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Market Dynamics Switchover To Come In Fast-Growing Soft Tissue Fixation Segment

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Global sales for arthroscopy and sports medicine devices are expected to reach $6.5bn by 2021, representing a CAGR of 4.1%. Of the two main market segments, soft tissue products and arthroscopy devices, soft tissue fixation represented the smaller segment with 35.7% market share in 2016 vs. 64.3% for arthroscopy devices. However, it will see the most significant growth over the next few years.

According to a new report by *Meddevicetracker*, "Global Market for Arthroscopy and Sports Medicine Devices", worldwide sales of soft tissue fixation devices totaled about $1.9bn in 2016 and are expected to achieve a CAGR of 6% during the five-year forecast period, double the expected growth rate for arthroscopy products. By 2021, the global arthroscopy products market is expected to reach $4bn vs. $2.5bn for soft tissue fixation products. (See Figure 1.)

SOFT TISSUE FIXATION PRODUCTS

When it comes to the soft tissue repair segment – which includes hip, meniscal, shoulder and cruciate ligament fixation – *Meddevicetracker* anticipates significant changes *(Also see "Innovation Is Alive And Well In Sports Medicine" - Medtech Insight, 30 Jan, 2014.)*.

In 2016, shoulder fixation accounted for the lion share of the market with an estimated 61.7%, followed by cruciate ligament fixation products with 17.3% and meniscal fixation devices with 15.8% with hip fixation making up the smallest part with 5.2%.

By 2021, *Meddevicetracker* expects that hip fixation implants will see the highest growth rate with 16.8% in the soft tissue fixation products market while the other segments will see single-digit growth. Meniscal fixation devices will see a growth rate of 6%, shoulder fixation devices will rise by 5.5% and cruciate ligament repair by only by 3.8% during the forecast period. (See Figure 2.)

Hip Fixation

So what's driving the high double-digit growth in the hip fixation devices segment?

The number of hip fixation procedures, especially in the US, has been on the rise in the last few years due to a variety of factors: They include significant improvements in surgical technologies, rising incidences of sports injuries and associated degenerative changes to the hip joint, and the growing number of surgeons being trained in these delicate procedures, all played a role. The rising obesity rate also continues to be a major risk factor.

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FROM THE EDITORS OF: **THE GRAY SHEET, CLINICA, START-UP** AND **MEDTECH INSIGHT NEWSLETTER**

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Go online for all you need to know about timelines and implementation of the European-wide Medical Device and IVD Regulations, which were published in final form this month after five years of debate.

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EU's Competent Authorities for Medical Devices group? It will have an important role in the implementation of the EU's new regulations and in managing an EU market-surveillance project, that's what.

COMMERCIAL

START-UP SPOTLIGHT

'Program Alignment' Falls Into Place: Everything You Need To Know About US FDA's New Inspectional Approach

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On the eve of US FDA rolling out an historic overhaul of its approach to facility inspections, the agency is finally offering a peek behind the curtain, giving details on how its "program alignment" scheme will operate and be structured.

The upshot: For the medical device industry, FDA's five regional offices – Pacific, Central, Northeast, Southwest, Southeast – will be replaced on May 15 by three distinct divisions across the US encompassing 20 FDA district offices. (Figure 1 shows – as of May 5 – where the divisions will be located, although FDA says adjustments could be made by launch date.)

About 140 investigators, plus management and support staff, will work out of the new device divisions, which will be situated in the northeast, central/southern, and western areas of the country, the agency says. Each division will have a director and 24 compliance officers, as well as compliance and investigations branches.

Under program alignment, inspections performed by the Office of Regulatory Affairs will be structured along commodity-specific product lines in an effort to make audits more predictable and consistent for investigators and manufacturers. ORA conducts all of the agency's field activities.

For a given product type, the entire reporting chain for ORA's inspection and compliance staff, from the employees on the frontlines to the assistant commissioners at headquarters, will specialize in that particular commodity. This is a significant departure from ORA's existing geography-based model, where employees, regardless of their areas of expertise, may do work in more than one program area – inspecting, say, a peanut producer one day and the maker of defibrillators the next.

"Ultimately, these changes will result in a high level of technical expertise and more uniform application of ORA's policies and processes," said Blake Bevill, director

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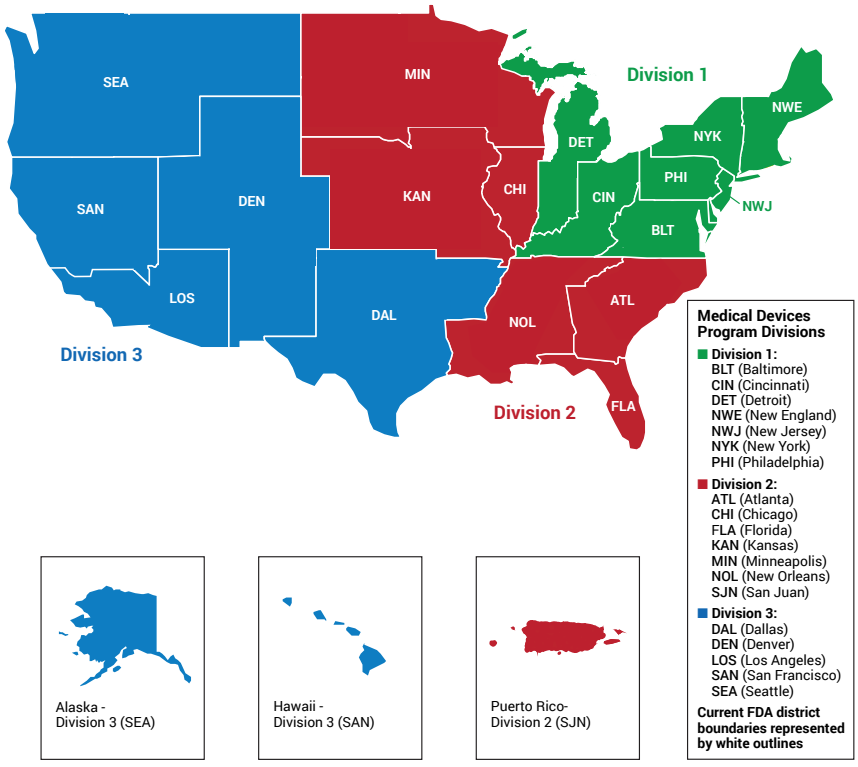
FIGURE 1

Office Of Medical Device And Radiological Health Operations

This map showing where the three medical device divisions will likely be located was presented on May 5 by FDA at MedCon 2017 in Cincinnati. An FDA spokeswoman tells *Medtech Insight,* "The map may change a lot, it may change a little, it may stay the same. Negotiations are ongoing, and until Monday [May 15], nothing is final." *Medtech Insight* will update the map then if changes have been made.



Source: US FDA

of compliance at FDA's Florida district office. "While operations will be aligned into programs, some functions will be retained based on geography. No offices will close, and no one will lose their job or be asked to move as a result of program alignment, although the roles and responsibilities associated with some positions may change."

When the five regions sunset on May 15, the agency will stand up "six specialized programs for operations, with an office director for each program area: biological products; bioresearch monitoring; human and animal food; medical devices and radiological health; pharmaceutical quality; and tobacco," Bevill explained May 5 at MedCon 2017 in Cincinnati.

"By specializing ORA staff, we will provide more seamless and coordinated interactions between the agency and industry, as well as our federal, state, tribal and local regulators. Our reorganization will drive new efficiency across each commodity," he said.

The directors in the 20 district offices will remain in place, but they will take on an additional title: program division director.

"Moreover, our district directors, while aligned operationally into one program area, will also have responsibility over a geographic area, overseeing state liaisons, emergency-to-response coordinators, and other key functions that need to remain geographically based," Bevill said.

District directors will also be joined by eight program division directors, whose only tasks will be related to program operation.

"The district director will remain the most senior official in the district, regardless of their operational program assignment. Thus, they will continue to support regulatory meetings held locally, and they will have oversight for employee safety in facilities across the district," Bevill said.

Manufacturers should continue sending responses to FDA-483 inspection forms to their current district director until further notice. "If there is a problem with the 483 response, or if the inspection is classified as OAI, a compliance officer will contact you, and your point of contact will then change," he said.

FDA classifies facility inspections as "no action indicated" (NAI), "voluntary action indicated" (VAI) or "official action indicated" (OAI). NAI results signify that there were no objectionable conditions or practices found during an inspection, while VAI and OAI results indicate that potentially serious problems were discovered.

Further, "all regional food and drug directors and regional staff will transition into other positions within ORA," Bevill said. "ORA will align import operations as its own program of specialization, although it will still oversee all products regulated by FDA.

"ORA's laboratories will also specialize and align into human and animal food labs, or medical products, tobacco and specialty labs," he added.

Firms should continue sending responses to FDA-483 inspection forms to their current district director until further notice.

FDA's 20th District Office – Imports

On the US map (Figure 1), there is no mention of FDA's 20th district office, the Southwest Import District. So how will it fit into the program alignment plan? This is what the agency told *Medtech Insight*:

"What we can confirm as of today, May 8, is that Imports will be aligned into its own program, which includes the Southwest Import District. Final details on ORA's new organizational structure are still being finalized and will be made available on Monday, May 15."

NEW OMPTO OFFICE

As part of program alignment, FDA has established an Office of Medical Products and Tobacco Operations (OMPTO), led by Ellen Morrison, associate commissioner of operations. She reports directly to the Associate Commissioner for Regulatory Affairs (ACRA).

OMPTO's leadership team includes four office directors: Jan Welch for the Office of Medical Devices and Radiological Health Operations; Chrissy Cochran for the Office of Biological Product Operations; Ginette Michaud for the Office of Bioresearch Monitoring Operations; Alonza Cruse for the Office of Pharmaceutical Quality Operations; and Anne Reid for the Office of Tobacco Operations (acting).

More recently, Reid was also named Welch's deputy director in the Office of Medical Devices and Radiological Health Operations, Bevill said.

"Over this past year, we've been doing program alignment activities and working on work groups with the [device] center. Program alignment has made the world much, much smaller," he said. "When you work with people over and over again, and you don't have to keep jumping from center to center, it just makes the world smaller, the relationships stronger, and more work gets done."

For example, "All field operations, including inspections, recalls and compliance activities for the Office of Medical Devices and Radiological Health Operations [will be] planned in coordination with the Center for Devices and Radiological Health," Bevill said.

3 DIVISIONS IN DEVICE OMDRHO OFFICE

The Office of Medical Devices and Radiological Health Operations will be responsible for:

- ORA's oversight of inspectional operations and compliance actions to protect and advance public health, leading ORA's collaboration and operational activities with CDRH;
- Working with ORA and its federal, state, local, tribal, territorial and foreign counterparts, and advancing outreach education and

cooperative endeavors to industry, trade groups, academia and other stakeholders to further the protection of public health;
- Implementing new authorities granted by legislation;
- Developing regulatory program standards for quality improvements;
- Enforcement of FDA regulations; and
- Investigations of consumer complaints and emergencies.

OMDRHO is divided into three parts: the Office of Medical Devices and Radiological Health Operations Divisions I, II and III. Further, the office will house the foreign medical device and radiological health inspections and operations staffs.

Within OMDRHO, "we have a number of vacancies that we're working internally to fill. As for now, [a manufacturer's] local contacts will remain the same," Bevill said. "Your existing contacts will help facilitate your inquiries when changes are made in the future. And contact information will be updated on FDA.gov."

WHY THIS WAS DONE

Because of program alignment, most manufacturers will likely be exposed to an entirely new, unfamiliar inspectorate, among other big changes.

"We will focus inspections on activities that are critical to both product and process quality to improve the inspection outcome," Bevill said. "We will have greater clarity and coherence in our communications and actions. Our new level of specialization will better mirror the increased specialization of the industries we regulate."

Program alignment was launched in 2013. Since then, the agency has been tight-lipped about the initiative. *(Also see "US FDA's 'Program Alignment' Inspection Scheme Coming Mid-May; Details Still Murky" - Medtech Insight, 29 Mar, 2017.)*

"That's a long time that we've been at this," Bevill said. At the time, "FDA's commissioner – it was Margaret Hamburg – charged the director at the centers and ORA to identify a path forward for the agency to modernize and strengthen FDA's workforce, to improve our public health response in a way that keeps pace with the acceleration of scientific innovation, global expansion of markets, and modern legal authorities."

Program alignment will "modernize and strengthen the FDA's workforce to improve our public health response," he said. "We are doing this to keep pace with the acceleration of scientific innovation, global expansion of markets, and modern legal authorities, including the 2009 Family Smoke and Prevention and Tobacco Control Act; the 2011 FDA Food Safety and Modernization Act, known as FSMA; the 2012 FDA Safety and Innovation Act, FDASIA; and the 2013 Drug Quality and Security Act, DQSA.

"Over the years, the products we regulate have become more complicated, the markets are more numerous, and the rules governing our actions are more complex. Changing our operational model will allow ORA to continue to adapt to meet those challenges and improve our efforts to protect public health," Bevill added.

NEED HELP?

But just because program alignment stands up on May 15, doesn't mean it won't have rough edges. Aside from the various staffing vacancies for the initiative, firms won't have to immediately communicate with the agency via the new structure.

"For now, continue to work with your current ORA offices and contacts, including district directors, state liaisons and your contacts in the Office of Partnerships. Any changes to your current contacts will be communicated," Bevill said. "However, we encourage you to let us know if you need assistance identifying a contact. We've established a mailbox for such inquiries. Please direct your questions to engageora@fda.hhs.gov."

He also suggested that companies reach out to ORA's new ombudsman, Jessica Zeller, if they have concerns or questions, at oraombudsman@fda.hhs.gov or jessica.zeller@fda.hha.gov.

"We have engaged all of our internal resources to ensure you continue to have a positive engagement with ORA. Our ombudsman is available to you to address any concerns regarding your engagement with ORA that would benefit from a third party," Bevill said.

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What If There's An Emergency?

Although investigators under program alignment will be siloed by commodity, they would still be expected to inspect commodities outside of their designated expertise should a national crisis arise.

"In an emergency, it's all-hands-on-deck," FDA's Bevill said. "If there's an emergency and we have the resources, we're going to help take care of that product. We'll have device people pulling cans of food off retail shelves. Nobody is above doing the work to protect public health. We're all in it together."

"Over the years, the products we regulate have become more complicated, the markets are more numerous, and the rules governing our actions are more complex. Changing our operational model will allow ORA to continue to adapt to meet those challenges," FDA's Blake Bevill says.

US FDA Continues Shift From Companion To Complementary PD-L1 Diagnostics With AstraZeneca Imfinzi Approval

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FDA's approval of **AstraZeneca PLC**'s *Imfinzi* (durvalumab) is the latest example of the agency's growing preference for complementary diagnostics over the companion diagnostic paradigm that dominated the early days of targeted therapy and immunotherapy for cancer.

While the indications for many targeted therapies and early immunotherapy approvals specified use of a companion diagnostic test, FDA has been moving toward a less prescriptive approach that describes clinical data organized by biomarker expression on a diagnostic test, but leaves use of the test to the physician's discretion – a complementary diagnostic.

Imfinzi is the third PD-1/L1 inhibitor approved by FDA for second-line bladder cancer use, and the third to keep PD-1/L1 expression data in labeling but out of the indication.

FDA cleared Imfinzi on May 1 for treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or who have disease progression within 12 months of neoadjuvant or adjuvant platinum therapy. *(Also see "AstraZeneca's Imfinzi Debuts In Bladder Cancer With Combo Coming Soon" - Scrip, 1 May, 2017.)*

The agency approved **Roche**'s *VENTANA PD-L1 (SP263)* assay as a complementary diagnostic. A similar Roche assay was approved as a complementary diagnostic with that firm's *Tecentriq* (atezolizumab), approved for urothelial carcinoma last year, and as a first-line therapy last month. *(Also see "Keeping Track: US FDA Expands Indications For Roche Tecentriq, Lucentis, Approves Second Infliximab Biosimilar" - Pink Sheet, 23 Apr, 2017.)*

For Imfinzi, PD-L1 status is not mentioned in the indication statement, although labeling describes clinical findings of higher response rates in patients with higher PD-L1 expression.

The complementary diagnostic approach has become a regular, if not an exclusive, feature of FDA's handling of biomarker-guided drug development. The first PD-1 inhibitors to reach the market, **Bristol-Myers Squibb Co.**'s *Opdivo* (nivolumab) and **Merck & Co. Inc.**'s *Keytruda* (pembrolizumab), illustrate the agency's flexibility: Keytruda's non-small cell lung cancer indication came with a required companion diagnostic from **Dako AS**, while Opdivo was approved with a complementary diagnostic, also from Dako.

Divergent approaches can also be seen with other personalized medicines. Just days before the Imfinzi approval, FDA approved **Novartis AG**'s *Rydapt* (midostaurin), a targeted kinase inhibitor with a conventional companion diagnostic claim in the indication, which reads "newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation-positive as detected by an FDA-approved test." *(Also see "Rydapt And Alunbrig Approvals Headline Good Week For Targeted Oncologics At US FDA" - Pink Sheet, 29 Apr, 2017.)*

In March, the agency approved a PARP inhibitor, **Tesaro Inc.**'s *Zejula* (niraparib) for breast cancer with a complementary approach to BRCA diagnostics, describing the data for patients with and without BRCA mutations but not including the diagnostic in the indication. *(Also see "US FDA Shows Relaxed Approach On Personalized Medicine In Zejula Approval" - Pink Sheet, 30 Mar, 2017.)*

CONSISTENTLY BETTER RESPONSE WITH HIGHER PD-L1 EXPRESSION

PD-1/L1 inhibitors are rapidly advancing in bladder cancer. In addition to Roche's Tecentriq, Bristol-Myers' Opdivo is also approved for similar indications in platinum-experienced metastatic urothelial carcinoma (mUC). Keytruda is under review for first-line and second-line indications, and **Merck KGAA** and **Pfizer Inc.**'s *Bavencio* (avelumab) is up for a second-line mUC indication.

Response rate data for the three immunotherapies approved in the post-platinum chemotherapy mUC setting is consistent in showing a greater benefit in patients with higher levels of PD-L1 expression (*see chart below*).

	ALL PATIENTS	LOW PD-L1 EXPRESSION	HIGH PD-L1 EXPRESSION
Infinzi	17% for 182 patients	4.1% for 73 patients	26.3% for 95 patients
Tecentriq	14.8% for 310 patients	9.5% for 210 patients	26% for 100 patients
Opdivo	19% for 270 patients	15.1% for 146 patients	25% for 124 patients

Source: FDA-approved labeling for treatment of metastatic urothelial carcinoma patients who progressed during or after platinum chemotherapy

The definition of high and low PD-L1 expression, however, is not consistent across the three development programs. Tecentriq used a threshold of PD-L1-stained tumor-infiltrating immune cells covering 5% of the tumor sample, using Roche's *Ventana PD-L1 (SP142)* as a complementary assay; the low PD-L1 cohort had less than 5%. For Opdivo, the standard was 1% or more to be in the high expression group, using Dako's *PD-L1 IHC 28-8 pharmDx* assay.

The Infinzi trials, relying on the Ventana PD-L1 (SP263) assay, used a more complicated PD-L1 cutoff with a 1% threshold.

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US FDA Ready To Accept 510(k) Devices To Expedited Access/Breakthrough Pathway

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US FDA is ready to implement a clause in the 21st Century Cures Act that requires the agency to accept 510(k) devices into the Expedited Access Pathway (EAP) for breakthrough devices, agency staff says. What types of 510(k) devices might qualify for the program in practice remains to be seen, but experts suggest devices that offer significant benefits to patients, even if not completely new, may be the most likely participants.

Introduced by FDA in 2015, EAP offers a faster development path to market for some devices that significantly improve treatment for an unaddressed debilitating or life-threatening disease or condition. The Cures Act, enacted last December, establishes the Breakthrough Devices Pathway, essentially putting the EAP program into statute, and expanding the PMA- and *de novo*-limited program to include eligibility for 510(k)s devices. The act also removes FDA's previous EAP requirement for sponsors to submit a long-term data-development plan as part of applications to enter the pathway, though the data plans remain optional. *(Also see "21st Century Cures: Device Provisions" - Medtech Insight, 14 Dec, 2016.)*

Previously, FDA has suggested that it might stretch its resources too thin to include 510(k)s into the EAP program, and it has also questioned whether such a pathway would offer value to 510(k) devices. *(Also see "CDRH Launches Expedited Access Pathway, Extends To De Novos" - Medtech Insight, 8 Apr, 2015.)*

According to FDA device center head Jeffrey Shuren, FDA always planned to expand the program to include 510(k)s. However, the agency might have waited longer without the legislative push, Shuren acknowledged at the Food & Drug Law Institute annual meeting on May 4 in Washington DC.

"We wanted to start with PMAs and *de novos* as a resource issue," he explained. However, he doesn't foresee major problems in adding 510(k) devices, which must meet the same criteria as PMA products to enter the program. One key distinction in the Cures language says that FDA can't shift data collection for 510(k) or *de novo* devices to the post-market period, thus blocking those devices from one of the key benefits of the EAP/breakthrough pathway.

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"It's hard to abstractly conceptualize that a 510(k) device could meet the requirements for the breakthrough pathway," says Beverly Lorell from King & Spalding. But the increased attention from senior FDA staff should offer a substantial benefit for 510(k) devices that are accepted, she notes.

Overall, the program is intended to provide a sponsor with outsized attention from agency reviewers as clinical trials are being designed to agree-upon the most efficient development plan early in the process. For PMA devices, this can mean a data plan that reduces pre-market evidence collection under an agreement that much more data will be collected post-approval to validate initial findings.

Shuren said that the data collection shift, which allows FDA to accept more uncertainty in approving devices, is inappropriate for 510(k) devices. However, he floated the possibility that future legislation might open the option for post-market data collection as a condition of clearance for *de novo* devices.

510(k) devices accepted into the program, meanwhile, would be able to benefit from the enhanced collaboration with reviewers and priority review once a submission is made.

WHEN IS A 510(K) A BREAKTHROUGH?

Because 510(k) devices are cleared as substantively equivalent to previous technol-

ogy, "it's hard to abstractly conceptualize that a 510(k) device could meet the requirements for the breakthrough pathway," said Beverly Lorell, senior medical and policy advisor at law firm King & Spalding, in an interview. But the increased attention from senior FDA staff should offer a substantial benefit for manufacturers of any 510(k) devices accepted into the pathway, she says.

Meanwhile, Alan Minsk, who heads the food & drug law team at Arnall Golden Gregory, expects any 510(k) devices accepted into the program to qualify because they significantly improve patients' quality of life or allow them to better manage their own care, rather than because the technology is completely new.

It's still unclear how portions of the Breakthrough Devices Pathway will look in practice. President Trump's administration has indicated that it wants fewer regulations, which Minsk speculates could slow work on detailed guidance documents. In addition, FDA's ability to implement the program is dependent on its resources.

The Cures Act mandated that the agency issue a guidance document on its Breakthrough provision within a year of enactment. *(Also see "Must-Do Guidance Development: What's On Tap From Cures, MDUFA IV" - Medtech Insight, 22 Dec, 2016.)* FDA spokeswoman Stephanie Caccomo said the agency is still on schedule to release a draft guidance document in December, but declined to offer further specifics.

Minsk believes the transition should go smoothly. "When you've got a secretary of [Health and Human Services] who is a doctor, and you also have an administration that wants to get devices on the market and cut through red tape, I don't think the breakthrough pathway will go away," he says. "The question will be what level of guidance, and maybe budget cuts, and morale issues, and all of the other things that FDA is having to deal with."

However, Lorell feels FDA's prior actions have shown the agency's commitment to offering an expedited pathway. The agency has been reviewing devices for inclusion since pilot programs began in 2011, she says. By submitting a request for acceptance into the breakthrough pathway early in the product lifecycle, manufacturers can benefit from the increased dialogue with FDA as early as possible, she says.

NO NEED TO DELAY

Since FDA launched the EAP program in 2015, devices have been steadily accepted into the program. So far, the feedback from several participating companies has been positive, particularly regarding the collaborative experience with FDA in designing trials, and the participation numbers are higher than FDA original predicted. *(Also see "CDRH's Expedited Access Pathway: 17 Devices And Counting" - Medtech Insight, 12 May, 2016.)*

The device pathway is partially modelled on the FDA drug breakthrough pathway, which launched in 2012.

"With breakthrough drugs there was an excitement," Minsk recounts. "Everyone and their mother was going to try to get it, it was kind of like the Willie Wonka ticket." But he expects a more cautious approach on the device side, as FDA's device center looks at what has and hasn't worked for the drug center. Still, he expects the pathway to create new opportunities for some manufacturers, especially smaller ones.

Minsk advises manufacturers who want to explore the breakthrough pathway to take a measured approach. But both experts agreed there's no need for companies considering the breakthrough pathway to put off starting the process. Sponsors considering breakthrough designation should review the statute with counsel or a consultant to make sure they fit the requirements, and then ask FDA for a pre-submission or pre-IDE meeting at which the agency's expectations can be discussed. Sponsors shouldn't expect a "slam dunk," Minsk said.

"It won't be 'Here's all my data, now sign off on my application,'" he said. "Manufacturers should have enough that FDA can make a decision, but it doesn't have to be so substantive."

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CLICK

Check out Medtech Insight's Expedited Access Tracker at http://bit.ly/2pwOn57 for a listing of publicly disclosed devices accepted into FDA's EAP program.

How EU's Competent Authority Group Is Flexing Its Muscles For New Roles

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Just at a time when the new EU Medical Device and IVD regulations are on the point of taking effect and the medtech sector is urgently in need of the latest information on the role of the Competent Authority for Medical Devices (CAMD) group in implementing the regulations and market surveillance, the chance of an update has slipped away.

John Wilkinson, head of devices at the UK's Medicines and Healthcare products Regulatory agency and head of CAMD's executive committee, was unable to confirm an interview date due to the UK "Purdah" ruling, which prevents government staff from carrying out any media activity until the election on June 8 is over.

So what exactly do we know at this point?

ROLE IN IMPLEMENTATION

Firstly, CAMD is playing a pivotal part in work on the European Commission's medical device roadmap and in supporting the implementation of the new regulations.

The group was one of the organizers, along with the European Commission,

CAMD is an umbrella group under which the national competent authorities in the EU work to enhance the level of collaboration in the single market for medical devices. Its aims are to enhance collaboration; improve market surveillance; and deliver better communication.

of the stakeholder meeting on the implementation of the regulations, which took part in Brussels on March 9 and where proposals to tackle implementation in the context of seven different clusters were reviewed. *(Also see "EU Implementation Plan For New Regs Starts To Take Shape" - Medtech Insight, 14 Mar, 2017.)*

As a result of that meeting, the Commission and CAMD are expected to publish the final implementation roadmap for the regulations in approximately one month.

The final texts of the Medical Devices and IVD Regulations were published in the Official Journal of the European Union on May 5, serving as a catalyst for the Commission to finish the final roadmap, *Medtech Insight* understands.

The roadmap should clearly lay out CAMD's role, in terms of its implementation objectives. Also, presumably, more information should start to populate its website, which is still at a relatively basic stage of development.

Industry is hoping that the publication of the roadmap will also help confirm timeframes for compliance, as there are many derogations in both the device and IVD texts, and these are creating some difficulty in interpretation.

MARKET SURVEILLANCE

In addition to work on implementation of the regulation, CAMD is also helping to manage the EU's market surveillance project. This project is being rolled out as part of the second wave response to the so-called Dalli plan of immediate actions set out in the PIP Action Plan, following follow through with a notified body project that has resulted in some 25% of notified bodies leaving the sector. *(Also see "EU Market Surveillance: It's About Rationalizing Resources, Not Seismic Changes" - Medtech Insight, 24 Nov, 2016.)*

CAMD aims plans to employ " Joint Actions" to enhance collaboration, improve market surveillance and coordinate better communication across the EU member states.

With the MHRA's John Wilkinson at the head of the CAMD executive group, the organization has launched a series of joint actions in market surveillance. That has led to the UK itself taken on a series of key work initiatives to support the roll out an EU-wide working market surveillance system, while Austria, the Netherlands and Ireland have taken on specific responsibilities.

PILOT MARKET SURVEILLANCE PROJECT

One pilot within this market surveillance project, led by Austria, has made progress. It is known as the "COEN Joint Action 2014: Instructions for use for re-useable and re-sterilizable medical devices." Organizers have set up a process for the collection and evaluation of data from manufacturers, and the pilot is due to be completed by the end of this year.

As part of this project, economic operators, including manufacturers, are sent checklists based on the European standard entitled "EN ISO 17664, Sterilization of medical devices – Information to be provided by the manufacturer for the processing of re-sterilisable medical devices." The economic operators are then inspected "in a harmonized way" to check the validation of their reprocessing procedures.

BIGGER MARKET SURVEILLANCE INITIATIVE

Following on from the pilot, the broader market surveillance initiative is also now underway.

On October 19, 2016, at the 39th meeting of the Competent Authorities for Medical Devices in Bratislava, Slovakia, MHRA officially launched the Joint Action in Market Surveillance of Medical Devices (JAMS).

The Joint Action is being implemented through five work packages:

1. Coordination (MHRA, UK)
2. Dissemination (MHRA, UK)
3. Evaluation (MHRA, UK)
4. Joint manufacturers' inspections (IGZ, the Netherlands)
5. Clinical process and resource development (HPRA, Ireland)

UK Responsibilities

MHRA in the UK is responsible under points one, two and three for:

- Coordination of the project: MHRA has to verify that the Joint Action is completed on time, within budget, and with high–quality deliverables;
- Dissemination of the information: MHRA has to collect and circulate the deliverables to the target groups; and
- Evaluation: MHRA has to check that the implementation of the project is developed as planned.

Dutch Lead

As part of the work package to improve joint inspections of manufacturer inspections, the Health Care Inspectorate (IGZ) in the Netherlands, in collaboration with European partners, is responsible for:

- Developing methods, agreed tools and guidance for a joint, consistent and proactive approach to manufacturer inspections by Competent Authorities: At the beginning of the project, it is expected to identify various approaches and differences between Competent Authorities in terms of how they approach market

Working With Partners

There are two types of partners involved in the Joint Action: beneficiaries and collaborating stakeholders.

• Beneficiaries are organizations that receive EU co-funding following the successful application and the signature of the Grant Agreement.

• Collaborating stakeholders do not have a contractual relationship with WU Consumer, Health, Agriculture and Food Executive Agency (Chafea) and do not receive any EU funding. They contribute to increase the technical and scientific content of the Joint Action, as well as its relevance for different users in the European Union

surveillance. A guidance document intended to define and specify good practice by sharing and exchanging information on performing inspections will also be developed.

- Establishing specific inspection scopes and objectives to complement those conducted by conformity assessment bodies: The joint manufacturer inspections will be complementary to the existing system to reinforce the current performances and permit the harmonization of manufacturer inspections. The Netherlands will develop a harmonized guidance regarding joint inspection planning strategies.
- Identification of information sources to be used as focus during the Joint inspections: An inspector training course will be developed to prepare inspectors to perform intended joint inspections and to perform inspection according to the joint approach.
- Developing and delivering collaborating mechanisms designed to maximize the efficiency and effectiveness of resource deployment: Competent Authorities will initiate a joint manufacturer inspection regime to reinforce market surveillance.

CLICK

The EU Medical Device and IVD Regulations were published in the Official Journal of the EU on May 5 and formally take effect on May 25. Check out MedtechInsight.com for updated news and analysis on the implications for industry.

Irish Lead

As part of its work package to improve clinical process and resource development, the Health Products Regulatory Authority (HPRA) in Ireland is coordinating:

- Identification and establishment of communication platforms and protocols: A communication platform will allow Competent Authorities to discuss, in real time, market surveillance issues in the clinical arena that affect some or all of the authorities, and provide a platform to discuss specific market surveillance issues in a confidential setting.
- Establishing current practices and identifying development and/or training needs in the evaluation of clinical data by authorities: Based on the findings from workshops and surveys, a training strategy will be defined. Training material will be developed to provide practical guidance on the assessment and review of clinical data as part of market surveillance activities.
- Identifying and prioritizing medical devices that require development of common specifications to define clinical criteria for safety and performance: Under the new proposals for a regulation on medical devices and *in vitro* diagnostic medical devices, common specifications will be developed addressing the clinical requirements for safety and performance. The work of the Joint Action will help identify the priorities for developing common specifications and help inform the activities for implementing the new regulations.

25% CASUALTY RATE?

This is a heavy workload involving close cooperation between the various authorities during the preparation stage. But once the market surveillance projects are off the ground, manufacturers and other economic operators will need to be very vigilant that they can demonstrate compliance at any moment.

The big question is whether we will see causalities here, like we have with some 25% of notified bodies that disappeared as a result of the joint audits of notified bodies emanating from the first stage of the Dalli plan of action. *(Also see "Will EU's New Market Surveillance Project Hit As Hard As Notified Body Action?" - Medtech Insight, 17 Nov, 2016.)*

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CONTINUED FROM PAGE 1

Worldwide, the market for hip fixation devices was valued at about $99.9m in 2016 and is expected to reach $217.1m by 2021, with the US seeing the highest growth. In 2016 alone, there were about 87,000 hip fixation surgeries performed in the US with the average hip fixation device cost per procedure being $643, resulting in a market value of $55.9m. The number of procedures is expected to more than double to 203,288 by 2021 with the average fixation device cost per procedure rising to $746.

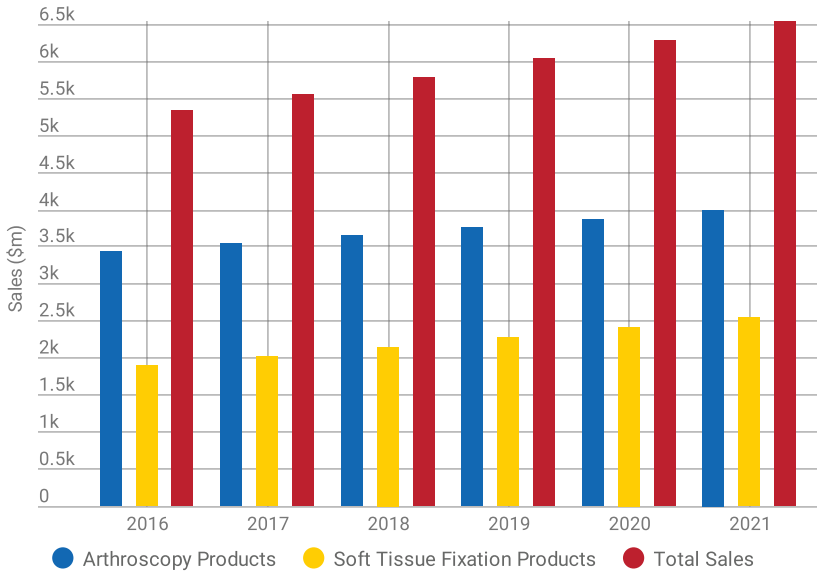
In 2016, this segment was dominated by two major rivals, **Smith & Nephew PLC** and **Arthrex Inc.**, which had a combined market share of 63%. Smith & Nephew dominated with a market share of 32% and estimated sales of $32m with rival Arthrex falling just slightly behind with a 31% market share and $31m in sales. Two other key players in this market, **Stryker Corp.** and **Zimmer Biomet Holdings Inc.**, each held a 11% market share with an estimated $11m in sales (each).

Smith & Nephew and Arthrex also just recently settled a major, long-running lawsuit over a patent for suture anchors, the companies reportedly told a court in February, just prior to the start of a final trial. Prior to the settlement, Arthrex was looking to obtain an injunction against Smith & Nephew, which could have resulted in the company losing its ability to sell products. But now that a settlement has been reached, that will no longer be the case. Details of the settlement, which puts to rest several lawsuits filed in federal court in Texas, were not revealed.

Arthrex markets multiple knotted and knotless suture anchors for soft tissue reattachment and reconstruction procedures in the hip joint under the *Hip PushLock* family, which includes the bioabsorbable *PLDLA* and *BioComposite* and nonabsorbable *PEEK* options *(Also see "S&N wins round in patent row with Arthrex" - Medtech Insight, 31 Oct, 2008.)*. Meanwhile, Smith & Nephew markets the *Bioraptor Hip Suture* anchors for labral refixation in the hip, including bioabsorbable anchors and non-absorbable anchors, *Healicoil PEEK-OPTIMA* suture anchor for repair of the gluteus medius and minimus and the *Osteoraptor PLLA/HA* knotted suture anchors.

FIGURE 1

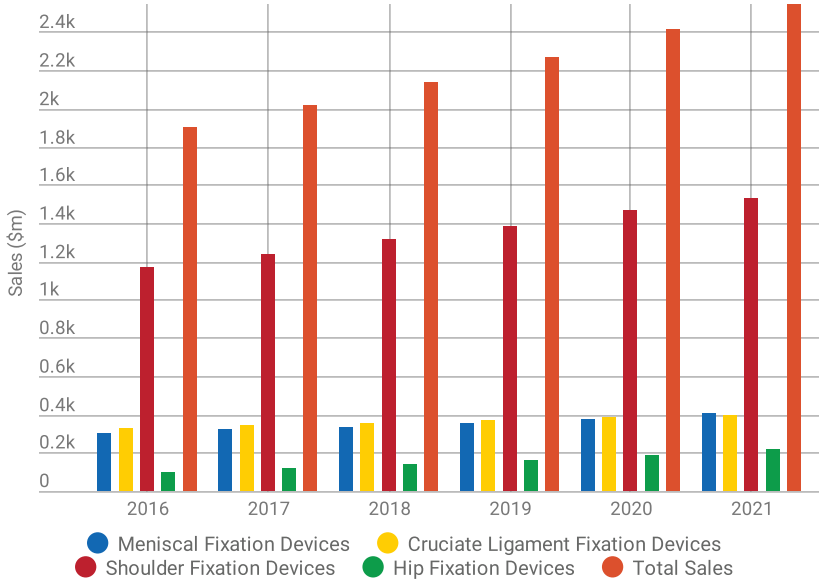
Arthroscopy And Sports Medicine Devices Market Forecast, 2016-21



Source: "Global Market for Arthroscopy and Sports Medicine," Meddevicetracker

FIGURE 2

Soft Tissue Fixation Devices, Combined Market Forecast 2016-21



Source: "Global Market for Arthroscopy and Sports Medicine," Meddevicetracker

The 2014 acquisition of **Pivot Medical Inc.**, a private company that develops hip arthroscopy products for repairing femoracetubular impingement syndrome (FAI), allowed Stryker to gain speed in this market segment. Stryker now markets the *Pivot Nanotack Flex* suture anchor system and the *Pivot CinchLock* knotless anchors for repair of the hip, knee, shoulder, and small joints, adding to its sports medicine solutions.

Zimmer Biomet also improved its position in this segment with its acquisition

WATCH

Visit our website at **medtech.pharmamedtechbi.com** to access videos detailing knotless approach to hip arthroscopy and Arthrex's SpeedBridge repair system.

of **Cayenne Medical Inc.** in 2016, which gave it the *JuggerKnot* all-suture anchor for acetabular labral repair and *SureLock* all-suture anchor. Zimmer Biomet also markets the *Quattro GL, a PEEK-OPTIMA* pre-loaded suture for labral repairs. The remaining 15% market share and $15m in sales for this market segment in 2016 included such suppliers as **ConMed Corp.** and **DePuy Synthes** .

Looking forward, *Meddevicetracker* expects that continued technological advances, such as the development of specialized instrumentation and new techniques for hip arthroscopy as well as computed tomography and magnetic imaging, will further the growth of hip fixation devices.

And with the rising public awareness of these advancements, more people will opt for minimally invasive surgery as an alternative to traditional surgery and to delay total joint replacement. Also aiding the expansion of hip repair procedures are widening indications for hip arthroscopy; although surgeons are becoming more aware of the limitations of using the procedure to treat older patients with arthritis.

Meniscal Fixation

The global meniscal fixation devices market, which includes all implants used in the repair of the meniscus, excluding sutures, was valued at about $300.4m in 2016 and is expected to reach $402.3m in 2021, a 6% rise.

The arthroscopic repair of a torn muscle has been simplified by the introduction of various fixation devices including arrows, darts, staples and tacks that are used to hold the edges of the meniscus together. Only tears that are located in the vascularized zone of the meniscus are amenable to repair, which accounts for about 25% of all meniscus injuries; the other indications for meniscal repair include a short size meniscus, patients younger than age 40, vertical tears and an associated cruciate ligament (ACL) tear.

This market segment also continues to be driven by the rising greying population, as well as sports injuries that occur in both adolescents and adults, and by people working in physically demanding jobs who get hurt.

As with all soft tissue repairs, the US leads the growth in this segment worldwide. In 2016, about 256,133 meniscal fixation repairs were performed in the US with an average device cost per procedure of $910, resulting in about $233.1m in sales.

On the competitive landscape, Smith & Nephew led this market segment in 2016 with sales of about $88m and a 29.3% market share. The company markets the *Ultra Fast-Fix* and the *Fast-Fix 360* meniscal repair systems, which are permanent implants that deliver strong fixation without an invasive surgical procedure

The second-leading global supplier in this segment in 2016 was DePuy Synthes with about $75.1m in sales and a 25% market share. In March 2017, DePuy Synthes introduced the *Truespan Meniscal Repair System* for arthroscopy procedures, which features a single trigger and auto-reloading mechanism for quick, one-handed use. The company also sells the *OmniSpa*n meniscal repair system for minimally invasive repair of meniscal tears, which includes a low-profile needle preloaded with two PEEK backstops and the company's proprietary *OrthoCord* suture, made from ultra-high molecular weight polyethylene and resorbable polydioxanone.

Arthrex, which markets *The Meniscal Cinch* and *Meniscal Dart* product lines, ranked third with roughly $59.2m in sales and a 19.7% market share in 2016. The Meniscal Cinch is designed for an all-inside arthroscopic repair, which eliminates the need for accessory incisions such as those required for traditional inside/out techniques. The Meniscal Dart system is a headless, reverse-barbed dart with a disposable inserter.

Zimmer Biomet also offers an all suture meniscal repair system, *MaxFire*, and takes its place among other suppliers that accounted for the remaining $78.1m in sales and a 26% market share.

In this market segment, companies that offer meniscal fixation devices that increase efficiency and provide strong fixation with minimal disruption to the meniscus will be the most successful, according to *Meddevicetracker*.

Shoulder Fixation

The worldwide shoulder fixation devices market remains by far the largest market segment in the soft tissue repair market with $1.1bn in 2016 sales, but is expected to grow modestly at 5.5% reaching $1.5bn in 2021.

As with the other segments in this market, the main growth factors are the aging population and rising prevalence of injuries, including rotator cuff degeneration, and those resulting from sports and trauma. However, two other growth factors also play a role, namely higher-priced knotless sutures and bioresorbable implants.

The US also leads this market segment worldwide, accounting for an estimated $625.8m in sales. In 2016, about 600,000 shoulder fixation procedures were performed with an average device cost per procedure of $1,043; that number is expected to climb to 726,489 procedures in 2021.

Among the big three leading companies, Arthrex dominated the market space in 2016 with sales of about $481.1m and a 41% share.

DePuy Synthes ranked second with sales of about $328.6m and a 28% market share,

followed by Smith & Nephew with about $246.4m in sales and a 21% market share. Other suppliers accounted for the remaining 10% share and $117.3m in sales.

Arthrex offers multiple knotted and knotless suture anchors for use in soft tissue reinforcement and repair procedures. The company offers a 5.5mm *Bio-Corkscrew FT suture* anchor, a resorbable anchor made of PLLA for use in rotator cuff repair procedures, and also developed a resorbable "push in" suture anchor called the *Bio-Suture Tak*.

The No. 2 player in this market, DePuy Synthes offers the *Healix TI dual-threaded suture anchor*, which is made from titanium and indicated for rotator cuff fixation and elbow, foot/ankle, hip and knee repairs. The company's *GII anchor* is a titanium device featuring nitinol arcs, a small size and high pull-out strength. In this segment, DePuy Synthes also offers the *Versalok PEEK Knotless Anchor System*, which is indicated for rotator cuff repair and biceps tenodesis in the shoulder.

The third-leading supplier, Smith & Nephew offers various suture anchors for shoulder repair and other indications. The company's acquisition of ArthroCare in May 2014, valued at $1.5bn, significantly enhanced Smith & Nephew's position in this market segment. It added shoulder anchor products to its sports medicine division and rebalanced its product portfolio toward higher-growth market segments.

In its 2016 financial statements, Smith & Nephew noted that its strength in the shoulder repair market continues to underpin the company's overall performance. The company faced a setback last December when a federal jury in the US ruled that it, along with **ArthroCare Corp.**, had infringed on two of Arthrex's patents on its knotless and cross-support suture anchor technology including the *Bioraptor, Footprint, Healicoil, LabraLock, Multifix, Spyromite, Speedfix, Speedlock, Spartan, Speedscrew, Titan Ti* and *TwinFix* products, according to published reports. The court granted Arthrex $17m in damages and the company announced it would seek an injunction prohibiting Smith & Nephew and ArthroCare from further manufacturing or selling the infringing devices in the US. The case has been settled, as mentioned earlier in this article.

Among the other suppliers in this area are Zimmer Biomet, which offers a broad portfolio of suture anchors, including the *ALLthread LactoSorb*. Stryker also sells the *ReelX PEEK* knotless anchors for shoulder and small joint repair.

Meddevicetracker expects that demand for bioresorbable implants will continue to rise while metal implants, which are less clinically efficient and require follow-up surgery to remove the implants, will decrease *(Also see " US PMAs Are The New Reality For Metal-On-Metal Hips" - Medtech Insight, 18 Feb, 2016.)*. Resorbable implants are higher priced, but they are more cost-effective in that they offer significantly better results in rotator cuff repair by reduce the need for revision surgery. The big limiter for growth are pricing pressures as hospitals and ambulatory surgery centers will continue to look for ways to lower implant costs in this cost-conscious health care environment.

Cruciate Ligament

The global market for cruciate ligament fixation devices, including sales of meniscal fixation systems and implants excluding sutures, used in fixation of anterior and posterior cruciate ligaments, is slightly bigger than the meniscal fixation repair market with roughly $329.3m in 2016 sales. However, this segment, which is driven mainly by work and sports-related injuries, is expected to see the slowest growth at 3.8% reaching $396.4m by 2021.

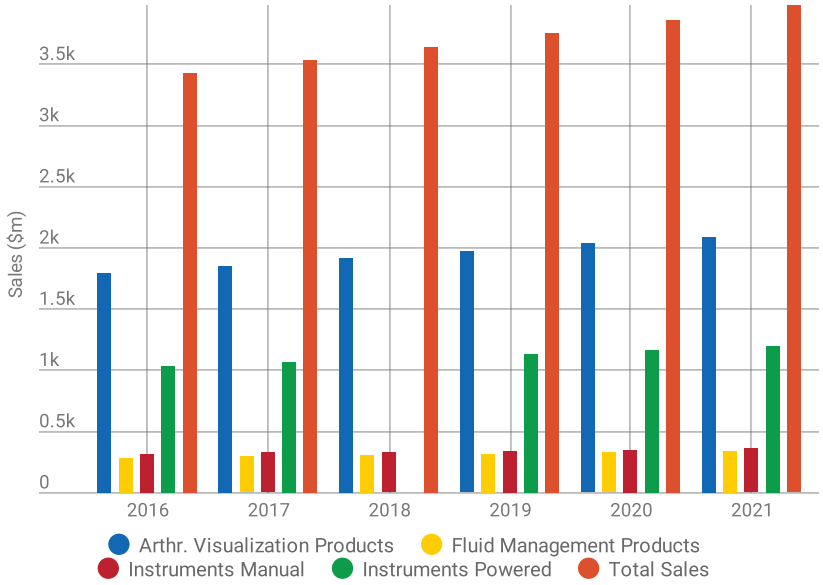
Here, the US market also takes the biggest share of the global market with an estimated $211.7m in sales in 2016 and some 374,600 cruciate ligament fixation procedures performed. The average device cost per procedure is $565.

In the cruciate ligament fixation devices market segment in 2016, Arthrex was the global leader with about $96.5m in sales and a 29.3% market share. Ranking not too far behind in second place was Smith & Nephew with a 22% market share and sales of about $72.4m, followed by DePuy Synthes with an 18% share and sales of about $59.3m. The other suppliers accounted for the remaining 30.7% share and $101.1m in sales.

During the forecast period, the primary drivers in this market segment will continue to be work- and sports-related injuries. Although nonresorbable fixation devices are used in the majority of ACL surgeries, *Meddevicetracker* expects the use of bioresorbable devices will climb by 2021, due

FIGURE 3

Arthroscopy Products, Combined Market Forecast 2016-21



Source: "Global Market for Arthroscopy and Sports Medicine," Meddevicetracker

in large part to refinements that enhance the properties of bioresorbable polymers.

Extremities Fixation

Fixation devices for repair of the extremities comprises one of the fastest-growing segments of the soft-tissue fixation market aided by the development of smaller anchors that allow surgeons to access tight joint spaces in the elbow, hand, wrist, foot and ankle, according to *Meddevicetracker*.

Most of the major orthopedic companies including Arthrex, ConMed, DePuy Synthes, Smith & Nephew, Stryker, **Tornier Inc.** and Zimmer Biomet sell soft-tissue fixation devices for the extremities including resorbable and nonresorbable suture anchors and tacks.

That said, the extremities soft-tissue fixation devices market is difficult to quantify as companies categorize extremities sales differently and not all orthopedic companies place small joint treatments into the extremities category. But *Meddevicetracker* anticipates that the growth in this segment will be driven by better implants and arthroscopic techniques and the rising numbers of surgeons who are trained in performing these types of surgeries.

GLOBAL ARTHROSCOPY MARKET

The global arthroscopy market totaled about $3.4bn in 2016 and is expected to reach $4bn in 2021, a modest growth of 3% and half the expected 6% CAGR for soft tissue fixation. The arthroscopy market is divided into four product segments - arthroscopic visualization products, manual arthroscopic instruments, power arthroscopic instruments and fluid management products – all of which are expected to grow in the low single-digits by 2021. .

Arthroscopic visualization products make up the lion share with 52.4% of the market, followed powered arthroscopic instruments with a 30.1% share, manual instruments with 9.2%, and fluid management products with 8.3%.

The arthroscopic market is largely driven by technological innovation and procedure-specific instrumentation. And sales have been positive for devices with wireless capabilities and integrated systems that provide value-based solutions that are cost-competitive and add efficiency.

Regional Outlook

Worldwide, the US dominated the arthroscopy market in terms of revenue in 2016, thanks to the greater adoption of less invasive arthroscopic procedures, which promote faster healing times, less downtime and faster recovery vs. open surgery.

In particular, arthroscopic hip and shoulder surgeries are expected to see continued growth due to the high incidences of age and sport-related injuries. There will also be a rise in knee procedures, supported by the aging population who will favor arthroscopic knee surgery to avoid knee replacements *(Also see "Latest Mako Tech Fleshes Out Stryker's Robotic Joint Replacement Line But Cost Critics Still There" - Medtech Insight, 20 Mar, 2017.)* . Although the practice of treating osteoarthritis of the knee with arthroscopic lavage and debridement has declined in the past decade or so, elderly people with radiologic evidence of advanced damage have undergone more of these procedures in recent years.

Looking to the major European markets – France, Germany, Italy, Spain and the UK – meniscal and articular repair of the knee accounts for the highest number of procedures, except in France, where carpal tunnel surgeries ranked the highest. But with Europe's rising geriatric population, arthroscopic hip surgeries will go upward in that part of the world as well, *Meddevicetracker* reported.

Looking East, the analysts expect that Japan's high prevalence of osteoarthritis among men and women 40 years and older will drive the demand for joint repair procedures *(Also see "Teijin To Solidify Ortho Biz With Bone-Fixation Investment" - Medtech Insight, 25 Jan, 2017.)*. The biggest growth, namely a 6% rise in arthroscopic procedures, is expected to take place in China. Here, the evolving middle class with higher disposable incomes coupled with a high incidence of musculoskeletal disorders and a rising aging population, will open up a big window of opportunities for companies.

Key players such as Smith & Nephew, Arthrex, ConMed and DePuy Synthes are all holding dominant positions in the various market segments. This market also has been driven by some major mergers and acquisitions.

COMPETITIVE LANDSCAPE

Arthroscopic Visualization

The global arthroscopic visualization products market, which includes arthroscopes, cameras, light sources and consoles/image management systems, is expected to grow from $1.8bn in 2016 to $2.1bn by 2021, a CAGR of 3.1%. The US accounted for 52% of sales in 2016 and is also expected to see the highest growth on the global market over the forecast period, namely 4%.

In 2016, Smith & Nephew led the global arthroscopic visualization products market with sales of about $378.6m and a 21% market share. ConMed was the second-leading supplier to the global arthroscopic visualization products market in 2016 with a 13% market share. Other leading competitors include Olympus with $200m in sales and a 11.1% market share and Stryker with $186.5m in sales and a 10.4% market share. The remainder of this market is highly fragmented and includes such big names as Arthrex, **DePuy Mitek Inc./Johnson & Johnson**, **Karl Storz Endoscopy-America,Richard Wolf Medical Instruments Corp.** and Zimmer Biomet.

While sales in Smith & Nephew's Arthroscopic Enabling Technologies division were flat on a year-to-year basis in 2015, the company took steps that allowed it to bolster sales in the US and in emerging markets in 2016.

The 2016 launch of its *LENS Surgical Imaging* system paid off in "strong sales" in 2016; and in the emerging markets, Smith & Nephew experienced some challenges early in the year, but then reported headwinds in the Gulf States and China, noting it expects long-term growth potential in the emerging markets.

Meanwhile, its competitor, ConMed, reported a 2.3% decline in revenue in its Orthopedic Surgery Division, primarily in the US, and also challenges in its Arthroscopy Enabling Devices unit, particularly for its resection and fluid management

products. ConMed also refocused its marketing efforts for the *Edge* arthroscopic radiofrequency system for soft tissue ablation, which it expects will stabilize sales.

In this market segment, *Meddevicetracker* expects that companies that offer products with advanced technologies -- including 4K and HD arthroscopes and cameras, consoles that enable wireless camera control and image management, and cameras featuring CMOS imaging -- will be on the cutting edge.

Companies that make small-diameter arthroscopes for small joint procedures can also expect rising sales, because of the expected greater demand for extremities surgeries. Other technologies in high demand include 3D video systems, data management systems, high-definition cameras and integrated arthroscopy systems. Companies that offer cameras with high-resolution images that may be displayed on flat screen monitors or broadcast for display in remote locations are also trending.

Arthrex's 4k camera and 4k 4.8mm and 4mm arthroscopes, introduced in 2015, meet the newest criteria. Also on the cutting edge is Smith & Nephew's digital *560 Series 3-CCD HD* camera system, which delivers high-resolution image via high-speed digital interface for display on flat screen monitors. The company's *LENS Surgical Imaging System* fits the trend of integrated systems with its included camera head, lens coupler and console. Smith & Nephew has done some strategic marketing that paid off. Rather than buying everything upfront, buyers can add on camera options and software upgrades as they become available.

Powered Instruments

Global sales of arthroscopic powered instruments, which include blades, burrs, shavers, wands and RF instruments, are expected to hit $1.2m in 2021, a CAGR of 3%. The US accounted for 52% of sales.

In 2016, Smith & Nephew was number. 1 on the worldwide market for arthroscopic powered instruments with sales of about $362.3m and a 35% market share. The company's 2014 acquisition of ArthroCare is largely behind this success. It enabled Smith & Nephew to rebalance its portfolio toward higher-growth segments, allowed it to expand its US presence, and gave it *ArthroCare's RF Coblation* technology, which complements Smith & Nephew's mechanical blade portfolio. In addition, Smith & Nephew also launched the *Werewolf Coblation* system in 2016, for which it reported strong sales in its annual results.

The second-leading worldwide supplier for powered instruments in 2016 was Arthrex with a 22% market share, followed by ConMed with a 12% share. The remaining 31% market was highly fragmented.

Fluid Management Products

In 2016, Smith & Nephew also led the global arthroscopic fluid management market, which includes pumps and accessories.

In 2016, fluid management products totaled about $282m worldwide and are expected to rise to $335.9m in 2021, a 3.6% rise. The US accounted for 52% of sales and is expected to grow 4.5%.

In 2016, Smith & Nephew led this segment with worldwide sales of about $50.5m and a 17.9% share, followed by Stryker with $39.5m in sales and 14% market share; ConMed with $36.1m in sales and a 12.8% share; and **Karl Storz Endoscopy-America** with $33.8m in sales and a 12% market share. The remaining 43.3% of the market was highly fragmented.

Fluid management products are used during arthroscopic procedures to irrigate and aspirate the operating field with a sterile saline solution, which helps surgeons with visualization and removing blood and debris.

Smith & Nephew markets the *Dyonics 25* fluid management system, which offers advanced irrigation and a stable system for all pump inflow and outflow functions.

Stryker offers the *CrossFlow, FloControl and FloSteady* fluid management systems.

ConMed sells the *24K Irrigation System Console*, which controls inflow, outflow, and shaver suction for managing arthroscopy fluids and the *Apex Universal Irrigation System*, a microcontroller-based system featuring a disposable cassette.

Karl Storz Endoscopy-America offers the *Arthropump Power*, a combination of single- and dual-roller pumps for more cost-effective and efficient fluid management during arthroscopy, and the *Arthropump* suction/irrigation pump.

Despite pricing pressures on medical device companies, the rise in arthroscopic procedures is expected to drive demand for fluid management systems. Companies that develop systems that are technologically advanced, cost-competitive and efficient for end-users will see the greatest demand.

Manual Arthroscopy Instruments

In the manual arthroscopy instruments segment, Arthrex and Smith & Nephew are the top leading suppliers.

In 2016, global sales of manual arthroscopy instruments totaled about $316m and are expected to reach $355.1m by 2021, a rise of 2.4%.

In 2016, Arthrex had sales of about $79m and a 25% market share, while Smith & Nephew had $75.7m in sales and a 24% market share. DePuy Synthes Mitek came in third with $60m in sales and a 19% market share. Other companies had estimated sales of $101.3m and a 32.1% market share.

Knee and shoulder repair kits are the most common manual instrument kits on the market. Examples include Arthrex's *Shoulder Repair Set*; DePuy Synthes/Johnson & Johnson's *Mitek Sports Medicine Graft Preparation System* for ACL reconstruction; Stryker's *Universal ACL Instrumentation System* and *Conquest Arthroscopic Manual Instruments* line.

This segment includes general instruments, which are sold by large companies in a highly competitive market, and surgical equipment, which are designed for use with specific implants and sold as a bundle by implant makers. Because the kits are often free or sold at substantial discounts to secure recurring implant business, this segment is expected to grow only at a slow to moderate pace.

Today, most major orthopedic/sports medicine companies have established a foothold in the hip arthroscopy arena with procedure-specific instrumentation for labral repair and reconstruction. In 2014, Stryker bought San Francisco startup company Pivot Medical in an all-cash deal, which gave Stryker a portfolio of instruments and devices to treat femoroacetabular impinge-

ment syndrome, one of the fastest-growing procedures in sports medicine.

Arthroscopic Extremities Procedures

Sports medicine companies market products that are designed specifically for arthroscopic extremity procedures. For example, Smith & Nephew's *Extremity Arthroscopy* line of products includes instruments, small joint arthroscopes, and suture anchors designed for hand/wrist and foot/ankle procedures.

For the ankle, diagnostic arthroscopy is appropriate for patients with a chronically painful symptomatic ankle for which nonoperative treatments and proper diagnosis have failed. In addition, athletes with severe ankle sprains that don't respond to conservative treatments may have localized synovitis that is amenable to arthroscopic treatment with entry through the anteromedial and anterolateral ports.

CHALLENGES FOR ARTHROSCOPIC AND SOFT TISSUE MARKETS

Among the biggest hurdles in the soft-tissue repair market are downward pressure on medical device reimbursement levels by third-party payers such as government healthcare programs, private insurance plans and managed care organizations. *(Also see "Total Joints: Bundled Payments Driving Procedural Innovation" - Medtech Insight, 26 Apr, 2016.)*

Consolidations and mergers by ambulatory surgery centers, hospitals and insurance companies will also enhance pricing pressures. And the rising purchasing power of entities that negotiate on behalf of Medicare, Medicaid and private sector beneficiaries will also limit device price increases.

The falling reimbursement rates for arthroscopic procedures is also constraining growth in the overall arthroscopy devices market. Other factors limiting growth include a strengthening US dollar vs. ex-US currencies and slow growth in China and the Gulf States.

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How GE Healthcare Is Taking Health Care Out Of Hospitals And Closer To Home

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With 32 years' experience in the ultrasound industry, Anders Wold, president and CEO of GE Healthcare's Clinical Care Solutions business has seen firsthand the impact of disruptive technologies in health care. The industry veteran joined GE in 1998 through the group's $230m acquisition of Diasonics/Vingmed Ultrasound, then a division of Haifa, Israel-based Elbit Medical Imaging.

Since then, he has led GE Healthcare's cardiovascular ultrasound and global ultrasound businesses and in July 2016 took over its new Clinical Care Solutions business. This division represents a $5bn business that provides health care professionals with a variety of medical technologies, covering ultrasound, monitoring technology, maternal infant care, anesthesia and respiratory care, and cardiology.

"There's been rapid changes in this industry because of two or three key drivers," says Wold. "Technology and smartphones have evolved and we are basically following that curve as a health care company. Globalization is a massive driver of production and new technology. Also, all the educational borders are falling too as people are gaining more access to technology and education."

But despite a technological revolution, the health care industry is navigating choppy economic waters to which even an industry heavyweight such as GE is not immune. Wold says that one of the major challenges is having to address the concerns of health care payers who are "completely frustrated."

"The costs are through the roof and everybody is putting in new legislation to minimize costs but the thing is this hits patients. There is no productivity in the hospitals anymore as governments are putting in brakes so there's a huge problem with [managing] costs. At the same time with technology and mobility there is so much

Source: GE Healthcare

> We face resistance and barriers from payers but ultimately this resistance is going to actually force the middle classes and other people to get access to technology at home. It's an opportunity, it will help us to work outside the hospital and develop more digital solutions for use in other areas with lower risk." – Anders Wold, president and CEO, GE Healthcare Clinical Care Solutions

information out there that can help us do better diagnosis if we use tools like artificial intelligence and analytics to get connected."

Wold says GE Healthcare is now in a "transformation phase" as it strives to evolve from a "standard industrial company to a leading digitalized one." In March, it acquired *Novii*, a wireless maternal and fetal monitoring device through its acquisition of UK-based company Monica Healthcare. *(Also see "GE Healthcare Patches In Wireless Fetal Monitoring Device" - Medtech Insight, 20 Mar, 2017.)* The wireless patch picks up maternal and fetal heart rates, as well as uterine activity simultaneously, then communicates this information wirelessly through Bluetooth to the fetal monitor. It is currently only available in the US, but will soon be distributed across the world at a time where demand for neonatal and fetal care equipment continues to grow.

According to Wold, this type of miniaturized monitoring technology with wireless capabilities is the future of health care. He believes diagnostics is shifting from outside the hospital and closer to clinics and homes. "These days we face resistance and barriers from payers but ultimately this resistance is going to actually force the middle classes and other people to get access to technology at home," he says. "It's an opportunity, it will help us to work outside the hospital and develop more digital solutions for use in other areas with lower risk. We want to increase accessibility to healthcare and start monitoring more health in the home. Hospital care is expensive and it can actually be a dangerous place, people go there to be treated but there is a risk of exposure to infection and other threats."

This increase in portable, miniaturized technology will also be instrumental in driving health care access in developing countries he says. In early 2017, GE Healthcare launched its first app-based wireless ultrasound device the *Vscan Extend*. *(Also see "GE Healthcare Extends Portfolio With First App-Based Ultrasound Device" - Medtech Insight, 19 Jan, 2017.)* The handheld device, includes two ultrasound probes built into a transducer head which is connected to a smartphone interface with wireless connectivity to integrate with hospitals DICOM systems. During development of the device, Wold travelled to Dhaka, Bangladesh. "I wanted to pick the most extreme, remote location to test it out in, so I went to three small slum cities around Dhaka. They had one medical doctor for the whole area, who was not actually a medically trained doctor but just the oldest woman in the village," he says. The miscarriage rate in the village was high due to a lack of diagnostics and available healthcare services. "When we gave them this device and saw that it improved diagnostics and natal care, we realized, there is something really good we can do here."

It's this solution-focused, global approach that is now at the centre of GE Healthcare's Clinical Care Solutions business, as it prepares to grow this year. And Wold insists the company is not concerned about its competitors. "We don't just sell boxes, we sell outcomes – something that is tangible for the payers and patients," he says. "We try to put as much quality as we can in our products using technology like data, analytics and the Cloud and putting it at the fingertips of the physicians so they can have much better diagnostics."

"At the same time the other part of the outcome is better productivity – can this do the process faster? Can we minimize workloads? That's what outcome is all about, to do this in a faster way. We are designing products and solutions specifically to meet productivity. Other players in this industry are still thinking about boxes, but we are not in the business of selling boxes; we are in the business of selling solutions. That's really the theme of where we are going."

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M&A ANALYSIS:

April Showers Big Name Acquisitions

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M&A deal-making picked up in April after a quiet March with 14 deals recorded by *Medtech Insight*'s M&A deal tracker. Deal volume was up by four from March's total but down two from the total in April 2016. The month was marked by two major billion-dollar transactions inked between medtech heavyweights Becton Dickinson and CR Bard, and Medtronic and Cardinal Health.

In the biggest deal of the year to date, **Becton Dickinson & Co.** reached a definitive agreement to acquire **CR Bard Inc.** for $24bn. *(Also see "BD, CR Bard Merger To Create Vascular Access Device Giant" - Medtech Insight, 24 Apr, 2017.)* It may be some way off in beating Medtronic's $43bn record breaking acquisition of Covidien in 2015, but it was close to Abbott's $25bn acquisition of St. Jude Medical, inked last year.

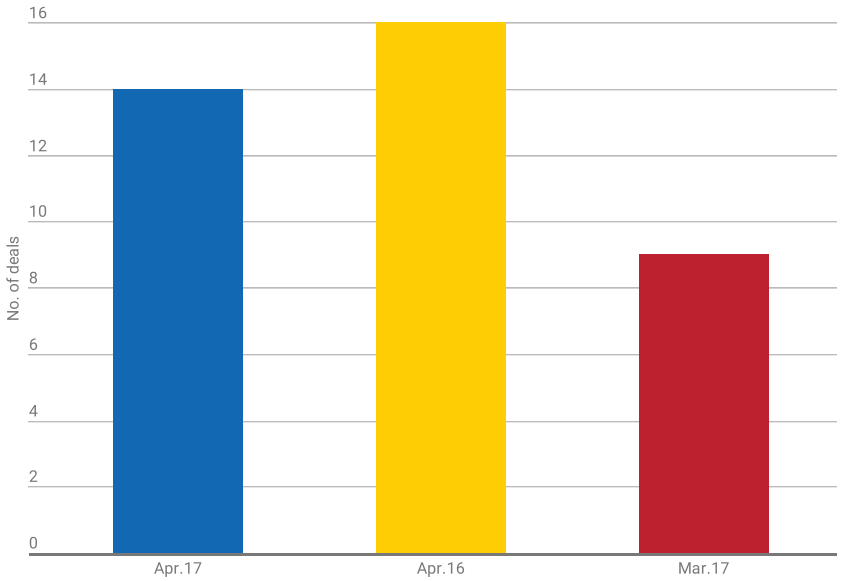
During an April 24 conference call to discuss the agreement, Becton Dickinson CEO Vincent Forlenza said the deal entered BD into "new-higher growth, therapy-oriented device segments." BD will add Bard's portfolio of peripheral vascular therapy, oncology and surgical products to its offerings with BD citing Bard's leading position in peripheral vascular disease and strong presence in general surgery as important assets motivating the deal.

Under the terms of the transaction, Bard shareholders will receive $222.93 in cash and 0.5077 shares of BD stock per Bard share, giving the share offer a total value of $317. BD will fund the deal with about $1.7bn in available cash, about $10bn of new debt, $4.5bn in equity and equity linked securities issued to the market, and bridge financing.

In its second deal for the month, BD also acquired Israeli-based Caesarea Medi-

FIGURE 1

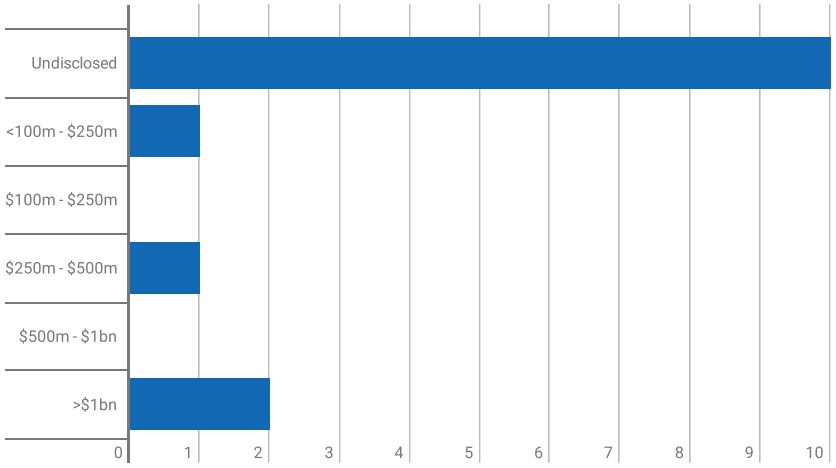
M&A Deal Volume, Apr. 2017 Vs Apr. 2016 Vs Mar.16



Source: Medtech Insight M&A tracker

FIGURE 2

No. Of M&A Deals By Value, April 2017



Source: Medtech Insight M&A tracker

cal Electronics (CME) for an undisclosed price. CME manufactures and markets infusion pump systems and will expand BD's infusion portfolio to include ambulatory, home and specialty acute care infusion pumps. In a statement, Mike Garrison, vice president and general manager of worldwide Infusion Solutions for BD said: "The integration of CME's technology into BD will strengthen our strategy of reinventing medication management across the health care continuum."

For April's second biggest deal, **Medtronic PLC** agreed to sell its medical supplies business to **Cardinal Health Inc.** for $6.1bn. *(Also see "Cardinal Health, Medtronic Tie Up $6.1bn Lower-Margin Assets Deal" - Medtech Insight, 18 Apr, 2017.)* The deal slims down Medtronic's offering in what it calls lower-growth, lower-margin segments, following the completion of its acquisition of **Covidien Ltd.** in 2015. The proceeds from the divestment of its patient care, deep vein thrombosis and nutritional insufficiency businesses will immediately boost Medtronic's debt situation. The three businesses had been inherited from Covidien and encompass 23 product categories. Shares in Medtronic rose 1.89% following the news but sent Cardinal Health's share price down by 12%, as the transaction will further weigh down on the latter's debt burden.

Johnson & Johnson had an active month as its orthopedics unit **DePuy Synthes** acquired a 3D printing technology for making skeletal reconstruction and bone regeneration scaffolds from **Tissue Regeneration Systems Inc.** (TRS) **(***Also see "DePuy Synthes Builds Out Trauma Offering With TRS' 3D-Printed Tech" - Medtech Insight, 20 Apr, 2017.***)** The 3D-printing methods developed by TRS will enable DePuy Synthes to create patient-specific, bioresorbable scaffold implants. Financial terms of the deal were not disclosed. It is the second transaction of the year so far for DePuy Synthes, who acquired orthopedics company **Interventional Spine** in January.

Codman Neuro, part of DePuy Synthes, also inked a deal to pick up **Neuravi Ltd.**, a privately held Irish stroke care company. Neuravi currently markets the *EmboTrap-Revascularization Device*, a thrombectomy system designed to restore blood flow to the brain by capturing and removing blood clots. The device is available in Europe, with clinical trials currently held in the US. Terms of the deal were not disclosed.

"Rapid restoration of flow is of utmost importance when treating stroke patients," said Shlomi Nachman, company group chairman of J&J's Cardiovascular & Specialty solutions in a statement. "The EmboTrap platform was designed to address this critical need and we are excited to combine Neuravi's expertise in clot research with Codman Neuro's global resources to accelerate innovation in acute ischemic stroke treatment."

The deal follows Codman Neuro's recent acquisition of Pulsar Vascular in Dec. 2016. Codman Neuro was previously the exclusive distributor of Pulsar Vascular Inc.'s *PulseRider* device, a nitinol implant used to bridge the neck of cerebral aneurysms. The acquisition follows the announcement in January that **Integra Life-**

Sciences would purchase Codman from Johnson & Johnson for $1.05bn.

Swiss firm LifeWatch was offered an attractive deal from US rival BioTelemetry, worth approximately $247m. The company had recently been subject to a proposed takeover by Swiss investment firm Aevis Victoria SA for a reduced price. LifeWatch rejected the offer, stating it was an "inadequate valuation." *(Also see "BioTelemetry Trumps Aevis' Takeover Bid For LifeWatch" - Medtech Insight, 12 Apr, 2017.)*

In other news, Abbott and Alere put their differences to one side with Abbott agreeing to buy the company for $5.1bn, an 8.9% cut from the deal originally announced in February 2016. Under the terms of the amended agreement, Abbott will pay $51 in cash per share for Alere, instead of $58 per share. *(Also see "Despite Legal Dispute, Abbott Set To Buy Alere for $5.3bn" - Medtech Insight, 18 Apr, 2017.)* The agreement ends months of acrimony between the two companies' after Abbott decided to back out from the planned deal just weeks after it was inked following the emergence of concerning revelations of Alere's overseas business practices. *(Also see "Abbott Steps Up Effort To Abandon Alere Deal" - Medtech Insight, 7 Dec, 2016.)*

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Can Alibaba Use Artificial Intelligence To Solve China Health Issues?

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Armed with big data and deep learning capabilities, Alibaba is decisively venturing into personalized healthcare, a fast-growing area in China.

Alibaba may be years behind established personalized healthcare players such as **PatientsLikeMe Inc.** and IBM's Watson, but the Chinese tech heavyweight believes it can catch up quickly. The Hangzhou-based group – which has been compared to the multinational ecommerce giant ebay – is armed with a rich trove of user information and it is preparing to make a big splash in user-based healthcare services, leveraging partnerships with both Chinese and overseas top academic institutes.

Just two years ago, personalized healthcare was still new to China, but now a new crop of companies including Alibaba is getting ready to tackle the issue. Even so, CEO Jack Ma stressed at a recent IT summit that "human beings should take the responsibility to develop machines as partners, not replacing humans."

Emerging China AI And Big Data Healthcare Firms

NAME	LOCATION	BUSINESS	FINANCING
Alihealth	Beijing	E-commerce, insurance, health management	
Linkheart	Beijing	Oncology information integration and sharing	CNY12m angel round
Vishu	Beijing	Biomarker identification	
Deepcare	Beijing	Medical imaging analysis software	CNY6m angel round

AUTONOMOUS AGENTS

One area Alibaba is initially developing is patient-hidden modeling, a service using the autonomous agent approach to aid the automated analysis of medical images, noted Yuan Quan, senior director and researcher at the Alibaba Intelligence and Precognitive Lab.

"The agent is like a guiding light amid a maze of organs to find a target," said Yuan during a medical imaging forum, held April 29 in Tsinghua University. A graduate of Tsinghua, Yuan said the Alibaba model uses tagging data to build a neural network and then use this to analyze images.

To help this goal, Alibaba in March launched a medical imaging competition offering RMB1m ($149,000) in prize money to attract the best talent to solve growing health issues. One of these was the diagnosis of sarcoidosis, an inflammatory disorder in which nodules form on organs including the lungs.

Despite undergoing CT scans, patients also usually require a biopsy to be diagnosed, which drives up medical costs and patient inconvenience. So far, the competition has attracted 1,290 teams including from Peking University, Tsinghua University, global medical facilities, and also the **Philips Healthcare** China Research Center.

PARTNERSHIPS CRITICAL

Additionally, Alibaba is partnering with Intel and the Beijing-based oncology diagnosis and big data firm **LinkDoc** in the competition to help scout talent, find appropriate algorithms, and analyze computer tomography lung images to precisely diagnose sarcoidosis.

Recognizing its own limited resources, Alibaba is also teaming up with overseas institutes to beef up its intelligent cognitive deep-learning capabilities. Projects include bilateral BiCNet and multi-agent mining for PubMed text, the goal being to help analyze gene expression, Yuan said.

It is also moving into other areas of health IT, setting up a healthcare subsidiary Alihealth to help drug makers trace counterfeit products.

EMERGING PLAYERS, TECH

Other China e-ecommerce giants like Baidu and Tencent have increased investment in offering personalized healthcare services *(Also see "Asia Execs To Watch: China's Tencent Snatches Up Healthcare Talent" - Scrip, 5 Apr, 2017.)*, and so has the Chinese government.

On April 25, the government of Fuzhou

launched the China National Healthcare Big Data Center, one of two recent such moves.

Facing a gap due to medical resources being heavily concentrated in large cities despite increasing demand from patients living in lower-tier cities, China is ripe for explosive growth in remote diagnosis powered by AI and big data, industry experts predict.

Already, companies like **BGI-Shenzhen** have been working on patient consent forms that can be read by machines, and IoT (internet of things)-supported biodata banks.

However, challenges remain, one of the main ones being a lack of data standards. That's one major purpose behind the building up the SnoMed CT (Systematized Nomenclature of Medicine – Clinical Terms) system in China, said Gong Mengchun, SnoMed China head and director of National Rare Diseases Registry System of China.

In addition, electronic medical records plus patient data will become increasingly adopted in China, he predicted.

Given the current activity and bright outlook, startups devoted to personalized medicine are popping up across China, including **Vishu Medical**, founded in 2011 and devoted to precision medicines. With its individual clinical medicine database, Vishu aims to provide biomarkers to help in the disease diagnosis and treatment of individual patients.

Another company is **Linkheart** (Lianxin) **Medical**, a startup devoted to the integration of oncology information, data sharing, and remote treatment. Started by a software engineer, the company aims to drive up radiology therapy rates in China based on data analysis and personalized treatment optimization.

The company is currently testing a system at the Sichuan Cancer Hospital, PLA Navy Hospital, and PLA Air Force hospitals.

Such real word data will be analyzed towards knowledge database building and information sharing, and will have huge potential in China as the country experiences a massive jump in the occurrence of chronic diseases, Gong predicted.

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START-UP SPOTLIGHT:

Atlantic Therapeutics, Stimulating The Stress Incontinence Market With Vaginal Mesh Alternative

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Vaginal mesh implants, devices used to treat pelvic organ prolapse and stress urinary incontinence, have repeatedly hit the headlines over the last few years, as women who suffered serious complications caused by the devices eroding through the tissue battle mesh makers in court. Payouts to these patients in the US have so far totalled several billion dollars and, more recently, over 800 women in the UK are taking legal action against the National Health Service. One member of UK Parliament has also advocated a further government investigation into the use of the surgical mesh.

"When pelvic mesh was first launched in the 1990s, it was not anticipated that it would have so many adverse events post-market," says Steve Atkinson, CEO of Irish firm **Atlantic Therapeutics Group**, which offers a viable noninvasive alternative to mesh. "As a result, mesh is now being relegated to a line of last resort," he tells *Medtech Insight*.

Atkinson notes that patients and regulators alike are seeking a safer, noninvasive and clinically effective solution. "I think our timing is perfect," he says of his company's first-line therapy, *Innovo*, an externally applied device that delivers electrical stimulation to treat stress urinary incontinence. Encircling the pelvic floor is an array of eight electrodes which elicits prominent contraction. "Our device retrains the pelvic floor muscle to become strong again."

Atkinson observes he has never encountered a medical device that garners such strong, positive, emotional feedback as Innovo. The therapy, designed primarily for home use, entails the user wearing two compression garments, each wrapping around a thigh and leg. The garment is then attached to a handheld controller, which automatically activates the electrical stimulation program. "You can change the intensity during therapy, based on your tolerance," Atkinson says. "The more you can tolerate, the more effective the treatment. But the therapy is not painful, just a strange sensation as your muscles internally contract."

Each 30-minute session consists of 180 contractions, and a typical treatment course would be five sessions a week for up to 12 weeks. Users tend to wear thong-type clothing underneath the device. They can also recline on a sofa with knees slightly bent; stand up and lean slightly forward; or lie down, flat on their back, with knees up. In each case, treatment is discreet, with the option of wearing a garment like a large pair of shorts or a sarong over the device, while watching TV, for example.

Atkinson acknowledges that Innovo would not be able to treat all patients. "There will still be a need for surgery, but it will likely be limited to the most severe cases with multiple complications, representing 5% to 10% of overall cases," he says.

Innovo is mostly being marketed to young active mothers, women going through menopause and men who have had prostate surgery in the UK, France, Germany and the US. This translates into a market opportunity of 47 million potential users; dollar-wise, this could lead to sales of $19bn, along with a recurring annuity of another two million new therapy candidates for an additional $800m.

The product was CE marked in 2012, and de novo 510(k) approval from the US FDA is expected late this year.

The principal inventor of Innovo is Conor Minogue, director of R&D for Biomedical Research Group in Galway, Ireland, which previously developed an abdominal toning and tightening product (marketed as *Slendertone* in Europe

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Website:
www.atlantictherapeutics.com

Contact: Steve Atkinson, CEO

Industry Segment: Gynecology/ Urology

Business: Novel noninvasive device to restore continence by providing strong, sustained repetitions that contract the entire pelvic floor muscle during 12 weeks of at-home therapy

Founded: Late 2015, as a subsdiary of Bio Medical Research; spun out as independent company in March 2017, after Series A financing

Founders: Steve Atkinson, CEO; Padraic Clarke, CFO; Conor Minogue, PhD (Biomedical Research Group, Galway, Ireland); Ruth Maher, PhD (Creighton University, Omaha, NE).

Employees: 30

Financing to Date: €15m ($16m)

Investors: Seroba Life Science Partners; Earlybird Venture Capital; Silicon Valley Bank

Board of Directors: Steve Atkinson, Daniel O'Mahoney, PhD (Seroba Life Science Partners); Thom Rasche (Earlybird Venture Capital); Bernard Collins, PhD (Biomedical Research Group).

Scientific Advisory Board: Francois Haab, MD; Roger Dmochowski, MD (Vanderbilt University, Nashville, TN); Ralf Tunn, MD; Linda Cardoza, MD (King's College London); Ash Monga, MD; Sonia Soeder; Ruth Maher; David Kaysen (formerly of Uroplasty Inc).

and *Flex Belt* in the US). "Unlike the abdomen, though, the pelvic muscles are deep inside the body and therefore it is difficult to access the nerves which cause them to contract," Atkinson explains. "Conor and his team not only invented and discovered the position of the electrodes, which is patented, but they figured out how to move the current between the electrodes to elicit a powerful contraction."

Live ultrasound was used to watch the pelvic floor muscles while experimenting with various electrode positioning and different current pathways. "It all came together with a eureka moment," Atkinson says. The time from proof-of-concept research to commercial launch was four years, starting in 2009, with first results published in *Journal of Women's Health* in 2010.

Atkinson has over 20 years' experience in the medical device field, including 10 years at Johnson & Johnson, from 1989 to 1999, where his last role was as managing director and vice president of J&J's patient monitoring franchise Critikon Dinamap. He also served as vice president of North Europe for CR Bard Inc., from 2002 to 2008, and as international senior vice president for Zeltiq Aesthetics Inc. – the body-sculpting specialist acquired recently by Allergan – from 2011 to 2013.

Atlantic Therapeutics has four issued and one pending patent. Additionally, it makes a small royalty payment to the University College Dublin, which co-developed the technology.

Innovo will initially be available in the US as a prescribed therapy, as is the case in France and Germany. "However, in the US, we plan on filing a second 510(k) next year for over-the-counter and direct-to-consumer indications, as it is in the UK, because this is a larger accessible market," Atkinson says. "Most people who suffer from incontinence are too embarrassed to even visit their doctor. They would rather purchase the product discreetly online."

Innovo's closest competitor class is an active electrostimulation probe, led by **InControl Medical LLC** (*InTone*), which is inserted in the vagina at home or in the clinic. "Tiny electroplates stimulate a small amount of muscle around the probe, but it does not elicit a full contractile response of the pelvic floor," Atkinson says. "The main difference is that probes are internal, whereas ours is external. Probes are also associated with a relatively high adverse event rate, causing bleeding, irritation and vaginitis."

The second closest competitor class are biofeedback probes from companies such as **Elvie** (*Elvie*) and **Analytica Limited** (*PeriCoach System*), both Kegel exercisers whereby the probe is also inserted in the vagina, but the user tries to squeeze the probe with her pelvic floor while simultaneously gamified (like a bouncing ball) on a smartphone. "However, between 30% and 50% of women are unable to perform Kegel exercises," Atkinson notes. "Clinical trials of biofeedback probes show they are also subject to infection and other adverse events."

The reimbursable Innovo, which retails for $399, debuted in March 2016 in the UK, followed shortly thereafter in Germany and France. The company uses a direct sales force in Germany; a contract sales force in France; and all-direct to consumer in the UK, which is handled by retail account managers.

The €15m ($16m) raised to date by the company represents a single Series A round, which closed in February and was jointly led by Seroba Life Science Partners and Earlybird Venture Capital. For the US launch in mid-2018, the company may raise roughly $5m in a Series B round, tapping a combination of a strategic in medical or consumer health and a financial investor.

The most likely exit plan is a trade sale in three to five years to a large medtech or consumer health firm. "If you want to be the major player in incontinence, then you will need to own Atlantic Therapeutics," Atkinson claims.

The second generation of Innovo will be even more consumer-friendly, with Spandex-type shorts that conceal the eight electrodes and a smartphone app to replace the controller. The shorts will debut next year, followed by the app in early 2019.

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