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Expanding Elderly Population Gives Leg Up To Osteoporosis Dx Growth

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The demand for products to diagnose osteoporosis – in particular, bone densitometer devices – continues to rise globally amid the growing aging population and high incidence rates of osteoporosis and associated fractures.

According to Datamonitor Healthcare, the number of adults with osteoporosis in the US will climb from 9.8 million in 2015 to an estimated 11 million in 2020, then to 13.3 million by 2030, representing a 34% increase from 2015. In the five major EU markets (France, Germany, Italy, Spain and the UK), 2015 saw around 28.9 million cases osteoporosis, and this is expected to reach 31.2 million in 2020 and 35.2 million by 2030. However, neither the US nor these EU big-five countries are able to beat Japan, where there is a very high incidence of osteoporosis in relation to its population; in 2015, Japan recorded 12.1 million cases, and this is expected to reach about 12.3 million cases in 2020 and 12.9 million by 2030.

In tandem with the global rise in osteoporosis, sales of products to diagnose this condition – which includes measuring bone mineral density using bone densitometers and biochemical marker tests to measure bone turnover or remodeling – are anticipated to expand from $253m in 2015 to $304.2m by 2020 (CAGR 3.8%), according to a new *Meddevicetracker* report, "Women's Health: Osteoporosis Diagnostic Products."

However, factors such as recent healthcare reform and reimbursement issues, are expected to stifle market growth in the US and Europe, whereas the emerging markets, especially Asia-Pacific, with its growing middle-class and aging population, offer manufacturers more lucrative opportunities.

GLOBAL MARKET ANALYSIS

Bone densitometer testing, known for its high degree of accuracy and wide acceptance by users, remains the gold standard for diagnosing osteoporosis.

That said, the system has its limitations. For instance, densitometers have a high predictive value for diagnosing fractures, but a low predictive value for diagnosing osteoporosis, according to the *Meddevicetracker* report. Conversely, biochemical marker tests have a high predictive rate for diagnosing osteoporosis, but a low predictive value for diagnosing fractures. Bone densitometry is recommended every one to five years; biochemical markers require retesting a patient's blood or urine every two to three months to obtain information

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

MDMA
MEDICAL DEVICE MANUFACTURERS ASSOCIATION

MDMA FDA Forum: PMA/510(k) Workshop

MARCH 8-9, 2017 | PALO ALTO, CA

Confirmed Speakers Include:

William Maisel
Deputy Center Director for Science and Chief Scientist, CDRH, FDA

John Sheets
Director, Office of Devices, CDRH, FDA

Thinh Nguyen
Director, Office of Combination Products, FDA

Bakul Patel
Associate Director for Digital Health, Office of Center Director, CDRH, FDA

Murray Sheldon
Associate Director for Technology and Innovation, CDRH, FDA

Marjorie Shulman
Director, Premarket Notification [510(k)] Program, Program Operations Staff, ODE/CDRH/FDA

John Weiner
Associate Director for Policy and Product Classification Officer, Office of Combination Products, FDA

Barbara Zimmerman
Deputy Director, Premarket Program Management, Office of Device Evaluation

MDMA's popular FDA Forum will be held in **Palo Alto, CA from March 8-9, 2017**.

The FDA Forum will focus on unique insights and strategies to govern the 510(k) and PMA regulatory pathways, as well as what changes to expect with the recently negotiated user fee reauthorization, FDA reform efforts and more. Numerous interactive panels will be led by FDA officials, industry leaders and policy experts.

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http://bit.ly/2kpfYH3
After a long search, Europe's no. 4 TAVR player Symetis has picked Middle Peak Medical as its maiden acquisition and portal to the mitral valve space.

Allergan builds aesthetics biz
http://bit.ly/2lgCX6I
Zeltiq's *CoolSculpting* body-contouring system will be the third "pillar" in Allergan's aesthetics business, along with its existing facial aesthetics and plastic and regenerative surgery lines, the company says.

Adverse-event trend
http://bit.ly/2lLmzMr
Overall US device adverse-event reports dipped slightly in 2016, while summary reporting ticked up.

Price capping in India
http://bit.ly/2kxHRb2
AdvaMed is crying foul in response to the Indian government setting a price ceiling for coronary stents for a year.

Device Week
http://bit.ly/2kxHRb2
Our weekly podcast, where *Medtech Insight* journalists discuss topics they are covering that impact the device and diagnostics sector.

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inside:

Medtech insight

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Q&A: Choosing An EU Notified Body For Drug/Device Combinations In A Rapidly Changing Environment

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It is no easy task to find a notified body that has experience with a company's particular device and also has the staff and capacity to manage it. With many notified bodies leaving the medtech sector, companies are forced to look around for alternatives.

The challenge is even more complex for manufacturers of drug/device combination products that are categorized as class III medical devices. There are not many notified bodies operating in this area, and there may be even less available in the coming year.

Such notified bodies that are working in the medtech field are under increasing pressure, and this is impacting companies too. Even if a company believes it has found an appropriate notified body for its device-type combination products, it then also has to work through the notified body with a drug authority. This adds an additional layer of complexity and variability as few drug authorities operate in this area, and those entities are also experiencing increasing demands.

Arkan Zwick

CLICK
to find part 2 online
This is the first of a two-part Q&A. Check out the second half online at http://bit.ly/2IjQ9Y3.

Medtech Insight asked Arkan Zwick, regulatory affairs and legal director at Croma Pharma GMBH (Austria), which makes aesthetic dermatology products, how his company proceeds and what advice he has for others in the area.

Medtech Insight: Can you explain, briefly, the bodies or organizations that need to be involved with class III device-type drug/device combination product in the EU and beyond?

Arkan Zwick: There are two main regulatory routes for drug/device combination products in the EU, according to the principal intended use of the combination. One is the path for drug/device combination products where the medicinal product has the primary action and the medical device acts as the administration kit. In this case, the medicinal product competent authorities or the European Medicines Agency are responsible under EU Directive 2001/83 for the medicinal product, and the device must be CE-marked separately under the CE-marking regime. The combination must then be reviewed by the medicinal product competent authority or the EMA [European Medicines Agency] during the drug approval.

For device-type device/drug combinations, where the device has the principal action and the drug enhances it, the main responsibility is with the EU notified body under EU medical device directives. This notified body must seek the scientific opinion of a drug competent authority for the drug component's quality and efficacy, and for the justification/usefulness of the medicinal substance.

The regulatory route for drug/device combinations beyond Europe is usually different. Normally, just one regulatory authority, for example in the US, FDA; Japan, PMDA; and Canada, Health Canada; or the Chinese CFDA, deals with both device and drug parts, although making use of its different departments.

Not all notified bodies in the EU have expertise in the drug/device combination area. How should companies go about selecting an appropriate notified body?

Zwick: The European Commission's Nando database offers a list of designated notified bodies and the product areas in which they work, so it is possible to find out which operate in the drug/device area.

When it comes to the notified body selection criteria, the most critical is scope and experience in dealing with drug/device combinations. Lots of notified bodies have never been active in this area, and others who are may be struggling to cope in the current increasingly strict environment.

If a notified body says it is active in the drug/device combination area, then the next question that needs to be asked is which of the competent authorities they have experience working with in Europe. It is also important to find out about the experience of both the notified body and that competent authority with the drug substance in the combination product that the company wants reviewed.

Is it an advantage for companies to stay with the same notified bodies?

Zwick: Companies should be prepared to shop around for different notified bodies. A new product offers the chance to go with a new notified body and this will provide future flexibility and mitigate risks in the event that a notified body ceases activity in their area – which could be an issue with the introduction of the new Medical Devices Regulation.

At Croma, our approach is to draw up a project plan and the key topics that we would like to discuss with the notified body via briefing books. We describe the drug and device, and the pre-clinical and clinical package, and then address the key questions we want clarified with the notified body via scientific advice meetings. These meetings serve to clarify the critical points with regard to the application requirements for both the device and drug part, format requirements, review steps and timelines, as well as cost implications.

It is also worth considering whether the notified body is co-operating in the MDSAP [Medical Device Single Audit Program], CMDCAS [Canadian Medical Device Conformity Assessment System] or the Taiwan cooperation programs, which would enable the manufacturer to gain easy access to these markets.

What about the time it takes for the review of products?

Zwick: Also important, and not just for combination products, is an agreement on binding timelines on the review of the medical device and drug elements. The notified body will usually ask for preliminary notification of new projects at least six months in advance. This timeline can extend to 12 months if an additional quality system ISO 13485 audit is involved. In addition, competent authorities have internal guidelines for complete or supplementary consultations of the drug part.

However, when it comes to the binding character of agreed timelines, most of the notified bodies try to limit their liability within their terms and conditions for not respecting the timelines. It is very difficult to negotiate these. The notified bodies are bound to their review slots for when companies submit their files. But when it comes to the ongoing review process, and especially in relation to the competent authority, they are reluctant to give any binding statements, just to commit to informing companies if the review is prolonged. They do not accept any liability for their own timelines, nor for the authorities.

To what degree have costs risen over the last 12 months?

Zwick: This year, I would say the preclinical modules and the manufacturing assessments have risen by around 15%, but the clinical review can be a challenging process, especially since the arrival of the latest fourth revision of the new clinical investigation guidance, MEDDEV 2.7.1, and related new interpretation of clinical requirements in the context of the upcoming EU Medical Devices Regulation (MDR), and so costs have risen even higher in this area. For those companies that were basing their clinical evaluation on the equivalence approach – the burden has significantly increased, reviews are taking longer, and there are more extended discussions and additional costs. This is the most critical for class III, high-risk products, implantable products, and drug/device combination products.

Also, with the notified bodies having to undergo joint audits by the European Commission and at least two designating authorities as a result of the European Commission's immediate plan of action (after the PIP scandal), there has been a significant increase in costs and administrative burdens due to unannounced inspections. At the same time, many notified bodies have stopped operating in the medtech area, or restricted their scope and excluded high-risk devices from their activities.

Now, with the new Medical Devices Regulation taking effect in a few months' time, there will be reaccreditation of all notified bodies during a transition period of up to 12 months. This will take time, and as notified bodies are struggling to recruit qualified staff, they are having to increase fees and transfer their extra costs to manufacturers.

Now, with all the costs having been raised significantly by all the notified bodies in the light of the much stricter requirements, it is difficult to find a cost advantage.

How many notified bodies, do you think, will continue to offer conformity assessment services for combination products under the new regulations, and during the transition to these regulations, and why?

Zwick: If you look at the European Commission's Nando database, you can see the active accreditations and the withdrawn ones in the medtech sector overall, and you can see that the numbers have decreased significantly – from over 80 a few years back to around 60 now. There is speculation that there will be an additional drop of 25% in medtech notified bodies during the MDR transition period because of the cost and quality challenges for notified bodies, and the lack of available qualified staff. So, that would leave just some 40 notified bodies in the medtech area. And probably no more than 10 notified bodies will offer services for high-risk combination products.

The ones who are likely to be reaccredited first in this combination area: TÜV Süd (Germany); SGS (UK); BSI (UK); LNE-GMed (France); DEKRA (Netherlands). There are likely to be up to five that follow, most likely including TÜV Rheinland and MDC, both in Germany. It is also possible that there will be newcomers in this area.

The MDR transition period is due to begin in May or June, with notified bodies invited to make applications for reaccreditation to start after six months. We should know within 12 months after the publication enters into force which are likely to be accredited in this area.

There is a very real risk that some notified bodies that operate in this area may decide to cease assessing device-type drug/device combination products because of the ever-increasing regulatory demands on them. How can companies reduce the risk of choosing a notified body that may cease its activities in this area?

Zwick: The key is active communication with the notified body, starting immediately with notified bodies the compa-

nies are working with. Companies can address these questions actively via audit preparation or new product submissions. They should ask about the notified body's internal planning to be re-designated under the MDR and other programs such as ISO 13485:2016 or MDSAP.

But will companies receive a straightforward answer?

Zwick: I would suggest preparing a written communication intended to assess the notified body's processes, capability and plans. I would ask the notified body for a written response. Where we receive replies and we see they have a good plan, then we would have no hesitation in hiring them. If there is a doubt, then it is reasonable to look for alternatives. At Croma, we offer regulatory services to other medtech manufacturers and we have a lot of customers that are searching for new notified bodies that work in the drug/device combination product area at the moment, and we support them in this.

It is an expensive and disruptive process to change notified bodies. It involves product reaccreditations including quality system audits against the medical device quality systems standard ISO 13485; it is difficult to find slots – if you ask notified bodies now, many do not have review slots until the end of the year, if at all.

It makes sense to work in parallel with several notified bodies in order to have alternatives for different product groups.

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As ACA 'Repeal-And-Replace' Plans Form, Some Senators Silent On Device Tax Repeal

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An Obamacare "repeal-and-replace" plan will not be ready until late 2017, President Trump says, and he has submitted a plan for OMB review to bolster insurance companies' confidence in the marketplace.

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While a majority of US House members are enthusiastically supporting legislation to permanently remove the medical device excise tax this year, alongside general Republican-led efforts to repeal and replace Obamacare, support for a permanent device tax repeal is less overt in the Senate.

Fewer Senators are cosponsoring device tax repeal bills than did in 2015, when the tax was suspended for a two-year period, and among the series of proposed repeal-and-replace bills that have been offered in the Senate this year as of Feb. 6, at least two make no mention of the excise tax.

The device industry, meanwhile, has stepped up its lobbying efforts to win permanent repeal of the device tax, including running an ad campaign aimed at lawmakers. *(Also see "AdvaMed Anti-Device Tax Campaign Takes Aim At Reconciliation Bill" - Medtech Insight, 3 Feb, 2017.)* And on Feb. 8, AdvaMed released data from the US Department of Commerce that it says demonstrated job losses that resulted from the device tax when it was in effect.

As to the administration's efforts to replace the broader Affordable Care Act (Obamacare), which was the legislative vehicle for the excise tax, President Trump recently backed off on campaign pledges and promises early in January to repeal Obamacare by the end of February. He told news outlets Feb.5 that the effort to replace the law probably will not be finished until late 2017 or early 2018.

In the interim, the White House submitted a proposed rule addressing important sections of ACA – details of which are not yet public – to the Office of Management and Budget. The proposal is designed to tighten eligibility standards for health insurance marketplace coverage, according to the *Associated Press*. Until OMB releases the proposed rule after a review, it is not expected to be publicly availability.

The draft rule is expected to shorten the time of "special enrollment periods" that allows consumers to sign-up for health insurance on ACA marketplace exchanges, while relaxing a provision of the law that stops insurers from charging older Americans more than three times the premium that younger adults are charged.

Similar provisions are also featured in some of the proposed Senate and House Obamacare "repeal-and-replace" plans, as discussed below. Under a discussion draft of a House bill aired at a Feb. 2 House subcommittee hearing, older citizens could be charged up to five times what younger adults could be charged for their marketplace insurance premiums.

So far, the "Medical Device Access and Innovation Act," introduced by Sen. Orrin Hatch, R-Utah, in mid-January, has garnered only nine cosponsors.

TAX REPEAL COSPONSORS: HOUSE, SENATE DIFFERENCES

Meanwhile, the current standalone House bill to repeal the device tax, H.R. 184, the "Protect Medical Innovation Act," introduced by Reps. Erik Paulsen, R-Minn., and Ron Kind, D-Wisc., is very popular and has gained 245 cosponsors, more than a majority; 11 have joined the list in the past two weeks. Companion legislation in the Senate, S. 108, the "Medical Device Access and Innovation Protection Act," introduced by Sens. Orrin Hatch, R-Utah, and Amy Klobuchar, D-Minn., includes only nine cosponsors (including Klobuchar).

By early February in the 2015-2016 Congress, an identical bill to S. 108 introduced in the Senate by Hatch and Klobuchar had already gained 30 sponsors.

While some senators who cosponsored S. 149 in the prior Congress are no longer members (for example, former Sens. Dan Coat, R-Ind., who retired, and Kelly Ayotte, R-NH, who was defeated in the November election), most of those who previously cosponsored the device tax have not added their names to the list for S. 108 this year.

Among the Senators who have not "re-upped" this year as cosponsors on the current version of device tax repeal, but did so at this time in 2015, are Sens. Lisa Murkowski, R-Alaska, Tim Scott, R-SC, Roger Wicker, R-Miss., John Barrasso, R-Wyo., Susan Collins, R-Maine, Mike Crapo, R-Idaho, Cory Gardner, R-Colo., James Inhofe, R-Okla., James Lankford, R-Okla., Jeff Flake, R-Ariz., Jerry Moran, R-Kan., Pat Roberts, R-Kan., Roy Blunt, R-Mo., Shelley Moore Capito, R-WVa., Mike Lee, R-Utah, and Thom Tillis, R-NC.

Of course, they may still plan to do so, such as Sen. Lamar Alexander, R-Tenn., who chairs the Senate's Health, Education, Labor, and Pensions Committee. A spokeswoman for the senator told *Medtech*

Affordable Care Act "Repeal-and-Replace" Plans Compared

INTRODUCED/ PROPOSED PLAN	DEVICE TAX REPEAL?	INSURANCE SUBSIDY PLAN	BAN ON LIMITS ON PREEXISTING CONDITIONS?	PARENTS MAY KEEP KIDS UP TO 26 ON POLICY?	OTHER PROVISIONS
S. 191, "The Patient Freedom Act" (Sens. Cassidy, R-La., and Susan Collins, R-Maine)	NO	Ends the individual mandate (except for states that want to keep it); lets states provide subsidies to citizens to buy health savings accounts (HSAs) to pay for higher deductible, lower-cost plans.	YES	YES	No minimum essential benefits must be included in purchased plans.
S. 222, "The Obamacare Replacement Act" (Sen. Rand Paul, R-Ky.)	NO	The individual mandate to buy insurance is repealed. Individuals have the option of taking a tax credit for up to $5,000 per taxpayer for contributions to an HAS, or for those contributing more than $5,000 to a plan, health-care contributions are tax-preferred.	YES, but provides only a two-year enrollment period for those with preexisting conditions to buy coverage.	YES, but only if they meet the test for being financial dependents of the beneficiary.	No minimum essential benefits must be included in plans.
S. __, "The Patient CARE Act" (white paper) (Sens. Orrin Hatch, R-Utah, Richard Burr, R-NC, 2016)	YES	Ends the individual mandate under ACA. Citizens could receive tax credits to buy insurance if they are low-income (up to 300% of the Federal Poverty Level), or if they work for a small business with a hundred or fewer employees. States would apply default enrollments into plans for individuals with no insurance, but individuals could opt out of them.	YES, but consumers with preexisting conditions would have to hold continuous coverage in a health insurance plan.	YES, dependent coverage up to age 26, but only for a two-year transition period.	No minimum benefits.
Four proposals by the House E&C Health Subcommittee	NO	Older beneficiaries could be charged up to five times what younger ones are charged by insurance companies for premiums.	Yes	Yes	Insurance could be purchased across state lines.

Insight: "Sen. Alexander believes Obamacare's medical device tax not only stifles investment and ultimately drives up prices for patients in need of medical help, but also hurts a crucial industry for Tennessee.

"Republicans are now at work to repair the damage caused by Obamacare by replacing [it] with better, lower-cost alternatives," the spokeswoman added.

CASSIDY/COLLINS, PAUL PLANS MAKE NO MENTION OF DEVICE TAX

In addition, Sens. Bill Cassidy, R-La., and Susan Collins, R-Maine, recently introduced an Obamacare repeal-and-replacement plan (the "Patient Freedom Act," S. 191) that makes no mention of medical device tax repeal, despite both senators' support for repeal of the tax during the previous Congress. Collins was an early supporter of device tax repeal in 2015, and was a cosponsor of S. 149 by Jan. 20th of that year; Cassidy signed onto it even earlier, on Jan. 13, 2015. But to date, neither Senator has signaled formal support for this year's bill.

The Cassidy-Collins bill offers a smorgasbord of options to states to make certain their citizens are covered by one health insurance plan or another; for example, those states who want to keep their ACA insurance market plans as is would be permitted to do so, but other states could opt for supplying subsidies in the form of federal tax credits for Health Savings Accounts (HSAs) to buy premiums. However, under Cassidy-Collins, insurers would not be required to supply an array of minimum essential benefits now offered by ACA plans.

Kentucky Sen. Rand Paul (R) – who voiced support for repeal of the tax in 2013 and voted for repeal in December 2015 (alongside most Republican Senators) – also did not put a device tax repeal provision in his "Obamacare Replacement Act," S. 222, introduced this year on Jan. 24.

Paul, a Tea Party member known in the Senate for fighting cronyism, may have been influenced by a series of blog pieces and articles published in the last four years by political conservatives depicting senators and representatives who voted for device tax repeal as crony capitalists. Among the anti-device tax repeal pieces by conservative writers were those published in *RedState*in September 2013,and in the *Washington Examiner*on Jan. 30, 2015.

Paul's Obamacare Replacement Plan, while not including a device tax repeal, would repeal the individual mandate provision of ACA that forces Americans to purchase at least minimal health insurance coverage or pay a penalty. In its place, the bill offers inducements in the form of $5,000-per-covered individual tax credits for beneficiaries to buy health insurance plans – which could include high-deductible, low-cost plans that simply cover catastrophic care.

Like the Cassidy-Collins bill, Paul's bill would protect those with preexisting conditions from being denied coverage and allow adult children who are dependents to remain on their parents' policies. It also states that no minimum essential benefits would be required in insurance plans eligible for coverage with the $5,000-per-person tax credit.

PATIENT CARE ACT DRAFT WOULD REPEAL DEVICE TAX

On the other hand, a working draft of another widely supported Obamacare repeal-and-replacement plan, the Patient CARE (Choice, Affordability, Responsibility and Empowerment) Act, that was floated by Sens. Richard Burr, R-NC, Hatch and former House Energy and Commerce Committee Chair Fred Upton, R-Mich., in 2016, *does* call for repeal of the device tax.

The proposal would also let adult dependents stay on parents' policies, and protect those with preexisting conditions – but it would set strict time limits for continuous coverage on those beneficiaries' with preexisting conditions ability to maintain that coverage.

Further, the Burr-Hatch-Upton proposal would impose medical liability tort reforms, and require no minimum benefits in health insurance plans that could be covered by tax-credited HSAs designed for people that earn lower incomes, and for those working for small business employers that would be eligible for the credits.

HOUSE ACA INSURANCE REPLACEMENT DRAFT BILLS

The more recent stab at "repeal-and-replace" by the House Energy and Commerce Health Subcommittee's also does not focus on the excise tax, but instead, offer substitutes for the ACA's insurance market and preexisting conditions provisions.

The four draft House bills, which focus more on replacement of the insurance market aspects of ACA, include:

Plan verification of individual beneficiaries;

Permitting higher coverage rates for older beneficiaries;

Providing more flexibility to align with state laws, by letting insurers lock beneficiaries out of plans if they go without coverage for three months prior to Jan. 1, 2018 and for a one-month grace period after that; and

Preserving a ban on insurer providers denying coverage to those with preexisting conditions.

ACA repeal-and-replace plans or draft legislation now under consideration by Congress are summarized in the table below.

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Obamacare Repeal May Be Delaying User-Fee Bills, Rep. DeGette Says

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US FDA's user-fee renewal seems to have taken a backseat temporarily to Obamacare reform on Capitol Hill, and discussions to build the necessary legislation now may be behind schedule.

Rep. Diana DeGette, D-Colo., said Feb. 8 that FDA staff now are talking to Hill staff about user-fee agreements, including the Medical Device User Fee Amendments of 2017 (MDUFA IV) that were delayed when the Trump administration took office and paused government communications.

But there have not been many in-depth talks at the member-level yet, in part because of the "chaos" surrounding Republican plans to repeal and replace the Affordable Care Act, DeGette said. "It's already February and there are some serious discussions that need to happen," she said following a panel discussion at a Holland and Knight health-care symposium.

Among the highest priorities of the administration is repealing and replacing Obamacare, although it is unclear when the legislation could emerge. *(Also see "As ACA 'Repeal-And-Replace' Plans Form, Some Senators Silent On Device Tax Repeal" - Medtech Insight, 9 Feb, 2017.)*

Both the medical device and prescription drug user-fee bills, because they are considered must-pass, also can take a long time to formulate and perfect. The legislation for each usually becomes a large package containing not only the reauthorization agreements, but many other enhancements for FDA and other health-care related issues.

Typically, Congress wants the bills completed long before the existing user fee agreements expire Oct. 1, in part so FDA does not have to notify employees that they could be laid off if the program is not renewed. To avoid those notices, Congress usually hopes to pass the legislation by June, and that is the GOP's current deadline.

In 2012, the House and Senate moved the medical device user fee bill in late June. *(Also see "FDA Subject To More Oversight Following User Fee Bill Passage" - Medtech Insight, 2 Jul, 2012.)* But the 2007 reauthorization nearly missed the deadline and was passed days before layoffs would have started. *(Also see "Congress Approves FDA Reform/User Fee Bill In The Nick Of Time" - Medtech Insight, 24 Sep, 2007.)*

Before Congress convened in January, there had been some Republican hope for a fast repeal of ACA, but discussion of Obamacare now includes debates about fixes, repairs and improvements, rather than completely abolishing the law.

If those broader reform efforts continue to take up the lion's share of health-care work on the Hill, Congress could be finishing the reauthorization bill much closer to the renewal date than ideal.

An Energy and Commerce Committee spokesperson said completing its work on the user-fee reauthorizations in a timely manner is an important priority.

The user-fee renewals are in a unique situation this year because they were negotiated under one administration and would be implemented by another. Some have worried that the Trump administration would try to reopen the agreements because it had no part in creating them.

In a recent interview with *Medtech Insight*, Medical Device Manufacturers Association President and CEO Mark Leahey acknowledged that a lot of the congressional debate over MDUFA IV this year "will be driven by the perspective of the [Trump] administration." *(Also see "Q&A: MDMA Strikes Optimistic Tone For Coming Year" - Medtech Insight, 31 Jan, 2017.)* His expectation, though, is that the user-fee talks will still be completed by July, as they have been in the past.

COMMISSIONER NOMINATION MIGHT DELAY USER-FEE BILL, TOO

Aside from the congressional fixation on ACA repeal, several factors are delaying the user-fee bill from moving forward, DeGette said, including the lack of a permanent FDA commissioner.

Several candidates have surfaced, but Trump has not announced his pick. One potential nominee for the FDA commissioner spot, Joseph Gulfo, told *Medtech Insight* in late January that if appointed, he would take a closer look at the recently negotiated user-fee agreements to find ways to cut any unnecessary and legal overreach. *(Also see "Gulfo Might Reevaluate Negotiated User Fees If Selected US FDA Commish" - Medtech Insight, 25 Jan, 2017.)*

The administration and Congress also may be holding up further user-fee discussion until after Rep. Tom Price, R-Ga., is confirmed as HHS Secretary. A Senate vote confirming Price's nomination is scheduled to take place on Feb. 9 or 10, following his approval by the Senate Finance Committee on Feb. 1. *(Also see "Senate Finance Advances Tom Price HHS Confirmation, Sans Democrats" - Medtech Insight, 1 Feb, 2017.)*

HIRING FREEZE RAISES LEGISLATIVE QUESTIONS, DEGETTE SAYS

In addition, Degette and others are waiting for answers to questions about the federal hiring freeze, which Trump implemented via executive order. *(Also see "A Burning FDA Hiring Freeze Question: What About User-Fee-Supported Staff?" - Medtech Insight, 24 Jan, 2017.)* It is unclear whether user fee-supported hiring will be allowed during the freeze. MDUFA IV includes a draft commitment from FDA to hire approximately 260 FTEs over five years to perform quality management, improve review times, enhance digital-health reviews, conduct supervisory oversight, and much more. Industry is likely to be unhappy to pay the increased fees if the agency can't hire the additional staff they are supposed to support. *(Also see "MDUFA IV Takes Shape: A Catalogue Of Draft Commitments" - Medtech Insight, 29 Aug, 2016.)*

The 21st Century Cures legislation also gave FDA enhanced hiring abilities, which DeGette wants clarified in relation to the hiring freeze. A coauthor of the Cures legislation, she reiterated that implementation of Cures would be in danger if FDA and other agencies do not get the necessary staff.

Among the changes Cures made was giving FDA the ability to offer higher salaries to attract the experts it needs. The agency has hundreds of openings that it has struggled to fill. *(Also see "CDER's 50 Open Leadership Posts Could Be Bigger Hiring Challenges After Trump Freeze" - Pink Sheet, 2 Feb, 2017.)*

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Registrations For Medical App-Makers Double In UK, But Noncompliance Still High

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Registrations of class I medical device app-makers in the UK have almost doubled since the Medicines and healthcare products Regulatory Agency clarified its expectations for standalone software and health apps last year, but there are still many manufacturers that are operating without having registered.

An additional 12 manufacturers registered with the MHRA after the agency released updated guidance on standalone software and health apps in August 2016, bringing the total number of registered manufacturers in the UK to just over 90.

But registration in this field is "still low … and we know there are a lot of apps out there" being made by manufacturers that have still not registered as required by EU law, Valerie Field, interim group manager for devices at MHRA, revealed at a conference in London last month.

It is "very difficult to tell" how many manufacturers are unregistered, a spokesperson for MHRA told *MedtechInsight* sister publication *Pink Sheet*. "But where we become aware of issues, particularly where patient safety is concerned, we will investigate and take action to bring the app into compliance."

Medical device apps can fall into any one of four risk classes under EU law, depending on their intended use, but most of them tend to fall into class 1, which is the lowest risk. Class I device manufacturers only have to register with the competent authority of the member state where they have their registered place of business, and self-certify that their product meets the general essential requirements of the relevant EU medical device directive. Higher-risk device-makers, on the other hand, must employ a notified body to check that they have met the essential requirements. All devices must have clinical data/evaluation to demonstrate that their results are accurate and they do what they claim.

"More people are now aware of what is needed," the MHRA's spokesperson said of the rise in registrations since the agency's updated guidance was launched. The guidance included new clarification on how to determine whether or not a product is a medical device, and it was published in an easy-to-navigate, interactive PDF format. *(Also see "UK MHRA Hones In On 'Medical Purpose' In Software And Apps Guidance" - Medtech Insight, 5 Sep, 2016.)*

Compared with the 2014 guidelines it replaced, the new guidance provided more advice on how to interpret the term "medical purpose" and how to differentiate apps that fall under the EU directives governing medical devices and IVDs from lifestyle or wellbeing apps, which are not subject to these laws. It has also been updated again since August. "We … had one minor update version in November 2016 taking onboard suggestions that we received from users and developers," the spokesperson said.

Poor manufacturer registration may be because there is still a "level of unawareness of the need to check if an app fulfils the requirements of a medical device," the spokesperson ventured. To help rectify the situation, the agency plans to "promote" the guidance and "spread the word by talking at conferences and to developers / manufacturers of medical device apps and [by] writing articles."

CHANGES AHEAD

App-makers should also remember that the rules governing medical device software in the EU are likely to change when the Medical Device Regulation – which is still being finalized – replaces the current medical device directives.

Software is covered for the first time in its own right under the MDR, Field said at the 16th Regulatory and Scientific Affairs Conference hosted by Medicines for Europe, the body that represents generic and biosimilar drug companies.

The MDR, for example, contains a new rule on definition and classification, Field noted. According to the latest version of the proposed MDR published on the European Commission's website in June 2016, the new rule would mean that:

Software intended to provide information which is used to take decisions with diagnosis or therapeutic purposes, is in class IIa, except if such decisions have an impact that may directly or indirectly cause:

- *The death or an irreversible deterioration of the state of health, in which case it is in class III;*
- *A serious deterioration of the state of health or a surgical intervention, in which case it is in class IIb.*

Software intended to monitor physiological processes is in class IIa, except if it is intended for monitoring of vital physiological parameters, where the nature of variations is such that it could result in immediate danger to the patient, in which case it is in class IIb.

All other software is in class I.

MHRA is planning to revise its guidance on standalone software and health apps once the new MDR is agreed.

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OUS APPROVALS ANALYSIS:

Medtronic, Abbott, Abionic Lead 2017 Upswing

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The year 2017 began with an uptick in non-US approvals, almost doubling the total in December 2016, and represents the largest month for CE marks since June of last year.

Medtech Insight's product approvals tracker recorded 19 CE marks plus one Health Canada license, bringing the total number of non-US approvals to 20. By comparison, there were only 11 non-US approvals in December, including just eight CE marks. There were more CE Marks in January than any month in 2016 except June, which was an outlier with 27 CE Marks.

January 2017 almost matched January 2016's total of 21 non-US approvals, which included 14 CE marks. (See Figure 1.)

The only non-European, non-US approval in January was Health Canada's license of **7D SurgicalSystem's** *Machine-vision Image Guided Surgery (MIGS)* system for spine surgery, announced Jan. 23 along with the US FDA 510(k) for the system. According to the Toronto company, MIGS combines 3D optical technologies and machine vision algorithms to make image-guided surgery more efficient and accessible for more surgeons. MIGS *Flash Registration* can register spinal surgery images of the patient's anatomy almost instantaneously using only visible light, whereas conventional image guided surgery systems that

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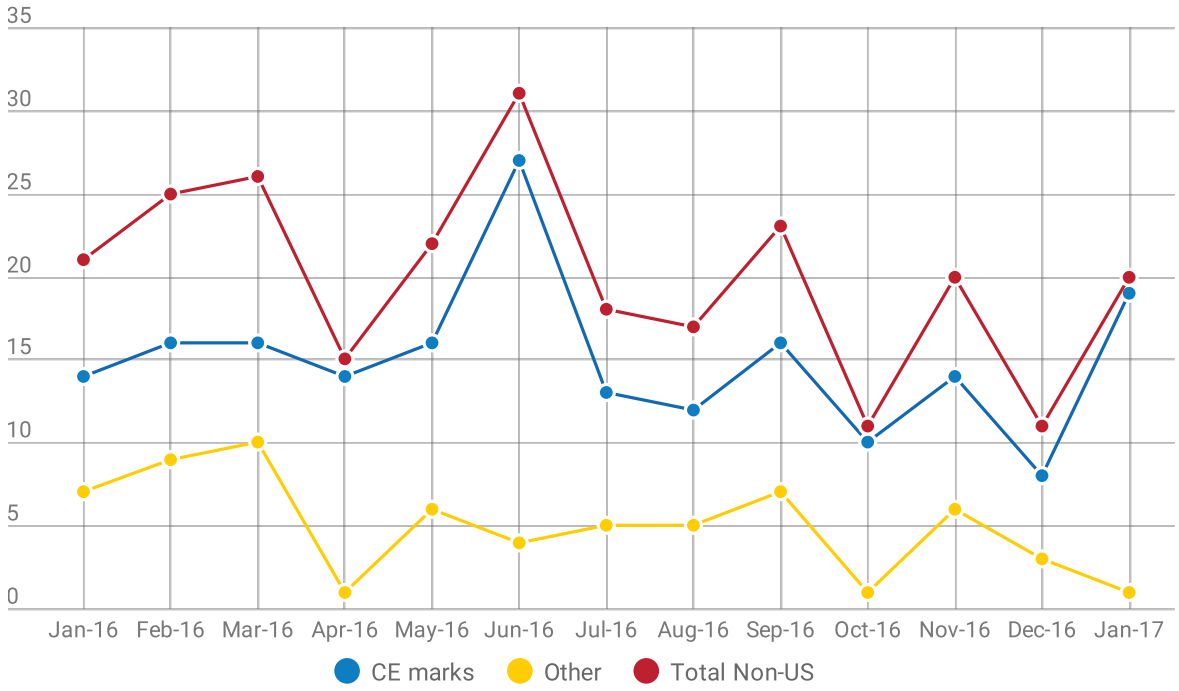
FIGURE 1

Non-US Approvals Jan 2016 - Jan 2017



Source: Medtech Insight Approvals Tracker

depend on intraoperative radiation and or laborious manual point-matching image-registration systems.

The company believes the difficulty of using these systems is why fewer than 20% of potential customers use image-guidance surgery systems, but that MIGS can break those barriers to market-penetration.

"We have achieved an unprecedented entire workflow time of less than 20 seconds for *de novo* spinal registration, unheard of in the spinal IGS world where such registration can interrupt surgery for up to 30 minutes," 7D Surgical president and chief scientific officer Victor Yang said. Yang is a neurosurgeon at Sunnybrook Health Sciences Centre in Toronto, which has used the prototype MIGS system in over 160 cases.

Like most months, January's approval totals were led by IVDs, with eight approvals in that category, followed by four in orthopedics, three in cardiovascular and two each in patient monitoring and imaging. (See Figure 2.)

The lone category outlier is Advanced Cooling Therapy Inc.'s CE Mark that allows the Chicago company to market its *Esophageal Cooling Device (ECD)* as compatible with Stryker Corp.'s *Altrix* precision management system. ECD control's patients' temperature with a triple-lumen tube that is inserted in the esophagus, like a standard gastric tube, and runs all the way down into the stomach. Two of the lumens are attached to temperature modulation systems, while the third lumen allows gastric decompression and drainage.

"The ECD's compatibility with a new line of control units, or heat exchangers, now available on the market, enables us to meet the growing needs of hospitals across Europe that are utilizing the Altrix Precision Temperature Management System in emergency departments, intensive-care units, and operating rooms for a wide range of cooling and warming needs," ACT international sales manager Markus Tödtling said in a release.

US FDA clearance of the Altrix Precision-compatibility indication is still pending. FDA *de novo*-cleared the ECD for use with Stryker's *Medi-Therm III* system and cleared it to be used with Cincinnati Sub-Zero's *Blanketrol II* and *III* hyper-hypothermia systems in January 2016.

Three companies recorded two non-US approvals in January: Medtronic PLC, Abbott Laboratories Inc., and Abionic SA. No company recorded more than two.

Medtronic announced the CE Mark for a lower profile size of its *HawkOne* directional atherectomy system on Jan. 24. The new version of the device, designed to treat peripheral artery disease both below and above the knee, is 6 Fr. in diameter. The 7 Fr. version of HawkOne was originally developed by Covidien before it merged with Medtronic two years ago. The 6 Fr. version has a 2.2mm crossing profile, compared to a 2.6mm profile for the 7 Fr. version. *(Also see "Market Update: Growth And Opportunities In Peripheral Artery Disease" - Medtech Insight, 18 Feb, 2016.)*

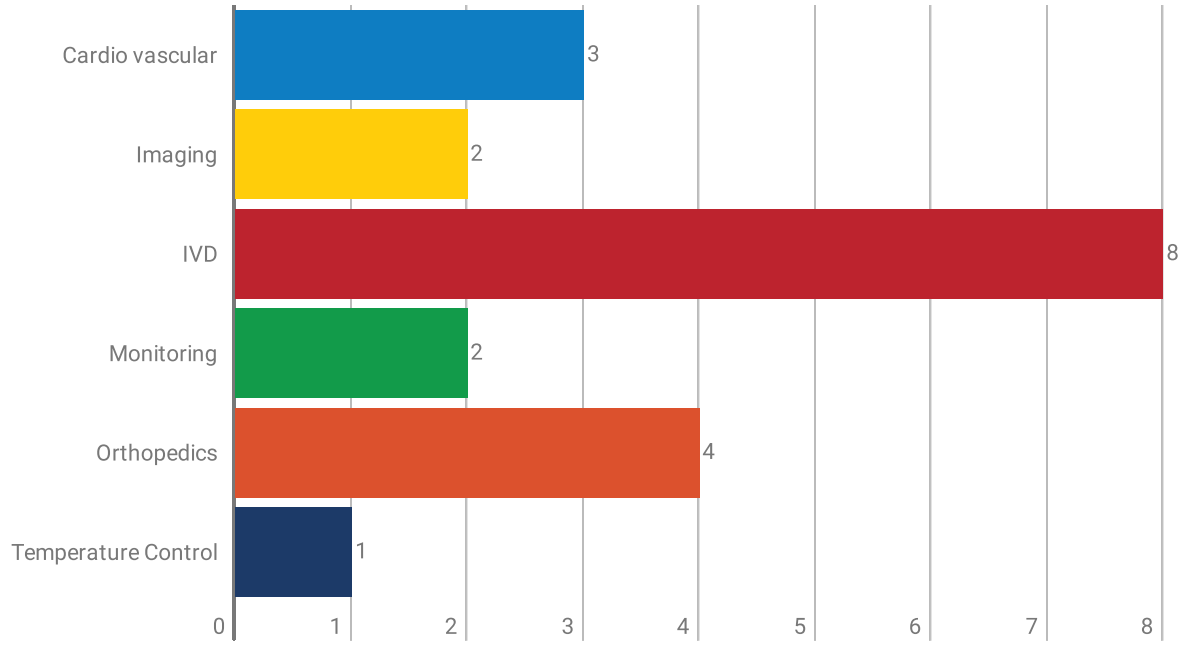
A week earlier, Medtronic announced the CE Mark and European launch of the 34mm diameter version of its *CoreValve Evolut R*, the largest diameter transcatheter aortic valve system available in Europe.

CLICK

Go to http://bit.ly/2kSlrnb to check out our 2016 Medical Product Approvals infographic and see http://bit.ly/2I8kZB4 for an analysis of January 2017 US approval trends.

FIGURE 2

January 2017 Non-US Approvals by Product Category



Source: Medtech Insight Approvals Tracker

The 34mm version is suitable for aortic annulus sizes from 26mm to 30mm, which represents 20% to 25% of European TAVR patients, according to the company. CoreValve Evolut R is also available in Europe in 23mm, 26mm, and 29mm versions.

On Jan. 10, just a few weeks after announcing the CE mark for its *i-STAT Alinity* point-of-care blood-test analyzer, Abbott announced the CE marks and European launch of its *Alinity s* system for blood and plasma screening, and the *Alinity ci* series of instruments for clinical chemistry and immunoassay. The c clinical chemistry instrument can be used independently or in conjunction with the i immunoassay system, the company explains, but are marketed together. The firm plans to launch the Alinity hematology system in Europe later this year, to be followed by a molecular system under the same brand. The Alinity line is "transformational" for Abbott's diagnostics business, Abbott Diagnostics' executive VP Brian Blaser told *Medtech Insight* in a recent interview. *(Also see "To Alinity And Beyond: Abbott Dx Launches Into Its Next Phase" - Medtech Insight, 26 Jan, 2017.)*.

Lausanne, Switzerland-based Abionic SA announced the CE Marks for the *PSP IVD Capsule* sepsis risk assessment and management test, and the *Ferritin IVD Capsule* iron deficiency test for the abioScope platform on Jan. 9. The iron deficiency test will be available in early 2017, whereas Abionic will launch the sepsis risk assessment test in 2018. *(Also see "Abionic's New POC Sepsis Test On Rapid Move To Market" - Medtech Insight, 20 Jan, 2017.)*

The PSP IVD Capsule test relies on pancreatic stone protein (PSP) as biomarker to aid in identifying patients at risk for sepsis. It has superior sensitivity and specificity versus other biomarkers currently used for sepsis, and the abioScope test can measure PSP in five minutes at the point-of-care, which can lead to "potentially life-saving" decisions.

The Ferritin IVD Capsule test measures the level of available iron stored within the body. Low iron is the most frequent nutritional deficiency worldwide, and ferritin testing is an important part of investigating potential iron metabolism-related diseases, such as iron-deficiency anemia, measures ferritin, according to the company. Because ferritin is present only in the blood at picomolar concentrations, abioScope is the only technology that can provide ferritin measurement within minutes at the point-of-care, according to Abionic.

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Anatomy Of A Medtech Carve-Out

JANE HOBSON
PHELIM O'DOHERTY

A carve-out typically can be structured either as the spin-off of an integrated business division or its divesture to a third party buyer by way of a business and/or share transfer. Recent years have seen an uptick in the number of carve-outs in the medical devices sector, such as the 2014 acquisition by EQT of Siemens Audiology Solutions and the acquisition by Montagu Private Equity of Rexam's health-care devices division. While the concept of a carve-out transaction is not new, the driver for performing carve-outs is shifting away from the reactive jettisoning of underperforming assets to a more proactive and continuing appraisal of a company's portfolio of businesses, and subsequent disposal of relatively well-performing but non-core assets.

Carve-outs, particularly in the medical devices sector, are often viewed as complex processes that offer up various challenges. The purpose of this article is to explore – with respect to divestures of assets to third parties (as opposed to spin-

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About The Authors

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ning them off as independent businesses) – some of the common carve-out issues that can arise for sellers and buyers, and how they can be readily addressed.

SNAPSHOT OF THE CARVED-OUT BUSINESS

A successful sale will likely be run as an auction with the seller keeping control of the process and maintaining competitive tension between the bidders. In auctions of carved-out businesses, aside from the general M&A issues, it will be critical for bidders to get a clear understanding of: (i) the scope of the business that is being transferred; (ii) its financial performance; and (iii) how it is being separated from the seller's group. Without this information, it will be challenging for a bidder to complete its diligence in a timely manner and to submit a confident price. A well-run seller process should try to position information on the business in a way that is quick and easy for bidders to analyze. To aid this analysis, sellers can use some of the following seller aids:

- Vendor due diligence reports (VDD Reports) and data room guides;
- Standalone carve-out financials and standalone costing analysis; and
- Carve-out "macro plans."

VDD REPORTS

VDD reports are now a well-established auction tool allowing a seller to quickly provide bidders with information on the business to be sold. In the context of a carve-out in the medical devices sector this is even more relevant because often the information available on the business is integrated within information relating to the retained business units and it can be challenging for bidders to try to separate this out. We often see shared/mixed contracts in the medtech industry, where contracts cover a number of the seller's businesses; a carve-out, on the other hand, would be the sale of one business so this would need to be clearly split from the seller's remaining interests.

Additionally, preparation of a VDD report will give the seller the opportunity to conduct due diligence on its own business and therefore understand more clearly any issues that may need to be remedied prior to the sale. Alongside a VDD report, a well-structured virtual data room, which will contain documents relating to the transferring business, together with a clear data room guide setting out how the data room has been established will assist the bidders in complying with the auction timeline.

> Most global medical device companies have centralized many of their services and processes so that the use of shared assets by different business divisions is common. From a carve-out perspective, it makes separation more difficult.

A well-structured carve-out macro plan allows:

- On the sell-side, the seller to present a clear and confident picture of the business, and it will identify long lead-time items that can have implications for the wider M&A transaction; and
- On the buy side, it enables the buyer to gain a deeper understanding of how the carved-out business will be sold, reduces the amount of due diligence that they would otherwise need to perform, and assists their integration planning.

STANDALONE CARVE-OUT FINANCIALS

The most time-consuming and potentially controversial of these aids are the standalone carve-out financials. These are separate (and preferably audited) financial statements that are created from the financial statements of the larger seller parent group/company. It is key that these financial statements are prepared early in the sale process so they are available to bidders at the initial stages but not too early so as to be "old" by the time you are taking the transaction to the market. These financials do not follow any standard form and can be adapted depending on the type and size of carve-out as well as the likely profile of the ultimate buyer. We explore the latter point more fully below but, regardless of the requirements of any bidder, a well-advised seller will be conscious that robust financial statements enable it to negotiate price and other terms from a position of strength. In addition to carve-out financials, bidders will want to understand the cost implications of making the business fully standalone. In this industry, where so often businesses rely on centralized support, this analysis will be critical in helping bidders arrive at their bid price. (See "Price" section, below.)

CARVE-OUT MACRO PLANS

Also in recent times, there has been a growing trend toward providing bidders with a legal macro plan summarizing the transferring business and the method by which it is to be separated from the seller group. The intention is for this to act as a roadmap to bidders to show them how the seller proposes to transfer the business to them. The carve-out will usually consist of a series of stock and business transfers in various jurisdictions and the macro plan will usually include, amongst other things:

- A summary of the legal steps required to effect the local transfer;

- An indication of the timing for implementation;
- Details of headcount and benefits together with a description of how the employees will transfer – for example, is a consultation required, and if so, when must that commence;
- A summary on real estate, owned and leased, with a focus on the strategy for shared sites;
- Treasury considerations such as whether the consideration for the local transfer needs to be paid at a local level and/or in local currency; and
- Tax considerations, such as whether any transfer taxes need to be paid and if so, by whom.

STANDALONE BUSINESS

Most global medical device companies have centralized many of their services and processes so the use of shared assets by different business divisions is common (for example, shared R&D facilities). Operational and financial benefits to such arrangements are plenty, but from a carve-out perspective, it makes separation more difficult and it means that very rarely is a seller able to offer a complete standalone business on closing. Ultimately, either the seller or the buyer will be required to replace some or all of these shared assets, and the analysis of what is shared and whether such shared assets will transfer or not will need be performed as early as possible, as the process to replace them can be time-consuming. In respect of shared assets not transferring to the buyer, the seller may need to continue to perform some of the shared services pending a full replacement of the relevant assets by the buyer and these services are often referred to as "transitional services."

The identification of the required transitional services and negotiation of their scope, the time period for the provision of such transitional services, as well as cost, will form a significant workstream on the transaction. Engaging in discussion on this as soon as possible is desirable but parties need to be mindful of potential "gun-jumping issues" pending receipt of any merger control approvals. While it is relatively common to see IT and other matters included in transitional service arrangements, the increasing trend on medical devices carve-outs is to close the transaction as soon as possible even if this means more complex arrangements. The means that the range of such transitional services can stretch from minor back-office functions to a seller continuing to run the business for the economic benefit of the buyer for a period post-closing of the wider transaction. This is particularly so in this industry where many contracts are with public bodies and the legal transfer of the contract is time-consuming and complex.

Thought will also need to be given to local law restrictions. As an example, there are strict rules on transitional services in the Middle East, in particular in UAE and Saudi Arabia, and often there can be no meaningful workarounds, meaning that a business will either need to transfer on the closing date on a standalone basis or not at all. In the latter instance, the consequences of failing to transfer such business must be taken into consideration – would the employees be terminated and who would pick up such costs?

> As the commercial drivers of the bidders will be different, a seller should ensure that the approach to the carve-out is structured in a flexible manner such that both types of bidders remain interested and competitive tension is maintained.

Finally, to assist bidders in arriving at their bid price, a seller will often provide the bidders with standalone costing analysis – the concept here is that the seller is explaining to the bidders what amount of services their central functions provide to the carve-out business presently and the costs of the same.

PROFILE OF BIDDERS

When organizing the auction process, a seller should consider the profile of the likely bidders and their respective motivations as well as their corporate structures. There will be predominantly two types of bidders – financial sponsors and corporates. Financial sponsors will be focused on the requirements to make the business standalone and tend to favor businesses with strong management teams. The motivations of a strategic buyer, on the other hand, will tend to revolve more around cost and profit synergies and they will be focused on integration planning.

As the commercial drivers of the bidders will be different, a seller should ensure that the approach to the carve-out is structured in a flexible manner such that both types of bidders remain interested and competitive tension is maintained. In particular, thought should be given to:

- **Financials:** As touched on above, the standard to which financials will need to be prepared may have to be adapted according to the profile of the bidder. For example, certain financial investors may be satisfied with an unaudited balance sheet and income statement for the previous financial year, whereas certain corporate bidders may require something more fulsome and may require it to be audited in order to satisfy their own regulatory processes. Whatever approach the seller takes, it is key that they are upfront around what standard the carve-out financials have been prepared to so that, in particular, corporate bidders can determine what work will be required in order that these carve-out financials can be included in their reporting going forward.

- **Structure:** A financial sponsor will likely not have an existing matrix of companies ready to accept the carved-out business. The carve-out process will therefore be focused making the business standalone, meaning the carve-out exercise may become more akin to prepping the business for a spin-off. Corporates on the other hand will likely have an existing network of companies, and many of the relevant shared services/back office functions into which the divested business can be more quickly integrated. In preparing for a carve-out, the seller will need to consider the likely profile of its bidders and determine what preparation of the business is required in advance. The fact that the carve-out exercise for a financial sponsor may be more fulsome than for a corporate can be offset in other ways. For example, it may be that the path to merger control clearance is easier for a financial investor, that the financial investor can offer the management team a better package and/or that the financial investor can be more nimble in the auction than a corporate. In any event, thought will need to be given to what additional work is required in respect of certain bidders over others, whose responsibility this extra work is and, ultimately, who picks up the cost.
- **Due Diligence:** The areas of focus for corporates and financial investors may differ somewhat in due diligence. For example:
- **Transitional Services:** The scope of any transitional services to be provided may depend on the profile of the buyer. Financial investors may require more transitional services for a longer length of time than corporates because they do not have an existing matrix of companies in which to plug the carve-out business. For example, if a Thai business is to transfer as part of the carve-out and the successful bidder does not have an existing entity with the requisite foreign business licenses, then as a result of the long lead time to incorporate the new company and have it licensed, the transitional services may stretch for up to two to three years.

PRICE

As mentioned above, one of the key factors in a transaction will be the price. However, in many ways on a carve-out, the headline price may not always be what it seems. One of the key points on a carve-out is to take a holistic view on price, and we would suggest the following points – which are also each linked to the profile of the buyer – be kept in mind when pricing your carve-out business:

> Where there is the likelihood that a deferred closing is necessary, then the carve-out and deal teams will need to work very closely to come up with a workable solution, and the principles of this solution will need to be in the main transaction documentation.

Deferred Closings: In implementing a multi-jurisdictional carve-out you will need to factor into your transaction timeline the differing local laws. There will be jurisdiction that will give rise to issues which have a long lead time associated with them. For example, R&D facilities in India will often have STPI (Software Technology Parks of India) licenses meaning their goods are bonded and the timeline to transfer such a business will need to factor in the period required to de-bond assets and/or have the transferee apply for an STPI registration (each process can take some months).

If such an issue arises then you need to consider the significance of the transaction value attributed to the particular jurisdiction in the context of the wider deal. If the jurisdiction is relatively insignificant then there may be benefit to progressing the transfer of the balance of the jurisdictions as soon as possible and not waiting for this jurisdiction-specific issue to be resolved; the transfer of this jurisdiction would therefore be "deferred" until the issue is resolved.

Where there is the likelihood that a deferred closing is necessary, then the carve-out and deal teams will need to work very closely to come up with a workable solution, of which the principles will need to be provided for in the main transaction documentation. This is usually done by way of an amendment after signing, when the timing becomes clearer. The solution will depend on the delaying issue, the jurisdiction in question and the deal dynamics, but it is likely that the deferred closing business will continue to be run by the seller until the deferred closing and a purchase price escrow arrangement may be looked into.

At one point it was relatively standard, where there were deferred closings, for the consideration attributable to the deferred company and/or business transfers to be placed in escrow. It is worth noting, that this is now less common on European health-care deals, and often notwithstanding that legal title to assets cannot transfer on the closing date, economic benefit moves. For this reason, it is more common now to see the entirety of the consideration paid on the closing date.

Cost of Carve-Out: The delivery of the carved-out business will have a cost associated with it, and it will be commercial negotiation for the seller and successful bidder to agree on which should bear such costs. Some of these costs will remain

static notwithstanding the identity of the successful bidder (for example, transfer taxes and notary fees). Other costs might shift, for example, costs associated with newco incorporations, costs of establishing employee benefit plans, *et cetera*. To the extent that the seller will bear some of all of this additional costs, this should be borne in mind when comparing rival bids.

Transitional Services: Similar to what was discussed previously, the transitional services required of the successful bidder will depend on who the successful bidder is – a financial investor bidder usually requires more and longer-term support than a corporate bidder. For example, it is relatively common for the successful bidder to be obligated to provide an employment offer to the transferring employees, the terms of which must be comparable – in the aggregate – to their existing employment terms. A corporate will have the advantage of existing benefits infrastructure, and it is reasonable to assume that, with some modifications, corporate could make qualifying offers to the majority of the transferring employees on the closing date. A financial investor bidder on the other hand, will not have such an infrastructure and will therefore likely seek some form of complex transitional services around benefits until it has had to set up in-country benefits infrastructure (work on which can often not commence until newcos are close to operational).

Again, when comparing price amongst bidders, thought should be given to the management time associated with such arrangements – even though they are usually compensated through the transactional services agreement, there is also missed opportunity cost as resources are diverted into a non-core business that has been divested, rather than refocusing on the strategic core business(es) that have been retained.

CONCLUSION

Carve-outs are complex procedures and significant resources are required on the seller's part, with various functions (whether that be legal, tax, treasury, accounting, quality, supply chain, regulatory, *et cetera*) having to engage in numerous tasks and consideration: producing standalone financials, inputting into detailed macro plans, computing purchase price allocations and providing asset lists, considering post-closing ongoing transitional services and other support, among other things.

However, asset carve-outs have been on the rise over the last number of years and we anticipate this trend will continue as companies continue re-focusing on their core business. We also expect the growing regulatory burdens being placed on companies, and the costs associated with this, as a likely catalyst for divestures.

Views expressed by guest columnists do not necessarily represent those of Medtech Insight.

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CONTINUED FROM PAGE 1

on the rate of bone remodeling.

Used as complementary tools, bone densitometer and biochemical marker testing allow doctors to identify patients at high risk for osteoporosis and prescribe appropriate and early treatment, according to the *Meddevicetracker* report.

To date, sales figures show that bone densitometers remain the most widely used diagnostic technique worldwide.

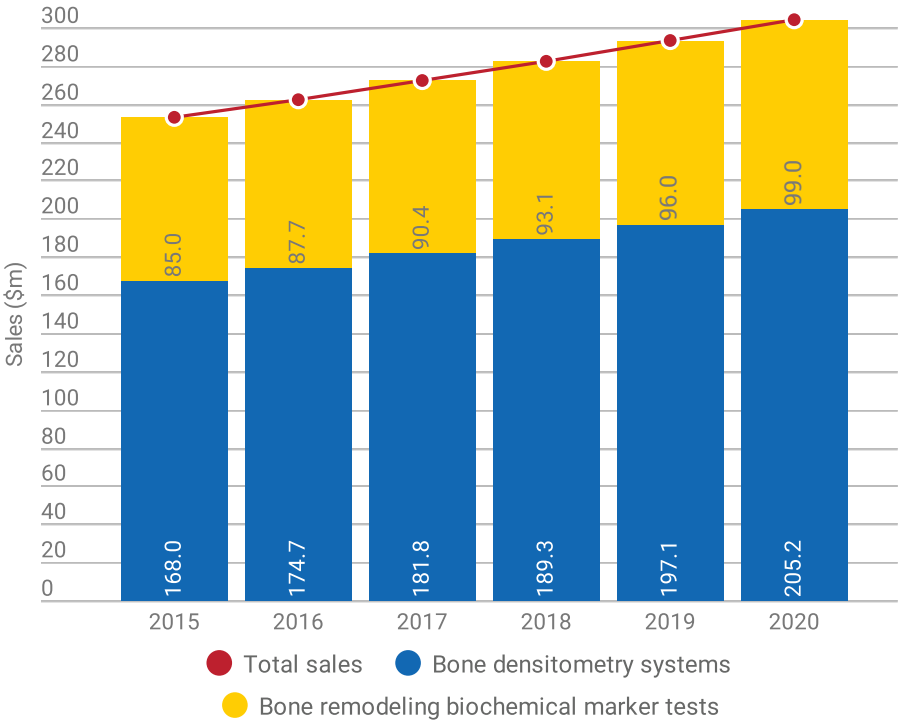
In 2015, sales of bone densitometry systems accounted for $168m or 66.4% of the global osteoporosis diagnostics product market and are expected to reach $205.2m by 2020, a CAGR of 4.1%. Bone remodeling biochemical marker tests, meanwhile, made up $85m or 33.6% of the global market in 2015 and are projected to reach $99m by 2020, a CAGR of 3.1%. (See Figure 1.)

REGIONAL INSIGHTS FOR BONE DENSITOMETERS

In 2015, the total market for bone densitometers – including DXA, radiographic absorptiometry (RA) and quantitative

FIGURE 1

Combined Market Forecast for Osteoporosis Diagnostic Products for the Years 2015-2020



Source: Meddevicetracker report, "Women's Health: Osteoporosis Diagnostic Products"

ultrasound (QUS) -- reached $168m with the US accounting for 60% of the market, followed by emerging countries, the five major European countries and Japan.

Growth in these regions will vary, however. By 2020, sales of bone densitometers are expected to grow only moderately in the US, Europe and Japan (around 3% in each region), with the highest growth rate of 9% expected in the emerging markets. (See Figure 2.)

While the largest bone densitometry (DXA) market, the US will continue to be driven, in large part, by favorable demographics (the growing elderly population and longer lifespans), there are also multiple barriers to growth.

Declining rates for DXA screenings, due to cuts in public and private health-care reimbursement, remains a major challenge in both the hospital and private doctor's office.

Regulation is another concern. Due to DXA's delivery of very low doses of radiation, regulations vary from state to state regarding what certifications are required to operate the system. Some states, like California, require coursework and a state-administered tests, while others have no requirements for DXA technicians, which is problematic, since DXA is highly susceptible to operating error and a lack of training may have a direct impact on the accuracy of the test results. Additionally, measurements may vary from one system to another, resulting in different devices producing different values.

Other factors constraining the growth of DXA screening in the US include declining prices for bone densitometers due to pressure by group purchasing organizations and managed care. Economic uncertainties and rising health-care costs that have cost-conscious consumers skip wellness screenings, an increase in sales of refurbished systems – which often cost half the price of a new system – uncertainty surrounding the Affordable Care Act, and the stronger dollar vs the Euro and other currencies, which has hurt overseas sales by US manufacturers, are all contributing factors for slower growth.

In the EU, Germany represents the largest market for bone densitometers given its large aging population – 16 million people were over the age of 65 in 2015 – which is 21.2% of the population.

The EU market was valued at about $25.2m in 2015 and is expected to reach $29.4m by 2020, fueled by the rising aging population and need for osteoporosis screening.

However, as seen in the US, growth of this product segment in the EU market is challenged on multiple fronts.

According to the *Meddevicetracker* report, an anemic economy and underutilization of DXA screening are two big limiting factors. *(Also see "Spanish osteoporosis vastly under-diagnosed "due to lack of bone densitometry"" - Medtech Insight, 26 Jul, 2011.)* Differing reimbursement rates between EU member states, as well as cost for DXA, which vary widely and bear little relationship to the wealth of the nation or to the availability of DXA machines, are also growth barriers in this sector.

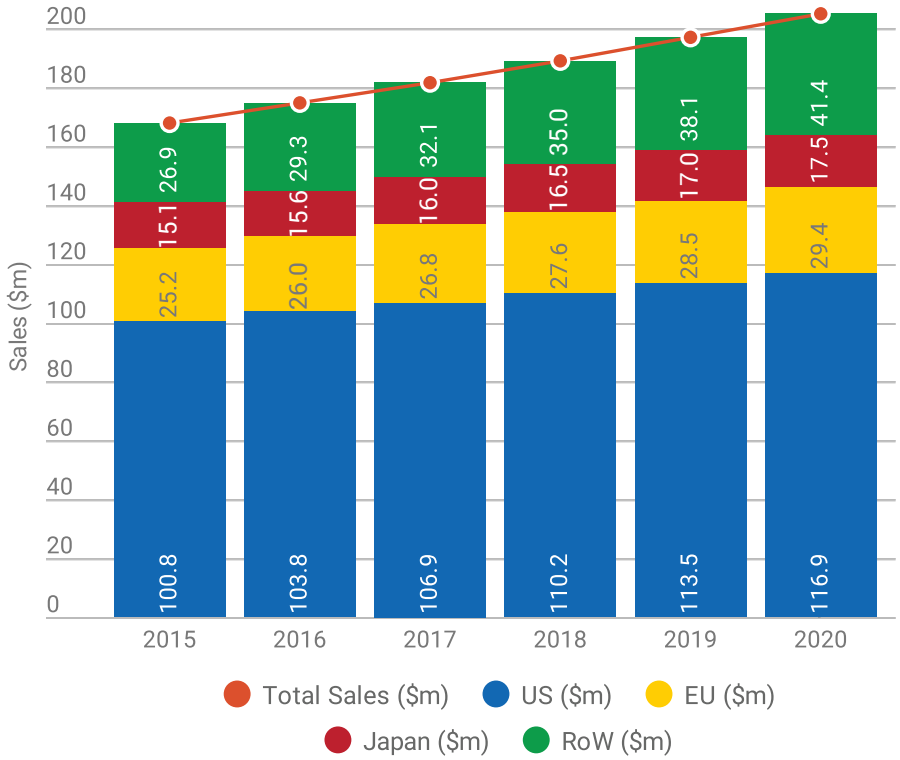
Looking east, in Japan, the bone densitometer market is projected to climb modestly to $17.5m in 2020, a CAGR increase of 3%, according to the *Meddevicetracker* report. A major driver in this market is the country's relatively prosperous senior population striving for a higher quality of life in their golden years, a goal that's backed by government initiatives in Japan.

Also boding well for growth in this sector is Japan's strong dependency on imports for medical devices, which according to *Meddevicetracker* estimates, is nearly 60% for US-made medical devices. On the downside, the government's efforts to contain health-care costs have also led to pricing pressures and lowering reimbursement.

The fastest growing region for bone densitometers will be the emerging markets, which are expected to reach $41.4m by 2020, a CAGR increase of 9% from 2015. Asia Pacific is considered the most lucrative market for bone densitometers, owing to an expansion in hospitals and diagnostic laboratories in India and China. The rising middle-class in this region

FIGURE 2

Bone Densitometry Systems Market Forecast by Region 2015-2020



Source: Meddevicetracker report, "Women's Health: Osteoporosis Diagnostic Products"

represent a source of fast, strong growth for the foreseeable future, particularly for minimally invasive therapies. That said, the dynamics of emerging markets tend to be different from major markets in that what may be applicable in one market may not hold true in another one. Companies that want to be successful in this region need to be able to adapt quickly to change and understand the local market insights.

COMPETITIVE ANALYSIS

In 2015, GE Healthcare and Hologic Inc. were the two major players in the global market for bone densitometers with a combined market share of 90%.

In 2015, GE Healthcare dominated the worldwide market with a 58% share (raking in roughly $97.4m in sales) followed by Hologic with a 32% share and ($53.8m in sales). The other 10% of the market were held by other suppliers, including **BeamMed**, CompuMed Inc., **Diagnostic Medical Systems**, **Furuno Electric Company**, Hitachi Medical Systems, Sectra AB and Swissray International Inc. (See Figure 3.)

GE Healthcare's large breadth of scale, brand recognition and broad product line give the company a competitive advantage in all regions worldwide, according to the *Meddevicetracker* report.

HOSPITAL VS PHYSICIAN AND COMMUNITY-BASED SETTING

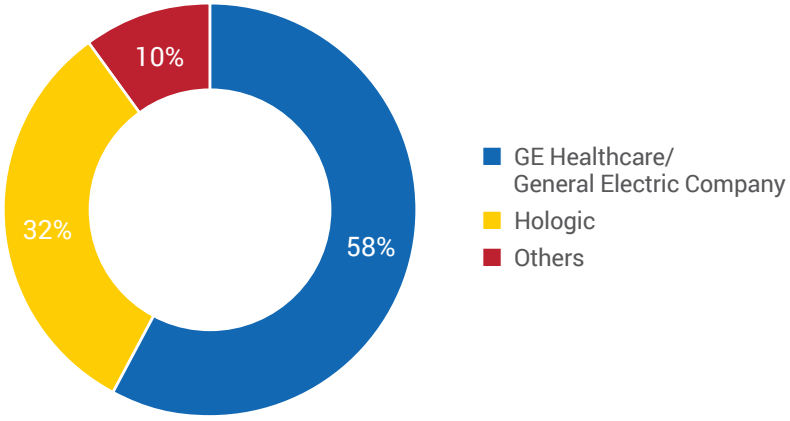
Most hospital-based bone densitometry uses DXA whole body imaging systems, and the key players in this space are Diagnostic Medical Systems, GE Healthcare/General Electric Company, Hologic and Swissray.

The relatively high equipment cost, large size and need for trained professionals are some of the key limiters for wider adoption. However, the *Meddevicetracker* report projects that DXA systems that offer advanced features and performance characteristics will see wider adoption and wider uses.

Among the forerunners is Hologic, which has made continual improvements since introducing its first DXA product in 1987. Hologic's newest-generation DXA system, *Horizon*, introduced in the second

FIGURE 3

Bone Densitometry Systems Global Market Share by Supplier, 2015



Source: Meddevicetracker report, "Women's Health: Osteoporosis Diagnostic Products"

Horizon DXA

Photo credit: Hologic

Prodigy DXA

Photo credit: GE Healthcare

quarter of 2014, can be used to assess osteoporosis at the hip and spine as well as vertebral fracture and to assess heart disease and obesity.

In addition, Jane Mazur, spokeswoman for Hologic, told *Medtech Insight*: "Hologic is starting to see growing interest in utilizing the technology (DXA) to assess body composition in the elite fitness, nutrition and weight loss markets."

GE Healthcare's Lunar Segment Leader, Claudio Mejia, said that the company's *Lunar iDXA* and *Prodigy DXA* systems, marketed to doctor's offices and in hospitals, are also increasingly used "beyond bone health."

"Other things you can test for related to body composition – weight management, diabetes, obesity, and lean muscle mass and sarcopenia – are getting increased visibility out there," Mejia said. "DXA can also be used for healthy populations where you can do body composition-type screening of healthy populations for athletic performance."

Many office-based and community-based bone density screening programs use pDXA and QUS systems, according to *Meddevicetracker*. Because these systems are limited to peripheral applications and offer information that is less definite than whole body DXA systems, they tend to be primarily viewed as screening tools.

However, benefits including low equipment costs, no radiation exposure and the system's usefulness to differentiate patients not at risk for fracture and those needing further evaluation by central DXA are catapulting QUS systems into doctor's offices, including those located in rural areas away from hospitals.

Suppliers of this technology include BeamMed, which markets its *Sunlight Omnisense 9000* model (which received the CE mark in 2014, but not yet US FDA approval); Diagnostic Medical Systems' *UBIS 5000*, which measures the speed of sound in the heel; and Furuno Electric Company's *CM-200*, *CM-200 Light* and *CM-300* models, which measure bone density of the heel.

Then there are also software-based densitometry systems, used to identify osteoporosis, that combine RA and image digitization to process an X-ray image of an appendage into a bone densitometry reading. Doctors in the US, however, tend to view RA technology as inferior to DXA, which translates into limited sales, according to the *Meddevicetracker* report. One of the suppliers of these systems is CompuMed.

Among the emerging companies is Artann Laboratories, which is developing its Bone UltraSonic Scanner (BUSS) technology to screen, diagnose and monitor osteoporosis.

GLOBAL MARKET FOR BONE REMODELING BIOCHEMICAL MARKER TESTS

Biochemical markers also represent an important diagnostic complement to bone-mass measurements, according to the *Meddevicetracker* report.

In 2015, global sales of BTM tests totaled roughly $85m with the US accounting for an estimated $39m in sales, the rest of the world accounted for $23m, the five major EU markets accounted for $15.3m, and Japan for $7.7m.

By 2020, global sales are expected to reach nearly $100m; growth in the developed markets will be in the low single-digit range, driven by the same forces as in the densitometry market, namely a rising aging population and growing prevalence of osteoporosis. (Figure 4.)

COMPETITION

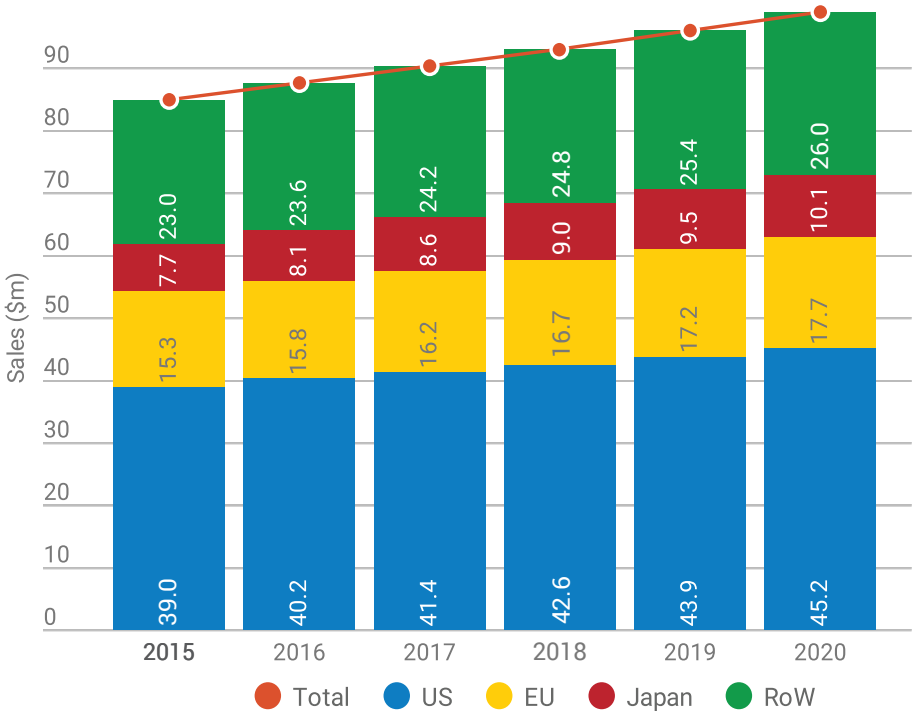
In the BTM test segment, competition is primarily based on price, quality, technology and speed of results, breadth of product line and distribution capabilities, according to the *Meddevicetracker* report.

In 2015, Roche was the leader in the global market for BTM tests, with a market share of 55% and an estimated $46.8m in sales. Alere Inc. ranked second, with an estimated 18% market share and about $15.3m in sales, followed by Quidel Corp. with a 9% share and $7.7m in sales.

Other suppliers of BTM tests accounted for an 18% market share and $15.3m in sales and include Beckman Coulter Inc., Immunodiagnostic Systems Ltd., Orion

FIGURE 4

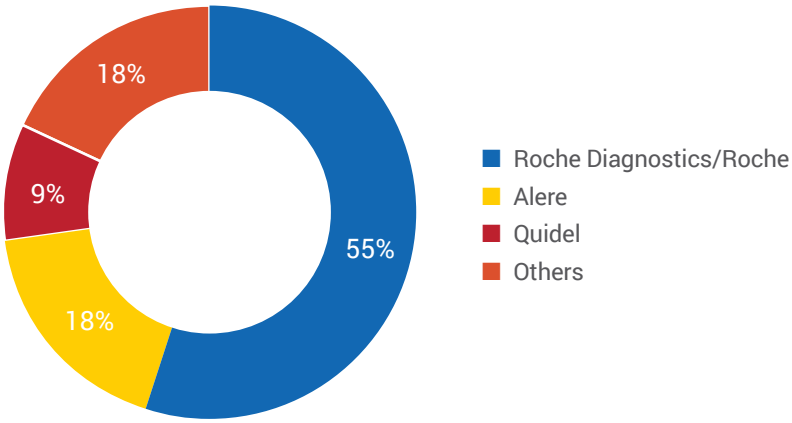
Bone Remodeling Biochemical Marker Tests Market Forecast by Region 2015-2020



Source: Meddevicetracker report, "Women's Health: Osteoporosis Diagnostic Products"

FIGURE 5

Bone Remodeling Biochemical Marker Tests Global Market, Supplier by Share, 2015



Source: Meddevicetracker report, "Women's Health: Osteoporosis Diagnostic Products"

Diagnostica and Quest Diagnostics Inc., among others. (See Figure 5.)

Roche, the world's leading supplier in the clinical diagnostics market, competes in the global market for BTM tests, with its *Elecsys* assays for bone resorption and formation, Quidel markets its *MicroVue BAP*, *DPD* and *PYD* marker tests for bone resorption globally.

Alere markets rapid diagnostic tests and competes in the global market for BTM tests with its *Osteomark NTx ELISA* markers for measuring bone absorption.

The company is currently embroiled in a lawsuit with Abbott Laboratories Inc., which last February signed an agreement to buy Alere in a $5.8bn deal. After learning about "damaging" revelations concerning Alere, Abbott is now trying to cut loose from the deal. In late January, the European Commission approved Abbott's pending buyout of Alere on condition it divest its *Epoc*, *Triage* and *BNP* businesses amid anti-trust concerns, but Abbott is still trying to get out of the deal.

PROS AND CONS OF BIOCHEMICAL MARKERS

The Pros

Biochemical markers are used for managing osteoporosis patients who are on long-term therapeutic regimens, specifically for monitoring the progress of therapy and patient compliance.

While bone scans can only detect bone density over long periods of time, biomarkers can detect changes within three months of initiating therapy.

According to the *Meddevicetracker* report, studies have repeatedly shown that only 50%-60% of osteoporotic patients continue taking oral medication for a year or longer for reasons that aren't quite clear, but may include cost, inconvenience in administration, side-effects and lack of sign that the drug works.

BTM may also have wider applications. For instance, the substance that biochemical markers measure via urine or blood tests can not only identify people who are "rapid bone losers," prone to the development of osteoporosis, they can also identify aggressive bone formation, which is typically a response to conditions such as Paget's disease or hyperparathyroidism.

BTM are also currently being evaluated in larger clinical trials for testing cross-linking region of type I collagen (or CTx, which is a bone resorption marker) used by oral surgeons to assess the risk of osteonecrosis of the jaw, following invasive dental procedures in patients treated with bisphosphonates.

The Cons

BMTs for bone turnover remain controversial due to the complexity of interpreting the value for patients as related to the intricacies inherent in bone metabolism.

Their usefulness for predicting fracture risk also still remains a topic of debate and the lack of standardization among commercially available marketed tests has led to variation between processing laboratories.

There is also no single test available to accurately reflect the balance between bone resorption and formation. Alkaline phosphatase, introduced into clinical use in 1929, was the first biochemical marker of bone turnover and remains the most widely used in clinical practice.

One of the major constraining factors for growth in this segment is the refusal of private payers in the US to reimburse for these tests, because they consider them "investigational" in diagnosing and managing osteoporosis, and managing patients with other conditions associated with high rates of bone turnover.

The US Centers for Medicare & Medicaid Services provides coverage for urine-based collagen cross-link BTM tests (Current Procedural Terminology (CPT) under code 82523. Coverage is also provided under CPT code 83937 for osteocalcin testing, and while there is no specific CPT code for BAP, several laboratories' websites identify CPT 84080 as being used for the (Access) Ostase test, according to the *Meddevicetracker* report.

Another issue is the lack of standardization. Scientific groups have called for greater standardization among tests. If that happens, the ability to combine BTM test results from osteoporosis clinical trials in a meta-analysis would give this market a boost. More knowledge derived from clinical trials may also open the door to use these tests for fracture-risk estimation together with physiologic and other factors contributing to variability of BTM concentrations.

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