significantly out-

weigh a possibly small increased risk for stent thrombosis," Debabrata Mukherjee, MD, a cardiologist with the **University of Michigan Health Center** (Ann Arbor). "As compared with bare metal stents, drug eluting stents are associated with a similar long-term incidence of death or myocardial infarction but provide a clinically important decrease in the rate of restenosis among high-risk patients."

But on top of the benefits, issues still tend to remain regarding the popular treatment option.

Mukherjee specifically spoke on the mechanisms of DES failures, and with a plethora of slides and talking points, he guided the audience through some of the key reasons for potential failures in DES.

"Restenosis following a DES implantation is an infrequent phenomenon but given widespread use of DES affects a significant amount of patients," Mukherjee said. "Stent thrombosis may be seen up to three years after implantation, a complication rarely or not seen with BMS."

He added that as compared with BMS, DES are associated with a similar long-term incidence of death or myocardial infarction but provide a clinically important decrease in the rate of restenosis among high-risk patients.

But the failures, he said, don't outweigh the benefit of these devices and measures have been taken to help ensure that there is a safer experience for patients who undergo DES implantation.

Perhaps one of the biggest advancements comes from thinner struts that are now used in the devices.

Panelists pointed to applications such as **Boston Scientific's** (Natick, Massachusetts) Taxus Liberté paclitaxel-eluting coronary stent, which incorporates the thin-strut feature. The company recently took part in the DAPT Clinical Study an independently managed large scale evaluation of DES.

"Thinner cobalt strut stents allow for easier delivery and have safer outcomes," said panel member David Moliterno MD, **University of Kentucky** (Lexington) College of Medicine division of cardiology chief. "I do think the thin struts are a step forward."

Moliterno also said that the amount of stenting procedures have increased and that the price of DES have also dropped tremendously, since inception.

"I think one of the most significant advances from the old to new generation of DES is that the devices were roughly \$3,600 now they're under \$2,000," Moliterno told the audience. "Also we're seeing a number of the [DES stenting procedures] increase."

But perhaps the next biggest push in the world of DES is the new polymer-free DES which is being touted as being even more effective than models on the market now.

"The durability of antirestenotic efficacy seen with

both the Endeavor and the polymer-free dual-drug-eluting stent is encouraging and lends some support to the hypothesis that modifications in second- and next-generation drug-eluting stent systems have the capacity to impact late patient outcomes," said Robert Byrne, of the **German Heart Center** (Munich).

The spread of these new stents could perhaps even further boost the DES market, which is slightly increasing since it stumbled a few years ago.

During a Tuesday afternoon meeting with reporters, David Holmes Jr., MD, a moderator for the press conference said that he only saw the market for DES on the uptake and that new and safer drugs would only continue to push the device in popularity.

"The concern with DES is stent thrombosis, but with new agents that are available that cuts the occurrence by half," Holmes said. "I think [the market] will only continue to increase."

### *Genetic test allows for proper Warfarin dosage*

Warfarin, like other blood thinners are very tricky medications. Oftentimes it takes weeks, sometimes months to get a patient on a steady dose. A great bit of it is actually due to trial and error, which can be taxing to the patient and also lead to hospitalization.

But according to results from the Medco-Mayo Warfarin Effectiveness Study presented at the meeting, a new genetic test will alleviate the dosing issue and help to significantly reduce the number of hospitalization.

**Mayo Clinic** (Rochester, New York) along with **Medco Health Solutions**, (Franklin Lakes, New Jersey) headed up the study.

Results proved that hospital admissions were cut by one third, for either excess bleeding or unwanted blood-clotting.

The assay tests for variations in two key genes that strongly influence the patient's sensitivity to the blood thinner warfarin.

"We found that the closer to the warfarin dosage the genotyping was done, the better the outcome," Robert Epstein, CMO and president of the Medco Research Institute, said during a Tuesday morning press conference. "We found that there was a nearly 30% reduction in a six-month period for people using the genotype."

For the study, researchers recruited 896 patients who were beginning warfarin therapy. All study participants were members of a prescription benefits plan managed by Medco Health Solutions. They came from 49 of 50 states and a variety of practice settings.

Shortly after starting warfarin therapy, patients gave a blood sample or a cheek swab, which was analyzed at the Mayo Clinic. For each patient, the ordering physician received a report on the genetic expression of two genes, CYP2C9 and VKORC1, as well as clinical information on

how to interpret the findings.

According to information presented on the study at the conference, a patient might be classified as having a high sensitivity to warfarin based on genotype. In this case, the physician would be advised to reduce the warfarin dose and monitor blood tests more frequently. If a patient were found to have a low sensitivity to warfarin, the report would recommend an increase in warfarin dose. Each physician was free to decide how to respond to the report and what action to take.

Patients in the gene-testing group were also 29% less likely to be hospitalized for bleeding or thromboembolism. The study's findings were even stronger when the analysis included only hospitalizations that occurred after genotyping. In this per-protocol analysis, patients who underwent genetic testing had a 33% lower risk of all-cause hospitalization and a 43% lower risk of hospitalization for bleeding or thromboembolism.

But in order for patients to get the maximum effect and benefit from the test it must be taken at the beginning of dosing.

Questions arose if the test, which carries a \$400 price tag, was truly worth it.

"If we're able to reduce the hospitalization it would be more than \$400," Epstein said. "Warfarin's been used for 50 years in this country but we still see a 22% hospital rate in the first six months of using."

He added that if a patient is already stable on the medication, that the test probably isn't needed.

"If you're on a stable dose you don't need the genotyping test," Epstein said.

To date, there are about two million people that use warfarin therapy each year in the U.S. to prevent unwanted blood clots in certain high-risk medical conditions, such as atrial fibrillation or following surgery to replace a heart valve.

It's widely known that warfarin sensitivity varies. It can take weeks or even months of repeated blood tests and dose adjustments to determine the right dose for each patient.

Often times patients during this trial and error phase of dose adjustment patients are at an extremely high risk for either unwanted blood clotting (thromboembolism) from too little warfarin, or dangerous bleeding from too much warfarin.

### *Women survive heart attacks with invasive therapies*

When it comes down to the rate at which men and women survive heart attacks and other cardio illnesses, there is a huge discrepancy between the two groups. A recent study shed more light on this discrepancy and revealed that women are more likely to survive a heart attack if they received the same level of therapy as males.

The multicenter study findings were presented dur-

ing last week's **American College of Cardiology's** (ACC; Washington) 59th annual scientific session, and shows that women are far less likely to go to the cardiac catheterization laboratory for angiography or angioplasty and about twice as likely to die within a month of having the heart attack.

"This suggests that we could reduce mortality in female patients by using more invasive procedures [on women]," said Francois Schiele, MD, professor of cardiology and cardiology chief at the **University Hospital of Besancon** (France). "When there are no clear contraindications, women should be treated with all recommended strategies, including invasive strategies."

For the study, researchers analyzed data from a regional registry that included all patients treated for a heart attack between January 2006 and December 2007. Of the 3,510 patients in the study, 1,119 (32%) were women.

A comparison of raw data showed that women were, on average, nine years older than men, had more health problems, received fewer effective treatments for heart attack, and were nearly twice as likely to die, both during the initial hospital stay (9.7% vs. 5%) and throughout the following month (12.4% vs. 7%).

In previous studies the reason for a woman's higher risk of death after a heart attack has been unclear. According to Schiele, possible explanations include biological differences in the atherosclerotic process and clinical differences when the heart attack occurs – such as women tend to be older and have poorer overall health.

To obtain data, researchers used a statistical method known as propensity score matching that tries to reduce bias of treatment-effect estimates from observational studies, to create pairs of men and women closely matched according to baseline characteristics. According to study results this created a population of 1,298 patients composed of 649 pairs. A second population of matched pairs was created by taking into account not only baseline characteristics but also the treatments and strategies actually used for each patient. This population of 584 pairs represented 1,168 patients.

When the researchers analyzed data from the first 649 pairs, they found that despite very similar clinical characteristics, men were 57% more likely than women to undergo coronary angiography.

Among patients who had an especially serious form of heart attack known as ST-elevation myocardial infarction, men were far more likely than women to receive therapy to reopen the blocked artery, whether by clot-busting drugs (used 72% more often in men) or by angioplasty (used 24% more often in men). The death rate during the initial hospital stay was 48% lower in men than in women, and the death rate within 30 days of the heart attack was about 30% lower in men, although this last finding was of borderline statistical significance. ❖

## International Report

### Sunrise Medical completes \$120 million refinancing, spins off DeVilbiss division

#### A *BB&T* Staff Report

**Sunrise Medical** (Malasch, Germany) last month reported that it has refinanced its existing senior secured credit facilities with the issuance of a new long-term €90 million (\$120 million) senior secured term loan. In connection with the refinancing, the company also reported the official separation of **DeVilbiss Healthcare** (Somerset, Pennsylvania), its respiratory and sleep therapy division, into an independent company.

Sunrise said the refinancing follows the strongest growth year in its history, with annual growth in earnings before interest, taxes, depreciation and amortization exceeding 100%. Additionally, the company has recently launched four new products including the Q7 custom wheelchair line.

"This financing is an important and exciting step for Sunrise as we continue to execute our strategic growth plans," said Thomas Rossnagel, president/CEO of Sunrise. "The refinancing of our senior secured facilities leaves us in a strong financial position to fund growth. This reorganization also allows Sunrise to pursue acquisitions in both Europe and North America."

Rossnagel added that the refinancing allows the company's European business to become the sole borrower, leaving North America debt-free and fully funded for growth.

DeVilbiss will operate as a separate, independent company, focused on its respiratory and sleep businesses. While DeVilbiss has been operating as a separate division since 2007, the refinancing will allow the company to officially stand alone as its own entity with no debt and separate long-term financing.

Existing investors including Vestar Capital Partners and Park Avenue Equity Partners maintain controlling investment interests in both organizations, and will serve on the boards of both companies. Management will also have an ownership stake in the companies.

Sunrise develops manual wheelchairs, power wheelchairs, motorized scooters and both standard and customized seating & positioning systems.

### **McKesson to sell Asia Pacific unit to Medibank**

**McKesson** (San Francisco) reported in April that it has agreed to sell its Asia Pacific business to Medibank Private, a private health services and insurer in Australia. The acquisition is expected to close in the second calendar quarter of 2010, subject to customary conditions, including regulatory review in Australia.

McKesson Asia Pacific (MAP) is a provider of phone- and web-based healthcare services, including telephone triage, health and wellness advice, chronic disease management and mental health services in Australia and New Zealand. Medibank is an existing MAP customer and offers many complementary services to its customers, McKesson noted.

The transaction is a share purchase, the company said. Financial terms of the sale were not disclosed.

### **Saladax in Japanese distribution accord**

**Saladax Biomedical** (Bethlehem, Pennsylvania) has executed an exclusive distribution agreement with **Falco SD Holdings** (Kyoto, Japan) for the Saladax My-5-FU MYCARE test kit in the Japanese market. The My-5-FU blood test enables oncologists to determine the precise amount of 5-fluorouracil (5-FU) chemotherapy in a patient's blood, allowing them to administer an accurate dose to each patient.

Under the terms of the agreement, Falco will pursue Japanese regulatory approval for the distribution and reimbursement of the My-5-FU test, both for sale of test kits and provision of testing services through their reference laboratory. Saladax will supply their My-5-FU kits to FALCO SD for their internal use and distribution to other laboratories.

### **Biotronik wins approval of ProMRI pacing devices**

**Biotronik** (Berlin) reported winning approval of its new ProMRI pacing systems – Evia pacemaker series and Safio S pacing leads – providing European patients the first portfolio of bradycardia systems that are MRI compatible under specific conditions.

According to the company, the approval of the ProMRI series is the first time an entire pacemaker series, including two single chamber and two dual chamber devices, has been cleared for use in combination with MRI. To gain approval, the Evia pacemakers and Safio S leads were “vigorously tested” in various combinations of device and lead positions and lengths, scanning time periods, and body positions in the MRI machines, all under strict regulation of the notified body, Biotronik said.

The company noted that its ProMRI portfolio includes four different Evia pacemakers and two different lengths of the Safio S pacing leads. The system was designed and approved for use with MRI under specific conditions.

The company notes that MRI is the gold standard for soft tissue imaging and an invaluable medical diagnostic tool for many common diseases and conditions in the area of oncology, neurology and orthopedic injuries. In 2007, there were roughly 30 million MRI scans conducted in the U.S. alone and that number continues to grow, the company said. Until recently, the two million European patients with an implanted pacemaker were prohibited from receiving MRI scans, because the strong forces applied as part of the MRI scanning could negatively affect the pacemaker system or patients' safety.

With a thin lead body (6.6 F), Safio S are active fixation leads with a flexible distal end, fractal coating and steroid elution to ensure optimal electrical performance and a stable fixation, Biotronik added.

The company also offers continuous remote patient monitoring before and after MRI scanning through its Biotronik Home Monitoring system. Physicians are alerted if there are any clinically relevant changes in their Evia patients' condition or pacemaker status before or after the MRI procedure and have immediate access to all relevant data, the company noted.

### **Tryton completes enrollment in two studies**

**Tryton Medical** (Durham, North Carolina) said last month it has completed enrollment in two European registry studies, E-Tryton 150 and E-Tryton Benelux, of the company's Side Branch Stent system for the treatment of atherosclerotic lesions in the side branch at the site of a bifurcation.

Tryton says it is conducting various registries in Europe evaluating the Side Branch Stent system in real-world clinical settings. In addition to E-Tryton 150 and E-Tryton Benelux, E-Tryton Spain (TRES) continues to enroll patients. More than 1,000 patients in Europe have been treated with the system so far, the company noted.

“Early data for the Tryton Side Branch Stent system is very promising. The E-Tryton studies will help us understand the use of the Tryton Side Branch Stent system in real-world practice,” said Pieter Stella, MD, PhD, director of the Heart Catheterization Laboratories and Clinical Cardiovascular Research at the **University Medical Centre** (Utrecht, the Netherlands), who participated in E-Tryton Benelux.

Areas of bifurcation in the vascular system are a common location for plaque and are particularly challenging to treat with currently available stent systems. As a result, the side branch is often left unstented, leaving it vulnerable to higher rates of restenosis, the re-narrowing of the stented vessel following implantation. Roughly 22% of patients treated for coronary artery disease have diseased bifurcated lesions, according to Tryton.

The E-Tryton 150 study enrolled 151 patients, and E-Tryton Benelux enrolled 155. The primary endpoint

of the studies is the overall rate of major adverse cardiac events (MACE) at six months following the procedure. MACE is defined as cardiac death, myocardial infarction and target lesion revascularization (main and/or side branch). The studies will also assess the technical success of the Tryton stent, procedural success, and the rate of target lesion revascularization at six months after the procedure.

#### ***Ness in \$44M deal to develop EHS in Slovakia***

**Ness Technologies** (Bratislava, Slovakia), a provider of information technology solutions and the leader of a consortium with its partner **Lynx** (Kosice, Slovakia), said last month it had on a public tender with the Ministry of Health of the Slovak Republic to provide the first phase of an electronic healthcare services system, valued at €32.4 million (about \$44 million), excluding VAT. The term of the initial phase is 24 months.

Ness will be responsible for the development of the system software and will serve as system integrator, in work representing €17.8 million (about \$24 million) excluding VAT, of the total phase one project budget. Lynx will be responsible for security and infrastructure, representing €14.6 million (about \$20 million), excluding VAT, with its partners.

Among other things, the objectives of the phase one implementation are to establish a national health portal to ensure the central provision of public health information to patients, healthcare personnel and external organizations.

#### ***JenaValve closes 19M 'B' round for TAVI entry***

**JenaValve Technology** (Munich, Germany), a device company developing transcatheter valve implantation (TAVI) systems, said it has closed on a €19 million Series B round led by two co-lead-investors, VI Partners, Switzerland and Sunstone Capital, Denmark. Gimv NV, Belgium, joined the consortium as a co-investor.

The company says the investment should ensure financing for its transapical and transfemoral systems up until its European market entry.

Existing investors include Edmond de Rothschild Investment Partners, NeoMed Management, and founding investor Atlas Venture.

JenaValve's systems feature the JenaClip stented aortic valve designed to provide accurate placement and the ability to retract and reposition the device if needed for enhanced patient safety.

#### ***German companies acquire 50% of VistaMed***

The **Freudenberg Group** and its affiliate **Helix Medical Europe** (both Kaiserslautern, Germany) have acquired a 50% share of **VistaMed** (Carrick-on-Shannon; Ireland), a manufacturer of components for medical devices. The

two companies say they expect the cooperation to provide synergies in the development of products and services as well as market penetration.

VistaMed has two production facilities in Ireland, where complex medical tubing systems and precision components for medical devices are produced under cleanroom conditions. Examples of applications include catheters for minimally invasive surgical procedures and endoscopic components.

#### ***biospace med reports raising \$18M***

**biospace med** (Paris) reported in April that it has raised \$18 million to accelerate market expansion in North America and Europe of its EOS ultra-low-dose 2-D/3-D imaging system.

The round included existing investors Edmond de Rothschild Investment Partners (Paris), Crédit Agricole Private Equity (Paris), UFG Private Equity (Paris), NBSI Ventures (London), COFA Invest (Paris); and new investor CDC Entreprises, acting on behalf of the SIF (Strategic Investment Fund).

EOS is a medical imaging technique that allows full-body 2-D and 3-D imaging of patients using radiation doses up to 89% lower than those required for a standard CR (computed radiography) X-ray. EOS is designed to reduce irradiation linked to radiological investigations, which has risen by 600% over the past 20 years, the company noted.

#### ***Torax wins CE mark for anti-reflux device***

**Torax Medical** (St. Paul, Minnesota) reported in April that it has received a CE mark for its Linx anti-reflux treatment. The company has started commercial launch of the Linx device at select centers in Europe.

According to Torax, the Linx device is a ring of interlinked, miniature titanium beads with magnetic cores. The device is placed around the esophagus just above the stomach using a standard laparoscopic procedure. The design is intended to augment the existing sphincter, preventing it from opening to acid and other reflux. When swallowing, the beads can momentarily separate, allowing food to pass into the stomach; magnetic attraction between beads helps the device to close. Patients are expected to resume normal activities and a normal diet upon discharge.

#### ***Oraya awarded CE mark for IRay system***

**Oraya Therapeutics** (Newark, California) said it has received the CE mark for its IRay stereotactic radiotherapy system. Under development since 2007, the IRay is designed specifically to treat diseases of the eye, and the technology enables precise delivery of low energy X-rays for the treatment of wet age-related macular degeneration (AMD), according to Oraya.

Clinical trials for the IRay are now underway in Europe, in the first-ever masked and sham-controlled study intended to demonstrate the efficacy and safety of radiation therapy for the treatment of AMD, the company noted. The one time radiation treatment is given in conjunction with the current standard of care anti-VEGF drug regimen, and with the expectation that visual acuity outcomes for the treated patients will be maintained with significantly less frequent drug injections as compared to the sham controlled group. Oraya said 150 patients from up to 10 sites will participate in the trial with roughly a third of those subjects receiving a sham exposure and the remainder receiving a radiation dose of either 16 or 24 Gray.

#### **KCI reports first Japanese placement of V.A.C.**

**Kinetic Concepts** (KCI; San Antonio) reported the first patient placement of its V.A.C. ATS therapy system in Japan. KCI said the event represented the commercial launch of the therapy in Japan and the beginning of a comprehensive market development strategy in the country.

Kyorin Hospital became the first institution in Japan to use V.A.C. therapy on a patient, who had a pressure ulcer. Typical patients eligible for V.A.C. therapy in Japan include those with dehisced and hard-to-heal open wounds, and wounds following trauma, surgery, amputation and debridement.

#### **Naviscan's PEM available in Columbia**

**Naviscan** (San Diego) said it has received approval from the Colombian Ministry of Health for the commercial introduction of its positron emission mammography (PEM) scanner into Colombia. Naviscan says it makes the only commercially available PEM imaging scanner and PEM-guided biopsy system. The scanner uses PET technology to produce tomographic images that allow physicians to visualize breast tumors down to 2 mm, the width of a grain of rice. The scanner is the size of a mammography unit and uses gentle breast immobilization, allowing for greater patient comfort, as well as reducing motion artifact and improving image resolution, the company said.

#### **USGI gets CE mark for IOP instruments**

**USGI Medical** (USGI; San Clemente, California) reported that European regulatory authorities have granted the CE mark to the instruments that make up its incisionless operating platform (IOP).

The IOP consists of the Transport multi-lumen access platform, the g-Lix Helical endoscopic tissue grasper, the g-Prox grasping/tissue approximation device, and the g-Cath tissue anchor delivery catheters with expandable tissue anchors. Each instrument received individual CE mark certification.

According to USGI, it has developed the first durable

suturing system for use in incisionless surgery. The instruments that make up the IOP have previously received 510(k) clearance and have been used in "hundreds" of incisionless procedures in the U.S., according to the company.

#### **Irvine Scientific kits get CE mark**

**Irvine Scientific** (Santa Ana, California), a developer of in assisted reproductive technology (ART), reported that it received the CE mark for its Vit Kit-Freeze, Vit Kit-Thaw and Oil for Embryo Culture. The regulatory milestone came on the heels of CE mark approval for a number of other media for ART from Irvine Scientific, the company noted.

In December the company received the CE mark for its complete range of culture media and andrology products.

#### **Exactech to start Japanese distribution**

**Exactech** (Gainesville, Florida) said it has received approval to market its Novation primary hip replacement system in Japan.

Japan's Ministry of Health, Labour and Welfare granted Exactech the approval to market elements of the Novation comprehensive hip system, including the tapered femoral hip stem, femoral heads and bi-polar implants. The hip system is designed to provide stability and excellent range of motion for the patient and ease-of-use for the surgeon. The company said it also is pursuing approval for additional components within the product line, to support femoral and acetabular reconstruction. ❖



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## Acquisitions & Agreements

- **CancerGuide Diagnostics** (Durham, North Carolina) has entered into a research collaboration and licensing agreement with **Duke University** (also Durham) to discover and develop tests to support individualized cancer treatment decisions. This relationship provides CancerGuide with exclusive commercial rights to a portfolio of molecular signatures that predict response for targeted therapeutics as well as collaborative access to clinical research and new molecular discoveries from Duke. CancerGuide will use these technologies with its pharmaceutical clients to improve the efficiency of the drug development process and to develop and commercialize novel clinical diagnostics through its existing agreement with **Laboratory Corporation of America Holdings** (LabCorp; Burlington, North Carolina).

- **CareFusion** (San Diego), a 2009 spinoff of **Cardinal Health** (Dublin, Ohio), has agreed to acquire **Medegen** (Ontario, California), a developer of needleless access valves and administration sets that deliver intravenous (IV) medication to patients, for \$225 million in cash.

- **ev3** (Plymouth, Minnesota) has initiated a supply agreement with **Medrad Interventional/Possis** (Warrendale, Pennsylvania). Under terms of the agreement, Medrad will make available its Cotavance peripheral drug-eluting balloon angioplasty catheter with Paccocath technology for study in combination with ev3's SilverHawk and TurboHawk Plaque Excision Systems for use in the DEFINITIVE AR European pilot study for treating lower extremity peripheral arterial disease (PAD). The DEFINITIVE AR (Anti-Restenosis) study is a prospective, multicenter, randomized pilot study evaluating the use of either the TurboHawk or SilverHawk Plaque Excision System followed by treatment with the Cotavance drug-eluting balloon catheter vs. the Cotavance balloon catheter alone in patients with peripheral arterial disease.

- **Given Imaging** (Yoqneam, Israel) said it has completed its acquisition of privately-held **Sierra Scientific Instruments** (Los Angeles, California) for \$35 million in cash. As a result, Sierra Scientific is now a subsidiary of Given Imaging. The company acquired Sierra Scientific from Water Street Healthcare Partners, a private equity firm focused on healthcare. According to Given Imaging, Sierra Scientific is recognized for its ManoScan family of products. Additionally, Sierra offers a line of reflux monitoring solutions (AccuTrac and DigiTrapper), as well as its Polygraf ID stationary gastrointestinal function testing platform.

- **Haemonetics** (Braintree, Massachusetts) reported that it plans to complete its tender offer to acquire **Global Med Technologies** (Denver). At the closure of the tender period 34.4 million shares of common stock

representing 90% of the outstanding common stock and 100% of the outstanding preferred shares were tendered. Haemonetics funded the \$58 million required for the acquisition of the shares and outstanding warrants from available cash. Haemonetics anticipates completing the merger with Global Med in 1Q11 with a final cash payment of \$3 million.

- **Iridex** (Mountain View, California) said it has acquired substantially all of the assets from **RetinaLabs** (Atlanta), a company that makes retinal instrumentation used by ophthalmologists to perform vitreoretinal procedures in the operating room and the surgery center. The assets Iridex acquired includes RetinaLabs' existing product family together with certain additional intellectual property that Iridex anticipates incorporating into future products, the company said. The purchase price consisted of \$250,000 in cash and 115,000 unregistered shares of Iridex common stock issued at closing, and an earn-out tied to future revenues that could result in additional cash and share payment to RetinaLabs based on the future performance of the acquired products. Other terms of the transaction were not disclosed.

- **NeuroTherm** (Wilmington, Massachusetts) said it has acquired the **Smith & Nephew** (S&N; London) Interventional Spine Pain Management assets from S&N's subsidiaries. The acquired product line includes several interventional spine pain products including the CDS Discography System, Spinecath & Acutherm catheters and a full radio frequency product line, the company noted. NeuroTherm said it will also be the distributor of the Trucath Injection System within the interventional spine pain market.

- **Trintech Group** (Addison, Texas) said it has completed the sale of its healthcare division, **Concuity** (Vernon Hills, Illinois), to **The Advisory Board Company** (Washington) for \$34.5 million in cash. The purchase price is subject to a working capital adjustment, and an escrow amount of \$6 million has been set aside with \$2 million to be released after 9 months and the remainder no later than Dec. 31, 2011, subject to the satisfaction of post-closing conditions.

- **U.S. Renal Care** (USRC; Plano, Texas) a privately-held provider of outpatient dialysis services, and **Dialysis Corporation of America** (DCA; Lithicum, Maryland), a provider of outpatient kidney dialysis centers, said that they have entered into a definitive merger agreement for USRC to acquire DCA for \$112 million. Upon the closing of the transaction, USRC will provide dialysis services to a base of nearly 5,500 patients through 84 outpatient dialysis facilities across nine states, more than 12 home dialysis programs, and 24 dialysis programs within acute and specialty hospital facilities.

## Market Developments

# CMS to cover NaF-18 PET for metastatic bone cancer under CED

By MARK McCARTY  
BB&T Washington Editor  
and Staff Reports

In a development that hardly catches medical societies and imaging providers flat-footed, the Centers for Medicare & Medicaid Services decided to use the coverage with evidence (CED) development rubric to reimburse for the use of a radioisotope of sodium fluoride for metastatic bone cancer. While a number of factors may have converged to prompt CMS to move in this direction, one of the prime drivers may have been the ongoing shortage of technetium-99 (Tc-99).

CMS said that CED coverage will be used to pay for the use of NaF-18 with PET scanning for both initial staging of the cancer and for ongoing staging after completion of initial treatments. The agency had tackled this topic last year and issued a proposed decision memo dated Nov. 30, 2009, stating at the time that the rate of false positives was an issue. CMS acknowledged the ongoing shortage of Tc-99 in the proposed decision memo, although the Tc-99 predicament was not specifically cited as a reason for the NaF-18 coverage analysis.

Robert Atcher, MD, past president of the **Society for Nuclear Medicine** (SNM; Reston, Virginia), is on record as saying that SNM had approached CMS on the issue, and that reimbursement for this application in the U.S. has lagged behind payment policy in Europe. Atcher also stated that SNM is interested in helping to bankroll a registry for NaF-18 when used with PET scanners.

### Quick turn-around on FDA warnings in place

The Dec. 3, 2009, warning letter to **Z-Medica** (Wallingford, Connecticut), maker of hemostatic devices, including the QuikClot combat gauze, was another instance in which FDA quickly hammered out a warning letter in what would have been record time in years gone by. The inspection ended Nov. 3, but a Nov. 20 response from the company to the inspectional findings was not enough to stave off the warning letter, which FDA issued exactly one month after the inspection ended.

The 30-day turn-around on this warning beats by five

days the elapsed time between the agency's inspection of **Guidewire Technologies** (Salem, New Hampshire), which was the recipient of a Feb. 26 warning letter addressing findings during an inspection that was completed by Jan. 22. The foreshortened time between inspections and warning letters suggests that the agency's emphasis on safety, especially as relates to sterility, is one of the prime drivers of the agency's regulatory activity. Sterility was an issue in the Guidewire warning letter as well, and was cited by FDA in its action against **Steris** (Mentor, Ohio), which had to recall all of its SS1 sterilizers over changes made to the system since its inception, even those units that bore the original cleared configuration.

In the case of Z-Medica, the agency managed to rapidly turn around a re-inspection as well. Denny Lo, senior VP of Z-Medica, told *BB&T* that FDA sent an investigator back out to review the proposed corrections between Jan. 27 and Feb. 2, the results of which earned the company a close-out letter.

### Boston Sci halts shipments, recalls inventory

In what may be one of the biggest medical device recalls ever, **Boston Scientific** (Natick, Massachusetts) reported in March that it had stopped shipment and is retrieving field inventory of all its implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds). The move caused a spike in trading and the company's stock dove 16.45% on the day of the announcement. Wall Street's reaction was brutal: the company was promptly labeled the Toyota of the medical industry in a Wall Street Journal blog.

"FDA didn't ask for a recall. But FDA will review the root cause for the ICDs recall as part of recall classification process," Dick Thompson, an FDA spokesman, told *BB&T*. "We were notified just last night."

Thompson said the reason for the recall will be reviewed as part of a 30-day notice submission. In the mean time, apparently there are no reports of adverse events for any patients who have received the devices. And there was no indication that the manufacturing process changes would prompt explanation of the devices already in patients.

"Preliminary information indicates that there are no product failures or adverse events related to this issue," Thompson said. The company pledged to work closely with FDA to resolve the situation quickly.

Device firms are required to report any manufacturing changes affecting the safety or effectiveness of a device. The news comes just over two weeks after Boston

Scientific negotiated a plea deal on behalf of Guidant, a subsidiary plagued with product liability problems when it was acquired for \$27.2 billion in 2006. Guidant was criminally charged with concealing information from the FDA regarding catastrophic failures in some of its

ICDs, including charges of submission of false and misleading reports to FDA and failure and refusal to report medical device corrections.

Boston Scientific said in a statement that it had identified two instances of changes to production that, while successfully validated, were not submitted to the FDA. The devices in question, which treat heart failure and manage heart rhythm, made up about 15% of the company's total sales of \$8.19 billion in 2009.

"A planned process review revealed that two manufacturing process changes were not submitted for FDA approval," Ray Elliott, President/CEO of Boston Scientific, said in a prepared statement. "We are acting voluntarily and expeditiously to resolve this situation, and we have seen no evidence of any risk to patient safety. We apologize for the inconvenience these actions will cause patients and physicians."

### ***Boston Sci wins at panel on indication for CRT-Ds***

**Boston Scientific** (Natick, Massachusetts) managed to rebound after its recall of cardiac electrophysiology equipment in a meeting of the circulatory systems advisory committee in March, but the development bodes well for all firms in the business of making CRT-D units. The company successfully sought the panel's approval of its attempt to expand the indication for CRT-Ds beyond those in class III or IV heart failure, and the firm's success suggests it will have a larger market for its hardware than any competitor. The only question is how long the company will have the expanded pool of patients to itself.

The current indications for CRT-D (at press time, FDA had yet to formally announce it will go along with the panel's recommendation) are for patients with left ventricular ejection fraction of 35% or less and a QRS interval equaling or exceeding 120 milliseconds (ms) who have been diagnosed with New York Heart Association class III or IV heart failure. The panel's recommendation was based on data from the well-known Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT), which enrolled more than 1,800 patients to establish whether CRT-D would reduce the risk of mortality and heart failure events by 25% in NYHA class I and II heart failure patients who exhibit a left ventricular ejection fractions of 30% or less and a QRS interval persisting for at least 130 ms.

Arthur Moss, MD, the principal investigator in MADIT-CRT, said double blinding was deemed "impractical if not impossible" because patients with implanted electrophysiology devices have to present a card to providers regarding the device. However, he said, "there was total and complete blinding" of the committee charged with adjudicating adverse events.

The patients in the control arm, who received only ICD units, numbered 731 and the remaining 1,089 were

randomized to CRT-D. Moss noted that the data indicated a 34% reduction in heart failure events at 48 months, well in excess of the 25% target, as well as a superior outcome for the combined endpoint of all-cause mortality and heart failure events. However, all-cause mortality was by itself statistically indistinguishable between the two groups at roughly 7%.

MADIT-CRT produced a rate of freedom from system-related complications (SRCs) at three months of 85%, substantially better than the target of 70%. Dislodgement of the lead attached to the left ventricle in the CRT-D unit was the source of a number of the SRCs in this arm, accounting for 51 events (in 46 patients) of the 214 reported. This 4.3% rate of problems with the ventricular lead is apparently seen as falling well within the historical range.

Presenting on behalf of FDA, Kimberly Selzman, MD, of the Office of Device Evaluation and the chief of cardiology at the **Salt Lake City Veterans Administration Hospital** (Salt Lake City, Utah) informed the panel that beta blockers were used by 90% of the enrollees in MADIT-CRT, but that 30% or less of the patients in each arm were at the appropriate dose of 150 milligrams a day of carvedilol (Coreg). She also cited "a fairly small representation of [NYHA] class I subjects," which she said "may have affected the combined results," including mortality.

All-cause mortality was about 7% in both groups, and Selzman said no treatment effect was observed in class I patients, perhaps "due to a small sample size." A total of 13 patients in class I NYHA heart failure made it to 48 months, suggesting "a need for more data" for this population.

Selzman pointed out that the presence of blockage of the left bundle branch – the cluster of nerves based in the left ventricle that delivers the electrical pulse responsible for ventricular contraction – was associated with an improvement in the study arm, but that the effect did not seem to hold for the patients in class I heart failure. She also acknowledged the greater benefit of CRT-D seen in women, but shrugged, "the cause of this is not readily apparent." Women were twice as likely to be non-ischemic as men and substantially more likely to suffer from blockage of the left bundle branch, but the source of the greater benefit in women was not discernible. "There were no differences in complications" between the two sexes, Selzman reported. She also remarked, "the benefit to CRT-D patients without left bundle branch blockage is not clear."

Panelist Bill Maisel, MD, an electrophysiologist at **Beth Israel Deaconess Hospital** (Boston), said he did not agree with the observation that no benefit was seen in class I NYHA patients because while enrollment in the study arm was greater than in the control arm and outcomes numerically similar, the hazard ratio for class I patients seemed to favor CRT-D. Maisel also posed the possibility that the trial would have had to enroll "about

three or four times the number" it did enroll in order to determine how many patients would have to have received a CRT-D unit to ward off a heart failure event in one patient.

Regarding the appropriate real-world population for CRT-D, Maisel said he could think of "several reasons I think it would be wrong to carve out class I patients from this trial," reminding panelists that a third of the class I patients in the trial had experienced more severe heart failure within a year of enrollment. Leaving class I patients with ejection fractions of 30% or thereabouts with no option but an ICD would force some of them back into the hospital for a CRT-D within 12 months or so, he said. Another panelist was heard to observe that he saw "a pretty fine line between class I and II" heart failure, a sentiment that drew support from several others. Panel chairman Hirshfeld summarized that the comments were "focused on the fact that patients with ejection fractions of less than 30% are by definition a sick population, and attempts to carve out a subset . . . are relatively weak."

As for the effects associated with left bundle branch block and QRS intervals, the remarks ranged from support for limiting use of the device in class I patients to those with blockage of the left bundle branch on one hand, to avoiding an overly prescriptive label that might tie an electrophysiologist's hands on the other. The panel concluded that the data on these issues might appear in the label, but the panel seemed disinclined to recommend any limitation on indications during discussions.

All the same, the voting procedure resulted in a recommendation that the use of CRT-D be limited in class I patients to those with left bundle branch blockage and sinus rhythm, and whose QRS intervals are 130 millisecond or longer. This proposal passed unanimously with the exception of one abstention. The panel then unanimously recommended that the post-approval study include a comparator group, and the final vote for approvability was likewise unanimous.

### **AGA Medical gets IDE for cardiac plug**

The abnormal heart rhythm known as atrial fibrillation (AF) carries a high risk of stroke, which is why many patients are put on a lifelong regimen of warfarin (Coumadin). But the side effects of this blood-thinning drug, mainly bleeding, can be dangerous. **AGA Medical Holdings** (Minneapolis) has for some time been working on a new technology, the Amplatzer Cardiac Plug (ACP), that would fix the underlying problem and eliminate the need for warfarin.

AGA won an investigational device exemption (IDE) in April for the ACP, which is intended to prevent thrombus embolization from the left atrial appendage (LAA) in patients who have nonvalvular atrial fibrillation. The ACP is designed to close the left atrial appendage.

"The reason you potentially want the left atrial appendage closed is, if you're a patient with atrial fibrillation, the left atrial appendage remodels and gets thicker. There are lots of nooks and crannies - hiding places where clots have been shown to form. Those clots are associated with 90% of strokes. If you close it off and seal it, then you no longer have a place for clots to form and hide," Rachel Ellingson, senior director of AGA's business development, told *BB&T*.

The IDE trial is designed to demonstrate efficacy and device safety and will randomize patients in a 2:1 ratio of patients on the device to controls, who will receive warfarin only, the current standard of care.

"Warfarin is a tough drug to tolerate," Ellingson said. "Many patients just can't tolerate it and it has a very narrow therapeutic window. If you take too much, you risk bleeding. If you take too little, there's not enough benefit."

President/CEO John Barr said, "Stroke can be a debilitating condition, and is a significant concern to the approximately 4.5 million people in the U.S. and Europe suffering from atrial fibrillation. Approval of this study will allow us to further evaluate our approach to reducing strokes in patients with atrial fibrillation by using our ACP to permanently seal the appendage, hopefully sparing patients from spending the rest of their lives on anticoagulants."

Ellingson said the company expects to enroll the first 400 patients sometime during the second half of 2010. Interim analyses will be performed after the first 400 patients are enrolled and at predetermined periodic intervals thereafter, until a possible maximum of 2,000 patients are enrolled. These analyses will determine when the trial has achieved its endpoints and whether AGA is able to conclude the trial prior to enrolling all 2,000 patients. The only other cardiac plug in development in the U.S. is the experimental Watchman, developed by **Atritech** (Plymouth, Minnesota). An FDA panel narrowly backed the device last spring, but the agency has since asked for a confirmatory trial to substantiate effectiveness.

AGA is accustomed to being a pioneer. In fact, last year, the company competed an initial public offering, raising \$199.4 million, one of the few to succeed in the dismal market. "We were the only medical device company to do an IPO last year," Ellingson said. "I think we truly view it as a significant testament to our company to go public when no other company could."

The ACP received European CE mark approval in December 2008, and is currently sold in Europe, South America and parts of the Pacific Rim.

### **Medical device tax costly for some companies**

A medical device excise tax that aims to raise \$20 billion throughout a 10-year-period is causing deep concerns and frustration for some parts of the med-tech in-

dustry. The tax is part of the newly adopted healthcare law, which is set to bring sweeping reform throughout the country. Members of industry argue that the tax could cause an undue financial burden for medical device companies—especially those smaller companies who have revenue in the \$60 million range.

“The tax is an absolute disaster,” Albert “Ace” Edwards, president of the **Southeastern Medical Device Association** (SEMDA; Norcross, Georgia), told *BB&T*. “You’ve got to explain the logic of taking money from a healthy industry not receiving any funding from the government and giving it to an industry [dependent upon federal funding]. I don’t see the logic in that.”

Members of SEMDA include a number of smaller companies who can’t weather the tax storm as easily as say **Medtronic** (Minneapolis) could. “Some of our companies are at \$50 million in revenue, but they aren’t to the point where they turn a profit yet,” Edwards said. He added that this tax has the potential to harm innovation; by taking away additional dollars that these companies would have to initiate clinical work or navigate through the PMA and 510(k) approval process.

In an unattributed statement, the **Medical Device Manufacturers Association** (MDMA; Washington) echoed similar statements and said it is “very concerned about the impact a \$20 billion device tax will have on patient care, innovation and small businesses,” making the case that under the tax, “many companies will owe more in taxes than they generate in profits.” MDMA says that such a scenario will force firms to lay off employees and cut budgets for research and development.

The statement also notes that absent an elimination of the tax, “structuring it to provide relief for smaller companies is critical,” urging that Congress address the issue “before the tax takes effect in 2013.”

“Minnesota is going to bear about 25% of the [medical device excise] tax,” said Don Gerhardt, the chief executive of **LifeScience Alley** (Minnesota), a trade group that represents med-tech companies. “With it being a tax on revenue instead of profit – well that’s going to be a bit difficult. This is an enormous issue for Minnesota, with the potential to effect 300,000 jobs at minimum.” Gerhardt said he has been in conversations with companies and they have said they’re considering layoffs. Other options include halting proposed expansions all together.

Legislators that support the tax contend that other industries – from pharmaceutical companies to hospitals – have agreed to commit billions to help pay for expanding health insurance coverage to most Americans, and they argue that it’s only fair that device companies contribute their fair share. In the meantime, companies are either adopting a “wait and see attitude” to see if the tax is scaled back a bit or approaching lawmakers and asking for the tax to be scrapped. ❖

## Product Briefs

### FDA clears ECG, blood pressure combo system

By AMANDA PEDERSEN  
*BB&T* Senior Staff Writer  
And Staff Reports

Doctors who want to monitor their patient’s ECG and blood pressure for a 24-hour period now have an alternative option to asking their patient to wear two separate monitoring devices to record the data – **Vasomedical** (Westbury, New York), said it recently received FDA clearance for a device designed to do both.

The company this week reported receiving FDA 510(k) clearance to market its Vasomedical-BIOX Model 2301 Combined ECG Holter and ambulatory blood pressure monitoring recorder and software analysis system. The company received FDA clearance for its Vasomedical BIOX Model 1305 Holter monitor and analysis software this time last year.

Traditionally, devices that record ECG signals and devices that monitor blood pressure are separate systems, Jun Ma, PhD, president/CEO of Vasomedical, said.

Ma explained that under certain conditions, doctors sometimes prescribe both devices for the patients to wear for a 24-hour period.

“Our combined two-in-one device eliminates the need of carrying two devices, so it becomes compact and a lot more comfortable to wear,” Ma said. He added that a second benefit of the system is that the interaction of the two signals allows the system to measure the patient’s blood pressure signal at the same time as they experience certain cardiac abnormalities, which provides added diagnostic value, he said.

“These are the first in a line of Vasomedical-BIOX ECG Holter and ambulatory blood pressure monitoring systems that Vasomedical intends to bring to the marketplace,” Ma said. “The introduction of Model 1305 Holter Monitor last year placed Vasomedical into the patient monitoring business with a high quality digital equipment that has enjoyed international success. The Model 2301, however, will make Vasomedical a supplier of ambulatory equipment, because it is so far the only combined ambulatory ECG/blood pressure recording device in the United States. In addition to being a compact de-

vice that replaces two separate recorders, it also provides interactive blood pressure recording at times of certain cardiac abnormalities, thus significantly enhancing the diagnostic value of the recorded data while increasing patient comfort and ease of use."

Ma said the company plans to add a few more ECG devices to the product line in the future.

According to Derek Enlander, MD, a New York City internal medicine physician, the Vasomedical BIOX 2301 is the only personal combined system to simultaneously and continuously record and store ECG and blood pressure data for 24 hours. "The ability to view these parameters simultaneously, side by side is unique," Enlander said. "It gives the physician more useful information to evaluate the patient's cardiovascular status and make appropriate clinical judgment."

Enlander noted that for the past few years, Holter monitors and other ambulatory devices have increased in use, allowing early diagnosis and disease management not only by cardiologists but by general practitioners. "I believe this product will have a great impact on the improvement of healthcare quality and reduction of healthcare cost," he said.

Vasomedical primarily makes enhanced external counterpulsation (EECP) systems based on its proprietary technology. According to the company, EECP therapy is a non-invasive, outpatient therapy for the treatment of diseases of the cardiovascular system currently indicated for use in cases of angina, cardiogenic shock, acute myocardial infarction and congestive heart failure. The therapy serves to increase circulation in areas of the heart with less than adequate blood supply and may restore systemic vascular function, the company said. Vasomedical received a U.S. patent for the technology three years ago.

**BIOX Instruments** (Jiangsu, China), is a strategic partner of Vasomedical. BIOX makes electrical medical instruments. Its core products include Holter recorders, ambulatory blood pressure monitors and comprehensive analysis software.

Elsewhere in the product line:

- **AdvanDx** (Woburn, Massachusetts/Vedbaek, Denmark) said it has received 510(k) clearance for a fast, 90 minutes protocol for its *C. albicans* PNA FISH and *C. albicans/C. glabrata* PNA FISH tests. The faster protocol reduces the PNA FISH turn-around time from the original 2.5 hours to 90 minutes by reducing PNA probe hybridization from 90 minutes to 30 minutes, AdvanDx said. Clinical validation studies performed at hospitals in the U.S. demonstrated 100% agreement between the 90 minutes protocol, the original PNA FISH protocol and conventional identification methods, ensuring the faster protocol maintains the very high sensitivity and specificity required versus slower, conventional methods, the company noted. According to AdvanDx, Candidemia, a

bloodstream infection caused by *Candida* species, is one of the most serious hospital acquired infections, afflicting more than 24,000 patients in the U.S. every year. Immunocompromised transplantation, oncology and AIDS patients are especially at risk for contracting the infection with mortality rates as high as 50%, the company said.

- **BD Diagnostics** (Baltimore), a segment of **BD** (Becton, Dickinson and Company), reported the addition of the BD Innova Preanalytical Automated Microbiology Specimen Processor, which is designed to help increase laboratory efficiency and automate the modern microbiology laboratory. By acquiring the Lab Systems division of Dynacon, a privately held corporation based in Ontario, BD said it adds innovative product platforms from a leader in preanalytical microbiology automation. These product platforms include the InocuLAB and Innova platforms.

- **Chronix Biomedical** (San Jose, California) reported publication of a study that supports the use of its serum DNA blood tests to predict clinical status and monitor disease activity and response to treatment in multiple sclerosis (MS). Chronix uses proprietary technology to identify disease-specific genetic fingerprints based on the circulating DNA that is released into the bloodstream by damaged and dying cells. Chronix claims publications and other researchers shows that this circulating DNA can be identified and analyzed to provide a diagnostic window into ongoing changes in the genome associated with specific diseases – changes that can be used to track the presence or absence of active disease. This new study is the first to show that the Chronix approach can be used to monitor the clinical status of a chronic disease. The findings are published in the current online edition of the *Journal of Molecular Diagnostics*.

- **ConvaTec** (Skillman, New Jersey) reported the launch of Aquacel Ag surgical cover dressings for the post-operative care of surgical incisions. ConvaTec says its patented hydrofiber technology is combined with skin-friendly hydrocolloid technology. The Aquacel Ag surgical cover dressings are supported by evidence showing significant reduction in the incidence of superficial surgical site infection (SSI), skin blistering and delayed discharge as compared to a non-woven post-operative surgical cover dressing regimen. "The innovative design of Aquacel Ag Surgical cover dressings has been proven to handle post-operative challenges – complications that can translate to increased time, expense and concern for the patient's well-being," said Michael Steadman, president of ConvaTec Wound Therapeutics.

- **DFine** (San Jose, California) said it has launched a new access system for the RF Kyphoplasty procedure using the StabiliT Vertebral Augmentation System. DFine claims the RF Kyphoplasty procedure with the

StabiliT system provides physicians greater control in the treatment of vertebral compression fractures through site and size specific cavity creation and an ultra high viscosity bone cement over an extended working time using a remotely controlled delivery system to stabilize the fracture, relieve pain and improve patient quality of life.

- As part of its I.V. Room of the Future initiative to cooperate with other industry leaders, **Health Robotics** (Bozen, Italy) reported the availability of its Virtual High-Availability Architecture, including virtualization compliant, cluster and fail-over, disaster recovery, and back-up solutions for its CytoCare and i.v.STATION robots (with future expansion to TPNstation when available), and its i.v.SOFT Workflow Engine for manual compounding. Health Robotics' core technology can be deployed on multiple configurations, ranging from one active node and a stand-by node, to active/passive clustered nodes with a remote disaster-recovery stand-by node. Virtualization is an irreversible process already initiated by many of the top-rated medical centers around the world, and it should be much more so when it comes to life-critical I.V. Admixtures. Health Robotics said it decided to engineer this concept as an additional option for customers and therefore safeguard their investments in I.V. automation, providing full support for the implementation of our core technology on all major virtual environments.

- **IZI Medical Products** (Baltimore) has introduced two new lines of flat mammography markers, which are being made in the U.S. and sold worldwide under the brand of Mammography Indicator Markers. The new markers, available in radiolucent and radiopaque varieties, function as reference points used by mammography

technologists to accurately and reliably indicate an area of interest on the breast (e.g. masses, scar tissue, moles, etc.) in diagnostic mammograms.

- **Medtronic** (Minneapolis) reported the launch of a new Frontal Handpiece for its Hydrodebrider System, made by the company's Ear Nose and Throat division. The Hydrodebrider System is a powered endoscopic irrigation system for removing bacteria from the paranasal sinuses. It is used for the treatment of chronic sinusitis. The new frontal handpiece has a 2.2 mm diameter with fixed 80° articulation for access to the hard-to-reach frontal sinuses. Surgeons can connect the Hydrodebrider console to the Frontal Handpiece, the Standard Handpiece for maxillary, ethmoid and sphenoid sinuses, or both. Each handpiece delivers a rotating spray of pressurized saline at 5 mL/sec, enabling access for direct irrigation of sinus mucosal surfaces. *In vitro* research has demonstrated a 99% reduction in bacterial coverage in chronic sinusitis specimens treated with the Hydrodebrider System.

- **Nextrials** (San Ramon, California) said that the latest version of its Prism electronic data capture and clinical trial data management platform will now support anytime/anywhere data access via the Apple iPad slate computer. Because Prism 3.0 is fully integrated with platforms traditionally used for electronic health records within the healthcare setting, its compatibility with the iPad enables physicians, researchers and others to have real-time access to data regardless of locale, and delivers that data in the familiar graphical formats traditionally generated by Prism on a desktop computer, Nextrials said. The company notes that the iPad has the potential of meeting many specific healthcare needs,

## Companies and organizations in this issue

AdvanDx.....	22	German Heart Center.....	12	RetinaLabs.....	17
AGA Medical Holdings.....	20	Given Imaging.....	17	Saladax Biomedical.....	14
American College of Cardiology.....	9, 13	Global Med Technologies.....	17	Salt Lake City Veterans Administration Hospital.....	19
Atritech.....	20	Guidewire Technologies.....	18	Sierra Scientific Instruments.....	17
BD.....	22	Haemonetics.....	17	Smith & Nephew.....	17
BD Diagnostics.....	22	Health Robotics.....	23	Society for Nuclear Medicine.....	18
Beth Israel Deaconess Hospital.....	19	Helix Medical Europe.....	15	Society of American Gastrointestinal and Endoscopic Surgeons.....	6
biospace med.....	15	Iridex.....	17	Southeastern Medical Device Association.....	21
Biotronik.....	14	Irvine Scientific.....	16	Steris.....	18
BIOX Instruments.....	22	IZI Medical Products.....	23	Sunrise Medical.....	13
Boston Scientific.....	11, 18, 19	JenaValve Technology.....	15	Sysmex America.....	24
CancerGuide Diagnostics.....	17	Johnson & Johnson.....	6	The Advisory Board Company.....	17
Cardinal Health.....	17	Karl Storz.....	7	TomoTherapy.....	24
CareFusion.....	17	Kinetic Concepts.....	16	Torax Medical.....	15
Chronix Biomedical.....	22	Laboratory Corporation of America Holdings.....	17	Trintech Group.....	17
Columbia University.....	9	LifeScience Alley.....	21	Tryton Medical.....	14
Concuity.....	17	Lynx.....	15	Unilife.....	24
ConvaTec.....	22	Mayo Clinic.....	12	University Hospital.....	7, 13
Cook Medical.....	23	McKesson.....	14	University Medical Centre.....	14
Copenhagen University.....	10	Medco Health Solutions.....	12	University of Kentucky.....	11
Covidien.....	6	Medegen.....	17	University of Michigan Health Center.....	11
DeVilbiss Healthcare.....	13	Medical Device Manufacturers Association.....	21	University of Texas Southwestern Medical Center.....	7
DFine.....	23	Medrad Interventional/Possis.....	17	USGI Medical.....	16
Dialysis Corporation of America.....	17	Medtronic.....	21, 24	U.S. Renal Care.....	17
Drexel University.....	7	Naviscan.....	16	Vasomedical.....	21
Duke University.....	17	Ness Technologies.....	15	Virtual Ports.....	9
Ethicon Endo-Surgery.....	6	NeuroTherm.....	17	VistaMed.....	15
ev3.....	17	Nextrials.....	24	Z-Medica.....	1
Exactech.....	16	Onze Lieve Vrouwe Gasthuis Hospital.....	11		
Falco SD Holdings.....	14	Oraya Therapeutics.....	15		
Freudenberg Group.....	15	ProSurgics.....	9		

such as serving as a handheld terminal for physician-led grand rounds, the examination of X-rays at remote locations and histology reviews. In the clinical trial setting, it can give researchers instant access to adverse event data, patient recruitment status, supply availability and other critical real-time data.

- **Sysmex America** (Mundelein, Illinois) said that its Sysmex XT-4000i Automated Hematology Analyzer has received FDA clearance. The Sysmex XT-4000i provides 34 parameters, including the advanced clinical parameters, IG (Immature Granulocyte) and RET-He (Reticulocyte Hemoglobin Equivalent) and a Body Fluid specific mode. It uses Sysmex's fluorescent flow cytometry and advanced cell counting methods to deliver rapid, reliable results essential in patient diagnosis and therapeutic monitoring. The company claims that the Sysmex XT-4000i automated hematology analyzer's IG parameter provides the reliable detection and quantification of circulating immature granulocytes that may be used by physicians as an early indicator of acute infection, inflammatory response or myeloproliferative disorder. Its RET-He parameter, which quantifies the hemoglobin content of reticulocytes, is an established parameter in the National Kidney Foundation's KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines for assessing the initial iron status of patients with chronic kidney disease on hemodialysis as well as I.V. iron replacement in these patients.

- **TomoTherapy** (Madison, Wisconsin) cited results of a study that showed the benefits of TomoTherapy

technology in a variety of cases requiring craniospinal irradiation (CSI) in children and young adults. The study concluded that the TomoTherapy platform offers a major dosimetric advantage in treating both standard and complicated cases by using integrated daily imaging and helical radiation delivery to more accurately target tumors and spare surrounding structures and organs. As reported in the study, "Helical TomoTherapy delivers continuous arc-based [intensity-modulated radiation therapy] (IMRT) that gives high conformality and excellent dose homogeneity for the target volume. Helical TomoTherapy allows for differential dosing of multiple targets resulting in very elegant dose distributions. By its conformal nature, IMRT is very sensitive to improper patient setup. The use of pretreatment [megavoltage CT] (MVCT) imaging with [helical TomoTherapy] allows for increased precision with respect to patient positioning and use of a reduced [planning target volume] (PTV) margin."

- **Unilife** (Lewisberry, Pennsylvania) has received FDA clearance for the Unitract 1 mL Insulin Syringes. The company says the Unitract range of 1mL syringes is the world's first and only known syringe that allows operators to control the speed of passive (automatic) needle retraction directly from the patient's body into the barrel of the syringe where it is locked in place. The products are well positioned to help prevent the transmission of blood-borne diseases such as HIV and hepatitis C via needlestick injuries, aerosol dispersal and syringe reuse. ❖

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