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EU Roadmap: Catalyst For More Work, And A Long Way To Go

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While there is a sense of relief that the Medical Devices Regulation/IVD Regulation Roadmap has been published, it also serves as a reality check for the sector.

Despite how the document has been described in the lead up to its release, this is not a roadmap to implementation. Rather, it is a roadmap to creating what will effectively be the real roadmap to implementation.

The roadmap, finalized Nov. 10, includes eight broad "work streams," does not tell stakeholders in the sector what work is now needed to comply with the regulations. Instead, it contains a series of instructions, mainly to the EU's working groups, on the work that they need to carry out – much of it comprehensive and detailed – to create the documents, guidance and structures on which implementation can then be built.

The sector is one step removed from where it should ideally be now that the regulations have entered into force, and there is a long way to go before there is consensus over how the new requirements should be interpreted. It still seems like a tall order for all of the involved parties to complete the necessary work and issue the documents so that full implementation can take place on May 26, 2020 for the Medical Devices Regulation and May 26, 2022 for the IVDR.

For now, manufacturers keen to get on with compliance are working through many of the stages in the dark, or, if they are lucky, in the dim light. But in these conditions, it is still easy to make mistakes that could be costly to correct. Other manufacturers may take this state of affairs to decide it is still too early to start on compliance; but this would be against generally perceived wisdom from medtech regulatory experts and notified bodies.

"The detail in this document is likely to evolve as the work programs develop," the Competent Authorities for Medical Devices group, which worked the European Commission on the roadmap, says on its website. What is more, the European Commission has invited the medtech sector to let it know of editorial errors in the regulation documents, but this may well lead to comments on inconsistencies and anomalies in the text, too. *(Also see "EU Commission May Open Floodgates By Inviting Input On Editorial Errors" - Medtech Insight, 18 Oct, 2017.)* Overall, it appears there could still be several moving targets and nothing is quite set in stone.

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Scott Huennekens, CEO of digital surgery company Verb Surgical, tells *Medtech Insight* how the new era of surgery will not just be about robotics, but will also include advanced computing elements to "democratize" surgery and unlock what remains a largely untapped market.

US Supreme Court preview
http://bit.ly/2iWJTmx
Patent validity reviews and state suits filed against product companies are among issues impacting medtech that could be addressed during the current term of the Supreme Court.

Azar nominated
http://bit.ly/2zHSkfh
President Trump has tapped former pharmaceutical industry executive and government official Alex Azar to run the US health department, which oversees FDA, CMS and other agencies.

M&A flow quickens
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The pace of M&A picked up in October, with 30 transactions, and a particularly busy month for orthopedics.

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around. *Medtech Insight* caught up with Pierre Chauvineau, Boston Scientific's former VP of Rhythm Management, Europe, and now VP executive advisor, to get an inside view.

R&D

POLICY & REGULATION

India Settles On Classifications For Nearly 600 Devices, IVDs

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India's new classification system has four risk classes

As the countdown begins to the introduction of new medical device rules in India on Jan. 1, 2018, the health-care products regulator has finalized and published a list of nearly 600 medical devices and IVDs clarifying how these products will need to be classified under the coming regulations.

The list, which classifies products according to their level of risk, contains around 100 fewer entries than the draft version of the document that was issued for public consultation in June.

It contains 351 medical devices and 247 IVDs that have been classified as either class A (low risk), class B (low moderate risk), class C (moderate high risk) or class D (high risk). The Central Drugs Standard Control Organisation (CDSCO) has previously noted that the classification is based on the system developed by the International Medical Device Regulators Forum.

The list is "dynamic," CDSCO says, and is subject to revision from time to time under the provisions of the new device rules.

While it includes a "general intended use" for each of the products, this is designed to guide manufacturers and importers, and a product may have a specific intended use as specified by its manufacturer, the regulator clarifies.

Some of the devices and IVDS may have dual use and they may be classified accordingly, CDSCO says. In addition, components and accessories to medical devices or companion IVDs have been classified separately.

The list notes that anticoagulant solutions, embolization particles, chitosan scaffolds (for cartilage repair), riboflavin (for corneal collagen cross-linking), silicone oil endotamponade, intraocular gases and injectable fillers "shall be regulated as drugs under the provisions of the Drugs and Cosmetics Act, and Drugs and Cosmetics Rules, 1945."

When the new Medical Devices Rules 2017 come into effect in January, this will mark India's first device-specific regulatory framework. Medtech products under the current rules are grouped into 15 categories and are regulated as drugs. The new rules will require manufacturers to meet risk-proportionate regulatory requirements that are based on best international practices.

When the draft classification list was first published, India's medical device industry association, AiMeD, told *Medtech Insight* that it had identified some devices that had been classified incorrectly. *(Also see "Indian Medtech Finds Errors In New Draft List Classifying Devices, IVDs" - Medtech Insight, 17 Jul, 2017.)*

It is not clear to what extent the list has been changed in response to the trade group's input. AIMEd had given one example of a scalp vein set for administering parental fluid/medication into a patient's vascular system being classified as a class C device in the draft list. According to the product's intended use and according to the rules, it should have been categorized as class B, the trade group said. A quick scan of the final list shows that scalp vein sets are now categorized as class B.

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THE CLOCK'S TICKING:

Tracking Global Regulatory Deadlines

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Beginning this March, no new certifications will be issued under the legacy 2003 version of the global ISO 13485 standard – a hard-stop warning for the imminent transition to the much-revised 2016 medical device quality management systems standard. Meanwhile, big medtech regulatory changes are afoot in Southeast Asia, centered around a January 2020 enforcement date for the broad-based ASEAN Medical Device Directive.

CLICK
Check out our Interactive Timeline of global regulatory deadlines at http://bit.ly/2An8xn8.

Those are just a couple of important dates for medtech firms to keep a sharp eye on in the coming three-to-five years, which promise to be a period of significant upheaval for the global regulatory environment. Companies have a lot to do to ensure compliance as the fundamental rules of the road shift under their feet in multiple regions.

Medtech Insight's new, evolving Interactive Timeline of global regulatory deadlines seeks to capture this reality. The timeline tracks the forward march of change that device and diagnostics firms are facing and intertwines links to MTI's in-depth stories and podcasts, providing needed context and insight.

As long-time FDA official-turned-consultant Kim Trautman said earlier this year, device firms are facing a "perfect storm" of global regulatory changes. To help weather the storm, check out the timeline, bookmark it, and look for updates.

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MEDTECH'S HIGH-EARNERS:

2016 Executive Payouts Boosted By Bonuses, Stock Awards

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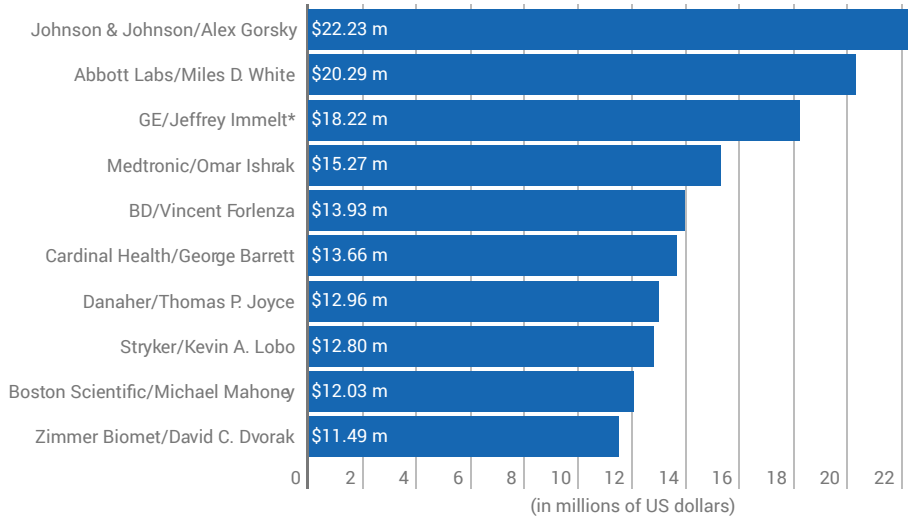
In the run-up to next month's launch of the annual MTI 100 league tables, *Medtech Insight* took a look back at last year's top 20 device companies to delve into how well these organizations rewarded their CEOs in 2016, the most recent full fiscal year.

Our analysis showed that the ten most highly-paid CEOs within these top 20 firms reaped generous compensation packages in 2016, thanks to their stock and options holdings in the companies they run. In a few cases, their pay packets were further inflated by some very healthy incentive bonuses.

Medtech Insight compiled its data on device and diagnostics company CEO pay packages by researching proxy statements at shareholders' meetings, and annual reports required to be filed and posted online by publicly traded companies with the US Securities and Exchange Commission (SEC).

The 2016 data on top executives' pay was the most recently available as of Oct. 30. Also, for large, diversified firms that make other products beyond devices, compensation information for leaders of the firms' device-specific divisions (such as the heads of GE Healthcare, or Johnson & Johnson's orthopedics subsidiary, DePuy Synthes) does not have to be filed with SEC. In these cases, we have included the pay of the group CEO. Below are the top 10 high-earners of 2016:

Top 10 Highest-Paid CEOs Of Device, Diagnostic Firms In 2016



*retired 6/2017

Source: Securities and Exchange Commission (SEC) filings

TWO CEOS DID WELL BUT LEADERSHIP QUESTIONED

Despite a boost in pay in 2016 for accomplishments and increase in sales and growth at their firms, two of the top 10 earners were facing severe challenges that threatened their leadership and bonuses by late 2016, and into 2017. Among these were Zimmer Biomet CEO David Dvorak, who stepped down from his post in mid-July, following a disappointing preliminary sales and earnings report for the second quarter of 2017. *(Also see "Zimmer Biomet Names New CEO Amid Disappointing Earnings" - Medtech Insight, 12 Jul, 2017.)*

Also, Cardinal Health CEO and George Barrett declined to accept an incentive bonus for the 2017 fiscal year after his company – which in addition to manufacturing and distributing devices is also a supplier of pharmaceuticals – became embroiled in an opioid supply scandal and agreed to pay settlements related to charges by the federal Drug Enforcement Administration (DEA) in 2016. His incentive bonuses for the two prior years, 2015 and 2016, amounted to $2.51m and $2.39m, respectively.

Barrett faced a challenge to his leadership initiated by a major shareholder, the Teamsters union, which argued in mid-October that the CEO failed to set the "correct tone at the top" for the company

due to the DEA settlements, and called for shareholders to vote to strip him of his Board Chairman's seat, at Cardinal's next stockholders' meeting on Nov. 8. *(Also see "Teamsters Ask Stockholders To Replace Cardinal Health Chairman" - Medtech Insight, 18 Oct, 2017.)*

But on Nov. 6, the question was settled when Cardinal announced that Barrett would step down as CEO on Jan. 1, 2018, (to be replaced in the CEO spot by current CFO Mike Kaufmann), and would remain as executive board chairman for only one more year – until after the next shareholders' meeting in November 2018. *(Also see "George Barrett To Step Down As Cardinal Health CEO" - Medtech Insight, 7 Nov, 2017.)* The company cited implementation of a "thoughtful succession plan" as the reason behind the change in CEOs.

INDUSTRY CEO PAY INCREASED BY 19% IN 2016, OVER 2015

In addition to receiving generous pay in 2016, the combined pay packages for the top six earners – **Johnson & Johnson**'s Alex Gorsky, **Abbott Laboratories Inc.**'s Miles D. White, **General Electric Co.**'s former CEO Jeffrey Immelt, **Medtronic PLC**'s Omar Ishrak, **Becton Dickinson & Co.**'s (BD) Vincent Forlenza, and **Cardinal Health Inc.**'s George Barrett – increased an average of 19% from 2015 to 2016.

For example, Gorsky saw an approximate 22.5% increase in his compensation in 2016 over the prior year, White received a 4.6% raise, and GE's Immelt enjoyed a huge increase of 71.68% in pay, primarily due to "other" compensation of $6.8m he was entitled to before departing the company in July of this year.

Further, compensation for Ishrak rose by 9.4% in 2016; Forlenza was paid 19% more in 2016 over 2015, while pay for Barrett was just slightly higher, at approximately 3% more, in 2016 than it was in the prior year.

COMPANIES APPLY DIFFERENT COMPENSATION APPROACHES

Different firms take varied approaches to compensating their executives. As a general rule of thumb, CEOs' base pay represents just 7.5% to 10% of their entire compensation package, although Jeffrey Immelt's base pay represented 20.86% of his pay package at GE in 2016. Some companies apply their greatest awards in the form of stocks or bonds, while others give more generous incentive bonuses or higher amounts to pension funds that can be tapped by a CEO upon retirement.

For example, in 2016, Miles White received a larger contribution to his pension funds – worth about $3.86m – than he did in his incentive bonus for the year, $3.2m. In another case, Forlenza had a $5.72m stock award, much higher than either his base pay of $1.11m, or pension fund/deferred amount of $485,787.

CLICK
to see the pie graphs showing the distribution of pay for each of the ten high-earners go to http://bit.ly/2ieBSJZ.

ALEX GORSKY, CHIEF OF JOHNSON & JOHNSON

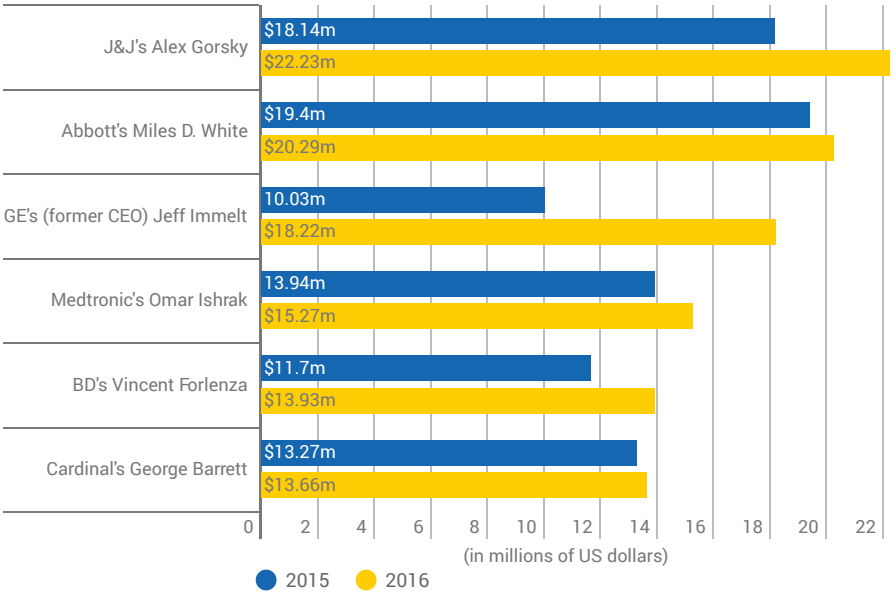
While J&J's device division and drug business grew only slowly in 2015 and 2016, overall the company was buoyed by strong growth in its consumer products segment, as the company's CEO Alex Gorsky predicted it would in January 2016. *(Also see "J&J Heralds Year Of 'Good Momentum' For Consumer Health Business" - Medtech Insight, 27 Jan, 2016.)* The uptick in sales, and a $16.65m incentive bonus for 2016, helped explain an increase in Gorsky's overall compensation package from $18.14m in 2015, to $22.23m in 2016.

J&J's outlook could improve even more over this fall and winter due to strong sales in its orthopedic division, as buyers continue to respond favorably to DePuy Synthes' hip and knee products. During a July 18 earnings call Gorsky said there was particular customer enthusiasm for the *Actis* hip implant system, and that the company plans some additional launches in its *Attune* knee group.

MILES D. WHITE, CEO AT ABBOTT LABORATORIES

Compensation for Abbott Laboratories' CEO Miles D. White rose by approximately 4.6% last year – from $19.4m in 2015, to $20.29m in 2016 – aided by a boost in stock awards and option awards of $5.25m in each category, and a $3.2m incentive bonus that year. And while revenue from Abbott's medical device unit was relatively flat at just 0.7% in the fourth quarter of 2015, by the first quarter of 2016, sales were up at Abbott 5% year-over-year, and were particularly

Raises For The Six Most Highly Paid Device Firm CEOs, 2015 vs. 2016 Compensation



Source: SEC filings

strong in emerging markets including China, India and Russia, where sales increased 12% on an operational level.

White remained upbeat during early 2016, saying he wanted to focus on "business fundamentals" for Abbott, and by January 2017, the company's diagnostic business was announcing CE marks and the European launch of its *Alinity* system for blood and plasma screening, and its *Alinity ci* series of instruments for clinical chemistry and immunoassays. *(Also see "To Alinity And Beyond: Abbott Dx Launches Into Its Next Phase" - Medtech Insight, 26 Jan, 2017.)* The move to increase Abbott's presence in the diagnostics sector "is an extremely ambitious undertaking and one that will strengthen our competitive position tremendously," White said during a Jan. 10 earnings call.

White could also benefit, and see an increase in his bonus for 2017, from Abbott's merger with St. Jude Medical in early January this year, giving it a share of the cardiac rhythm management market *(Also see "Abbott Becomes CRM Player Overnight By Completing St. Jude Deal" - Medtech Insight, 5 Jan, 2017.)*, alongside a strong series of novel device approvals this summer, including the *HeartMate 3* left-ventricular assist device and the firm's companion diagnostic *RealTime IDH2* assay, indicated for select candidates to be treated with *Idhifa* (enasidenib) for relapsed or refractory acute myeloid leukemia, marketed by **Celgene Corp.** and **Agios Pharmaceuticals Inc.** *(Also see "US Approvals Analysis: Abbott Leads Another Strong Month For Novel Approvals" - Medtech Insight, 13 Sep, 2017.)*

Alternatively, when reviewing White's performance over the last year, Abbott's board of directors could take a dim look at the company's trial failures on its *Absorb GT1 BVS* bioresorbable drug-eluting stent during the first quarter of 2017, which showed Absorb was statistically inferior to the firm's earlier, *Xience* everolimus-eluting stent or coronary artery bypass graft (CABG). Abbott ultimately decided to pull its *Absorb* first-generation bioabsorbable coronary stent off the market Sept. 8, although it will continue with an ongoing trial on its Absorb GT1 BVS. *(Also see "Abbott Pulls Absorb Stent Off The Market, Citing Low Sales" - Medtech Insight, 8 Sep, 2017.)*

> As a general rule of thumb, CEOs' base pay represents just 7.5% to 10% of their entire compensation package.

INCOMING GE CEO JOHN FLANNERY HERALDS BELT-TIGHTENING PHASE

As already pointed out, GE's former group CEO Jeffrey Immelt did quite well as head of the conglomerate, and, as a result, garnered a 71.68% increase in his pay from 2015 to 2016 when he earned $18.22m upon his mid-June retirement. But the new CEO, John Flannery, who formerly ran GE's Healthcare division and officially took over the lead post at GE on Aug. 1, *(Also see "GE Taps Healthcare Again For New Group Head" - Medtech Insight, 12 Jun, 2017.)* has already signaled a desire to boost profits even more at the overall company (including the **GE Healthcare** division) by cutting operating costs and shutting down some divisions and sectors.

Flannery also has started at a much lower annual compensation level than Immelt – with base pay of $2m (Immelt's base pay was $3.8m in 2016), plus a target of $3m for Flannery's incentive bonus (Immelt's incentive bonus was $4.3m last year) for a total of $5m, according to a June 12 8-K report filing by GE with the SEC. Of course, Flannery is also expected to be paid in shares of GE common stock, on top of his base pay and incentive bonus, depending on his performance this year and next, said the 8-K report.

As a key sign of Flannery's drive to save dollars at GE, during an Oct. 20 third-quarter 2017 earnings call, he told investors that third quarter results "are completely unacceptable," and that his future plans are to "drive sweeping change" in the firm's varied businesses and corporate culture, and be "much more disciplined at all levels of the company on capital allocations," and reduce the overall company's complexity.

GROUNDING THE CORPORATE JETS

Another example of Flannery's desire to cut costs is his early August decision to ground all six of GE's corporate jets, stopping the practice of the company running a second, empty "backup" jet behind former CEO Immelt's plane as he flew around the world. The second jet was required so that Immelt wouldn't be held up by mechanical or security problems with his primary jet, said a recent *Wall Street Journal* report.

Flannery also promised during the Oct. 20 earnings call to divest certain businesses – including non-health-care segments in GE's power and transportation divisions, although GE Healthcare itself did quite well and will probably be spared. Company executives reported during the earnings call that health-care orders were up 6% in the third quarter of 2017 over the 2016 third quarter, driven by an 11% increase for ultrasound products (including GE's *LOGIQ, Voluson* and *Vivid*), and an 8% increase in orders for its mammography equipment (such as the *Senographe Pristina* system) and CT equipment (*Revolution CT GSI Xstream*).

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Amazon's Medtech Retail Plans: Analyst Finds More Evidence

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The same market analysts who argued online retail giant **Amazon.com Inc.** is gearing up to dominate the medical device and supplies distribution market say they have found more evidence the company is focused on the device sector rather than pharmaceuticals.

After Amazon reported receiving licenses to sell medical products from a slew of states, stocks for pharmaceutical retailers saw a major plunge. However, Brian Tanquilut, an analyst with Jefferies says that the market's response may be unfounded. Based on his team's analysis, Tanquilut says, Amazon is taking a path of least regulatory resistance by focusing on staking a claim in the medical device and supplies retail sector rather than immediately challenging drug retailers such as **Walgreens Boots Alliance Inc.** and **CVS Health Corp**. *(Also see "Analyst: Amazon Possibly Priming Itself As Medical Device Retailer" - Medtech Insight, 30 Oct, 2017.)*

The conclusions are based on scrutiny of Amazon's communications to Tennessee's, and to some extent Indiana's, pharmacy board.

"As we dug deeper into news of Amazon's wholesale pharmacy licenses -- which drove a sell-off in pharmaceutical supply chain stocks -- we found specific examples of correspondence between the Indiana and Tennessee pharmaceutical boards and Amazon stating that the licenses can only be used for medical device/supplies distribution," writes Tanquilut in a Nov. 8 analyst note. "While this renders the sell-off on the news of the licenses unwarranted, investor anxiety over Amazon's future plans still puts a cloud over the group that impacts near-term valuations."

READING BETWEEN THE LINES

Tanquilut and his team used a Freedom of Information Act (FOIA) request to the Tennessee state pharmacy board to obtain communication between Amazon and the board. Based on the online retailer's responses to questions posed by the board about their license requests, the analysts argue company is looking to get licenses to distribute medical devices rather than drugs.

In one correspondence, the company was asked if it is licensed or registered with FDA. Amazon's response was that it plans to distribute prescription devices and therefore does not require a license or registration with FDA because, Amazon suggested, the agency does not require them for medical devices. In another answer to the board, company stated it's three Indiana fulfillment centers do not meet Tennessee's definition as drug outsourcing facilities because they do not intend to store or ship drugs from those warehouses.

Similarly, in an email captured in the correspondence with the Tennessee pharmacy board, Amazon revealed its communication with the Indiana pharmacy board about its plans for its Indiana facilities.

"[I]n Feb '16, before Amazon officially decided to pursue the distribution of prescription med devices/supplies and apply for licenses in other states, the company's representatives asked for details surrounding the regulations that the fulfillment centers would be subject to if they were to distribute medical devices/supplies in the state of Indiana," said Tanquilut. "Based on the director of the Indiana Board of Pharmacy's answer and without knowing the direct question from Amazon representatives, we believe that Amazon's intent behind this email exchange was to confirm that the company would not be subject to the major regulatory requirements within the state's Wholesale Drug Distribution Act if they chose to solely distribute medical device/supplies, suggesting that avoidance of these more comprehensive regulatory requirements was top of mind in the decision to enter that space and not prescription drugs."

DRUG RETAILERS LOOKING TO PARTNER

The analysts argue that despite the fact Amazon has sent signals every year that it is interested in entering the drug-supply sector, the company has not done so because there are less-regulated business lines, such as supplying medical devices, that are easier for the company to get into. The Jeffries team also argues that pharmaceutical suppliers such as Walgreens are aware of this position by Amazon and are operating on that assumption.

As evidence, Tanquilut quotes recent comments by Alex Gourley, Walgreen's co-chief operating officer, during a recent investor conference. The comments seem to indicate that pharmaceutical retailers know Amazon has an uphill battle to navigate the pharmaceutical regulations they already understand, which is probably the reason the company hasn't posed a threat yet. The entrenched drug retailers are even potentially willing to develop partnerships with the online giant to avoid competition.

"I still think that Amazon... in a regulated market, will find it different in other markets, for example, wine and spirits, as one example, to enter... that questions still got to be answered I think," said Gourley. "But when they come and if they come, we'll be more than willing to work with them or to compete with them. We feel good and strong about our position."

By the analysts' count, Amazon has begun distributing medical devices and supplies to 30 states that don't require distribution licenses for the products. The company has acquired distribution licenses for medical devices and supplies in another 17 states that require some licensing for the products, but have so far have skipped California, Maryland and South Carolina because the regulations in those states are especially complex.

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Exec Chat: From Cameron To Boston Scientific, Navigating Through CRM Challenges

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Boston Scientific Corp. entered the cardiac rhythm management market in 2006 after acquiring Guidant for a hefty $27bn, which, at that time, was the biggest deal in medtech history. Some market spectators had balked at the offer price, which enable Boston Scientific to take Guidant away from Johnson & Johnson, but the Massachusetts firm had justified the deal – which it described as a "transforming event" in its annual 2007 report filing with the US Securities and Exchange Commission – with the significant high-growth potential it saw in the CRM sector and the opportunity for Boston Scientific to be an well-rounded heart device player.

The immediate years after the acquisition did see CRM top-line make modest increases but then things started slipping after 2009, with sales of this business declining every year (dropping 10% between 2009-2010, then by 4% in 2011, and another 8% in 2012). However, the damage seemed to have been brought under control after 2012, when Boston Scientific saw a change at the helm, with new CEO Mike Mahoney coming on board and promising to take the company back to growth. That year also saw the firm acquire Cameron Health, the developer of the S-ICD subcutaneous implantable cardioverter defibrillator, which it had first invested in back in 2004. From this acquisition, Boston Scientific took on a technology that is now one of the key drivers of growth for the CRM unit. It also gained management expertise in the form of Pierre Chauvineau, who not only oversaw Cameron's international business, but also had 20 years at Medtronic, the CRM market leader.

Pierre Chauvnieau, VP executive advisor, Boston Scientific

Speaking at the Oct 19 *Med In Ireland* event in Dublin, Chauvineau said candidly that Boston Scientific's CRM business "was challenged" when he came on board with the Cameron Health acquisition. Unlike more nimble start-ups, big multinationals tend to find it harder to build a disruptive culture within the organization, Chauvineau told delegates, but Boston Scientific is aiming to address this challenge by nurturing a strong culture that can adapt quickly to the changing healthcare environment and the needs of their customers and patients.

Medtech Insight caught up with Chauvineau for a quick chat to touch on topics including this cultural shift and how it has helped, in part, to change the trajectory of Boston Scientific's CRM business and also about his perspectives on the bigger CRM market, the continued challenges – in the reimbursement and regulation of medtech – and the opportunities for innovation in this field.

Medtech Insight: When Cameron Health was bought by Boston Scientific in 2012, did you move into the role that you are in now?

Pierre Chauvineau: No. I was at Boston Scientific after the acquisition to help with the integration of Cameron. Then a few months later, Boston announced it was changing the way the company was organized from a geographic focus perspective to a business focus. That's when they asked me if I wanted to take the leadership job for CRM in Europe. I said 'no' at the beginning because I spent 20 years at Medtronic, before I went to Cameron and going back into a corporate role was not my favorite option. What changed my mind though was meeting the leaders of Boston Scientific; [CEO] Mike Mahoney, Joe Fitzgerald [the president of RM) and Michael Onuscheck [then President Europe]. I thought those people were very special and that we could do something together. At that time, I would not have called Boston Scientific a 'winning' company so it was about trusting the people to change the trajectory of the business.

You have been very candid about Boston Scientific's CRM business not being in a good place when you came to the company in 2012. It has been said that it had been a difficult integration and that Boston Scientific's mistake had been to run the CRM business like a stent business. What's the difference between running a business that sells stents and one that sells cardiac rhythm management devices?

The big difference between the two is that with stents, you deliver the implant to the patient one-time and then you rarely see the patient again. In a CRM environment, you take care of the patients for life. After you implant a CRM device in a patient, you have the patient coming back every six months

or so for a follow-up, so as a physician you need to have complete trust in your device provider.

Your provider is not someone who just sells you the product. Customer service and support is critical. You need to have someone who goes back regularly to the physicians and help them with the patient follow-up, understand the parameters of the programmer, and can support the physicians in fine-tuning the program for the patient.

That's a huge difference between stents and CRM.

In the five years that you've been at Boston Scientific, how has the CRM business evolved from where it was when you first joined to where it is now?

When I started, it was not doing so well. We had to completely transform the business in terms of remotivating the team and making the team win again. The addition of releasing highly competitive new product lines and the acquisition of new technologies also were of great help. For me, it's all about people and together with my close leadership team, we developed a change management process. It took two years of really hard change and for the last three years, we have been winning against the competition.

But has the CRM market itself improved?

No, it's been pretty flat. It's been flat to decreasing over the last five years, it's a very difficult market and the tensions have been building up even more this year.

Are your other CRM rivals also being impacted?

We all feel the pain. It's the market conditions. And the pricing pressures continue to be very intense. It's organized pressure by consortiums that get together and do bulk purchasing.

What are the key challenges that Boston Scientific's CRM business continue to face?

The reimbursement environment is one, but it could be an opportunity rather than a challenge.

Reimbursement is slowly moving away from measuring activity to measuring outcomes. By rewarding activity, the more cases you do, the more money you make as a hospital. However, for high value-high one off price items like implantable cardioverter defibrillators, what's happened is that this has led to hospitals wanting the prices of these devices to be reduced when they do volume purchasing.

So measuring value-based outcomes for reimbursement, rather than activity, is actually a way to solve this problem and can be a great opportunity for companies. Especially if you have an implantable defibrillator [like Boston Scientific's extended longevity ICDs] which lasts twice as long as your competitors, then you know you are bringing a real benefit to the patient, to the patient outcome, and to the healthcare provider.

The new EU medtech regulations must also be a big concern.

We have until 2020 to comply with the new rules. We are getting ready for this.

Will the US start becoming your first go-to market for new products?

There may be a risk. If you were a company what would you do? If you have a market as large as the US, with one language one regulation and if you can get regulatory approval faster in the US, or at least at the same time as Europe, you'd want to invest in the US, not in Europe. We hope it isn't going to cause too much disruption in the technological innovation. That said, we do agree that we need quality products with quality outcomes – but there needs to be a fine balance.

The market for CRM devices is still substantial and there is a need for technologies in this field to continuously improve. In this context, in which direction is CRM innovation going?

Leadless is where it's heading. The lead has always been the weak link of the system, even though we pride ourselves at Boston Scientific on having excellent long term results. In the near future, we will be connecting our leadless pacemaker and S-ICD so that they can wirelessly communicate with each other, so there's less hardware in the body and the venous system is not clogged up. It will keep options open for the patients, and for us, that is the most important aspect of what we do.

We're looking at innovations on the diagnostic side too and we feel excited about the potential benefits this may bring in the next 12 months

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TCT 2017: ORBITA Ignites Controversy, Twitter Storm Over Stents, But Analysts Expect Little Impact

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Analysts closely following drug-eluting stent manufacturers do not expect the controversial results of the ORBITA trial to have much impact, at least in the short-term, on the coronary stent market even though the sham-controlled trial found percutaneous coronary intervention with drug-eluting stents did not increase patients' exercise duration by more than the effect of placebo procedure.

ORBITA, funded by the UK's National Institute for Health Research, the Foundation for Circulatory Health, Imperial College Healthcare Charity in London, and **Philips Volcano** is the latest trial effort to determine the proper role of PCI in patients with stable angina. Primary investigator Rasha Al-Lamee from Imperial College London presented results of ORBITA on Nov. 2 at the Transcatheter Cardiovascular Therapeutics (TCT) scientific symposium in Denver. The results were also simultaneously published in *The Lancet*.

"The necessity for placebo-controlled trials has been rediscovered several times in cardiology, typically to considerable surprise. Often a therapy is thought to be so beneficial that a placebo-controlled trial is deemed unnecessary and perhaps unethical," Al-Lamee and colleagues explain in *The Lancet*. "However, 40 years after the first PCI, ORBITA's findings show that placebo-controlled randomised trials remain necessary."

Al-Lamee and colleagues explain that although multiple trials have shown PCI reduces the risk of death and myocardial infarction in patients presenting with acute coronary syndromes, no blinded randomized trial has shown a benefit of PCI over optimal medical management alone. And, in 2007, the COURAGE trial found no difference in myocardial infarction and death rates between patients with stable coronary artery disease treated with PCI and optimal medical therapy versus optimal medical therapy alone and professional guidelines recommend PCI only for patients who remain symptomatic after trying to resolve their angina with medication. *(Also see "Large Registry Finds Questionable PCI Procedures Before Surgery Remain Common" - Medtech Insight, 30 Mar, 2016.)*

Nevertheless, PCI remains a common treatment for patients with stable angina, Al-Lamee et al point out in *The Lancet*. "Angina relief remains the primary reason for PCI in stable coronary artery disease," the authors explain. However, none of the trials showing a benefit of PCI in stable angina patients were blinded and "in the absence of blinding, the effect size of PCI on symptomatic endpoints can be overestimated because of the addition of the placebo effect to the true physiological effect of intervention." So, to eliminate the possible placebo effect, ORBITA compared PCI with drug-eluting stents plus optimal medical management to a sham intervention with optimal medical management. The patients, the recovery staff, and the physicians who evaluated the patients after the procedure knew if they were treated with the real PCI procedure or the sham.

"While the study findings do suggest to a degree of placebo effect in PCI procedures for improving exercise capabilities, the study design makes the results more food for thought than immediately practice-changing," Jefferies analyst Raj Denhoy said in a Nov. 6 note. "Among the issues raised: the study is relatively small; the follow-up time was short; there was a higher exercise threshold in the placebo group pretrial—with the implication being the result could be a regression back to baseline. Having said all that, the ORBITA trial is the first truly randomized trial PCI and the results shouldn't be dismissed outright. So, while the largest stent companies might not see an immediate decreases in PCI utilization, with stent sales representing annual global sales of just north of $1bn each for **Boston Scientific**, **Abbott**, and **Medtronic**, the resonance of the trial into clinical practice will be closely watched."

After seeing how COURAGE impacted the drug-eluting stent market, Wells Fargo's Larry Biegelsen is confident the ORBITA results will not have a huge impact. "[The] potential Impact of ORBITA on DES companies is likely small," he wrote Nov. 5.

"We continue to see the COURAGE study as a good analog for ORBITA because both studies evaluated stable angina patients undergoing stenting." Biegelsen's team analyzed the major published studies of the impact on COURAGE on the volume of PCI in stable angina patients suggest that these patients account for about one third of stent patients, and the COURAGE results caused a 16% to 26% reduction in stent procedures in stable angina patients ranged, and therefore about an 8% reduction in total stent volume (33% x 25% = 8%).

"Like COURAGE, we would expect any impact from ORBITA to be seen in the US [rather than outside . US DES exposure by manufacturer is relatively low at 5.2% of total sales for Boston Scientific, followed by 1.1% for Abbott and 1.2% for Medtronic. If we assume half the impact of COURAGE or a 5% reduction in PCI volume in the US over the next 12 months, the financial impact to all three companies would be very small," Biegelsen concludes. "Even if we assume the impact of ORBITA is similar to that of COURAGE, the impact for all three companies would be manageable in our view. Our best estimate at this time is that the impact from ORBITA is less than 50% of the impact of COURAGE or less than a 5% reduction in PCI volume over the next year."

ORBITA RESULTS CREATE TWITTER-STORM

The ORBITA results immediately triggered an unprecedented avalanche reaction from cardiovascular interventionalists, other physicians, patients, and the general public on Twitter and the discussion about the results and what they mean for clinical prac-

tice has continued on social media and in other online media that shows no sign of dissipating soon.

While both interventionalists and non-interventionalists commended the ORBITA authors for their design and execution of a sham-controlled trial, many interventionalists were especially angry with the coverage of the trial in the mainstream press, especially the *The New York Times*. Interventionalists such as Ajay Kirtane from Columbia University suggested that many of the articles on ORBITA failed to emphasize that it only applies to stable angina and that it was a relatively small study with a short follow-up.

Ajay Kirtane MD SM
@ajaykirtane

.@ginakolata What do you think about this from principal investigtor @TCTMD Where is the nuance in your article? Try cardiobrief.org/2017/11/02/divi...

9:07 PM - Nov 2, 2017

1 4 5

Kirtane was among the commenters also took issue with the editorial by David Brown and Rita Redberg, pointing out statistical errors and suggesting that the authors may be biased against PCI.

Ajay Kirtane MD SM
@ajaykirtane

Was the @DavidLBrownMD @RDRedberg ORBITA editorial in @The Lancet...

Fair 15%
A little bit of a stretch 37%
Unhinged **48%**

247 votes · Final results

11/2/17, 6:10 PM

Ajay Kirtane MD SM
@ajaykirtane

That's what an editor / reviewer is supposed to pick up if you didn't know it. Also AKI number way too high. Within field this is obvious.

10:13 PM - Nov 3, 2017

1 5

One of the major limitations of ORBITA cited by many commenters, including Gregg Stone of Columbia University and Sunil Rao of Duke University, is that about 27% of the patients in the trial who were evaluated with physiological evaluation with fractional flow reserve, showed an FFR ratio over 0.8 and lesions with FFR ratios that high are not considered appropriate for PCI under current professional guidelines. However, in real-world clinical practice PCI is chosen based on angiography alone without physiologic evaluation, so the ORBITA investigators allowed these patients to undergo PCI based on angiography alone.

Greg W. Stone MD
@GreggWStone

Corresponds with the ~27% of lesions in this trial with FFR >0.80 for which PCI is inappropriate. Class III to have treated these pts. twitter.com/jreinermd/status...

11:48 PM - Nov 2, 2017

4 16 35

Sunil V. Rao
@SVRaoMD

Important point. Physiology assessment w/ deferral of non-sig lesions routine in our lab @manesh_patelMD @RVSwaminathanMD twitter.com/angioplastyorg...

1:57 PM - Nov 2, 2017

7 6 21

Supporting the prediction that ORBITA would show a benefit of PCI if it had excluded the patients with high FFR ratios, several interventionalists point to the results of the FAME 2 trial which results showed that FFR can identify stable coronary disease patients who benefit more from PCI that medical therapy alone. William Fearon of Stanford University presented three-year outcomes from FAME 2 at the TCT conference on Nov 2 by and the paper with the results was simultaneously published in Circulation. FAME 2 is sponsored by St. Jude Medical/Abbott**.**

FAME 2 randomized 888 patients with stable, single or multivessel coronary artery disease with an FFR ratio of 0.80 to treatment with FFR-guided PCI plus medical therapy or medical therapy alone. At the three-year follow-up, the PCI group had a lower rate of major adverse events than the medical management group (10.1% vs 22.0%; p<0.001). The difference was primarily driven by a lower rate of urgent revascularization in the PCI group versus the medical management group. (4.3% vs 17.2%; p<0.001). Death and myocardial infarction were slightly lower in the PCI group and angina was significantly less severe in the PCI group at all follow-up points. FAME 2 also found that although the average initial treatment costs were higher in the PCI group ($9,944 vs. $4,440; p<0.001), the total costs over three years were about the same ($16,792 vs. $16,737), so the incremental cost-effectiveness ratio (ICER) for PCI compared with

medical therapy was $17,300 per quality-adjusted live year at two years and $1,600/QALY at three years.

> **Mehrdad Saririan, MD** @DrSaririan 2 Nov
> Replying to @SukNijjer and 2 others
> How should be message to pts, in light of FAME II 3-yr?

> **Ethan Korngold, MD**
> @SVRaoMD
> Conflicting data! Maybe a positive stress test isn't enough, and ALL lesions need FFR/iFR before treating. #TCTDENVER #ORBITA
> 12:13 PM - Nov 2, 2017
> 2 2 6

One of ORBITA's primary investigators, Darrel Francis of the Imperial College London, London rejected that criticism of the study design.

> **Prof Darrel Francis [Cardio, logically speaking]**
> @ProfDFrancis
> Inane #ORBITA criticism #4: "You shouldn't have randomized FFR>0.80".
> I accept this as invalidating ORBITA, if EITHER of the following holds:
> (a) Show me how we know lesions cause ANGINA <0.80 but not >0.80
> (b) Confirm you never PCI lesions like ORBITA appx if angina on 3 drugs
> 3:38 PM - Nov 9, 2017
> 1 9 12

> **Stefan Harb** @stefan_harb 8 Nov
> Replying to @ProfDFrancis and 3 others
> The FFR cutoff is bound to maximum post-stenotic hyperemia during the short testing time. It cannot be expected to be the same in many other functional states.
> PA-reduction works both prestenotic and poststenotic, but apparently not to the same extent.

> **Prof Darrel Francis [Cardio, logically speaking]**
> @ProfDFrancis
> That's what I feared. We didn't use an FFR cutoff for entry for #ORBITA because, there isn't one that specifies when *angina* should occur.
> I do worry that changes of medication (e.g. anti-anginals) affect a pts FFR threshold for angina.
> And why should different pts have same?
> 4:04 PM - Nov 8, 2017
> 1 1 3

The significance of the ORBITA results will likely be a topic of debate for a long time, just as the COURAGE results were. Some physicians, like Peter Cram of the University of Toronto, argue that the results mean that PCI in stable angina patients is inappropriate.

But it appears that the interventional cardiology community is not ready to change professional guidelines based on the results, according to Duke's Daniel Mark and Ameya Kulkarni from the Mid-Atlantic Permanente Medical Group in Washington, DC.

And lead investigator Rasha Al-Lamee said at the TCT meeting: "To use [the ORBITA results] to downgrade angioplasty in the guidelines – and I say this as one of the investigators – would be an incredibly large overreach."

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US Approvals Analysis: Original PMA Slowdown, De Novo Upswing Among Recent Trends

DAVID FILMORE david.filmore@informa.com

October was a relatively light month for FDA approvals, with two original PMAs, one panel-track supplement and one *de novo* getting through the agency, according to *Medtech Insight*'s Approvals Tracker.

Even with the slower month, the agency remains on a relatively even pace in 2017 with recent calendar-year record volumes in novel device and indication approval categories. *(Also see "US Approvals Analysis: 2016 Another Record Year For FDA Novel Device Approvals" - Medtech Insight, 13 Jan, 2017.)* But, for original PMAs – the pathway for the novel, high-risk devices – a slowdown might be

coming, as the number of submissions formally filed with FDA has recently declined.

According to performance-review data posted by FDA on Nov. 6, as of Sept. 30, sponsors filed only 33 original PMAs with the agency during FY 2017 (which ended Sept. 30). That is down from 55 filed in the full-year FY 2016, a 40% drop.

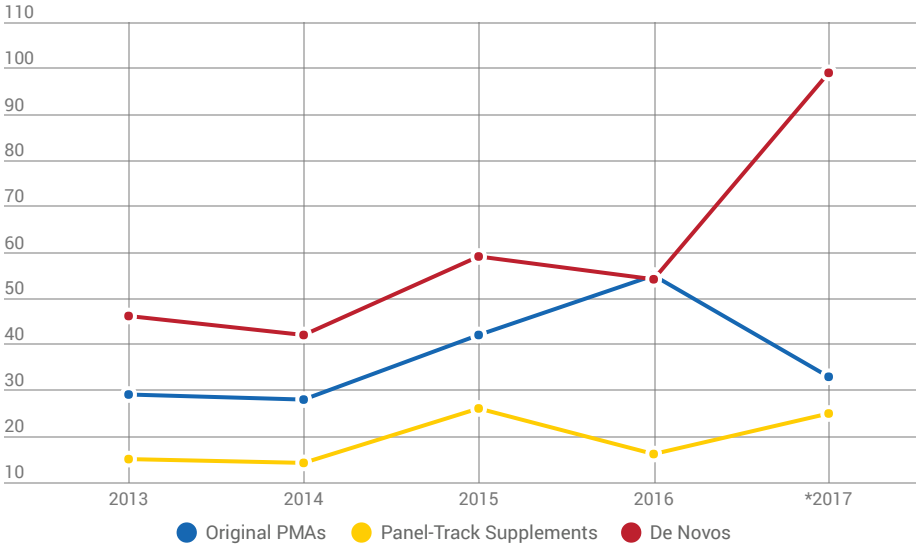
A submission is officially filed after it gets through FDA's "refuse to accept" and "refuse to file" review processes. There will likely be several more more FY 2017 submissions that reach the filing stage, as five original PMA and/or panel-track supplement submissions remained within the typical timeline for an RTA review, and at least two more might still have been stuck in the RTF process as of Sept. 30. But even if all of the pending submissions are original PMAs that are ultimately filed with FDA, it will still be a noteworthy drop.

Meanwhile, the number of panel-track supplement and *de novo* submissions are on an upswing, FDA's most recent data shows. Twenty-five panel-track supplements were formally filed with FDA in FY 2017, as of Sept. 30, up from 16 in FY 2016. Meanwhile, *de novo* classification requests received by FDA (with no formal RTA or RTF processes in place) almost doubled from 54 in FY 2016 to 99 in the recently ended fiscal year.

Submission and filing volumes are, of course, only one part of the equation in determining how many and what products actually get through FDA and on to the market. Review efficiency and the proportion of submissions that are ultimately approved are other major factors. FDA appears to be on track to maintain PMA

FIGURE 1

Filed PMAs/Panel-Track Supplements And Received De Novos, By Fiscal Year



Original PMAs and panel-track supplements filed as of Sept. 30, 2017. *Seven FY 2017 submissions remained in acceptance filing review stages as of that date, so the FY 2017 numbers could increase slightly. *De novos* received by FDA as of Sept. 30.

Source: FDA MDUFA III Performance Report, Nov. 3, 2017

FDA Novel Device Approvals: October 2017

PRODUCT	COMPANY	APPROVAL DATE	PRODUCT CODE	TYPE	CLINICAL SPECIALTY	INDICATION
Cheatham Platinum Stent System - Covered CP Stent, Covered Mounted CP Stent, CP Stent, Mounted CP Stent	NUMED, INC.	10/24/17	PNF	Panel-Track	Cardiovascular	"Expanded indication to include use in the right ventricular outflow tract and additional sizes (10-zig and lengths up to 60 mm for 8- and 10-zig configurations). "
RHA 2, RHA 3, RHA 4	TEOXANE S.A.	10/19/17	LMH	Original	General & Plastic Surgery	Indicated for injection into the mid-to-deep dermis for the correction of moderate to severe dynamic facial wrinkles and folds, such as nasolabial folds
remede® System	RESPICARDIA	10/06/17	PSR	Original	Anesthesiology	Indicated for the treatment of moderate to severe central sleep apnea (CSA) in adult patients.
VENTANA MMR IHC Panel	Ventana Medical Systems	10/27/17	PZJ	De Novo (direct)	Pathology	Indicated in patients diagnosed with colorectal cancer (CRC) to detect mismatch repair (MMR) proteins deficiency as an aid in the identification of probable Lynch syndrome and to detect BRAFV600E protein as an aid to differentiate between sporadic CRC and probable Lynch syndrome.

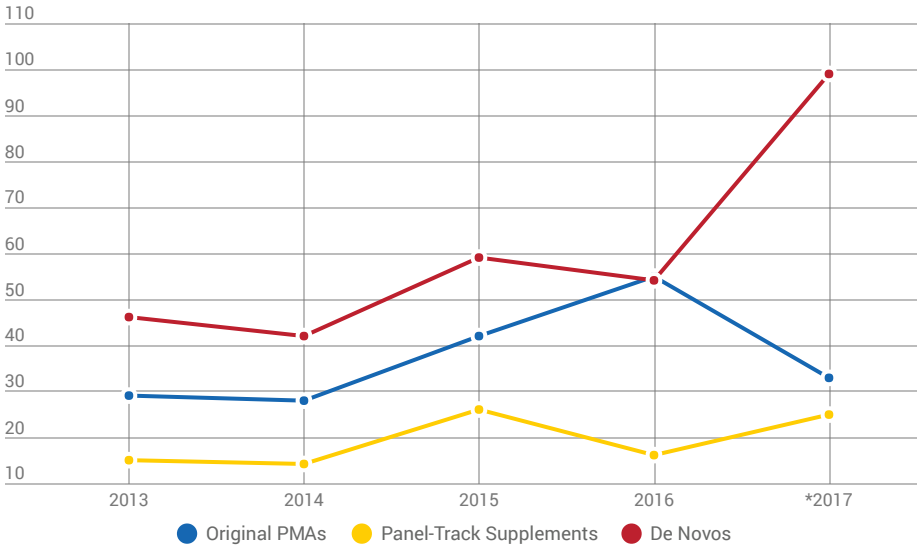
original/panel-track supplement average total-time-to-decisions of between 250-300 days, as it has since the FY 2014 cohort, and an approximately 90% approval rate.

For *de novos*, FDA's recent review-performance trend remains to be seen. Average decision times for requests received in FY 2016 are so far down by about 34days from those received in the year prior, but five FY 2016 submissions are still pending, which could end up increasing the average.

The *de novo* program is currently undergoing a transition. Starting in FY 2018, which began Oct. 1, companies must for the first time pay a user fee with each *de novo* submission, and FDA is implementing an RTA process to ensure quality submissions. These steps could potentially constrain *de novo* review volumes. In the meantime, the agency has also committed to performance goals for *de novos*, which could improve speed and predictability of reviews. *(Also see "'Refuse-To-Accept' Policy Outlined For De Novos In New US FDA Draft Guidance" - Medtech Insight, 31 Oct, 2017.)*

FIGURE 2

510(k) Submissions Received By FDA



Original PMAs and panel-track supplements filed as of Sept. 30, 2017. *Seven FY 2017 submissions remained in acceptance or filing review stages as of that date, so the FY 2017 numbers could increase slightly. *De novos* received by FDA as of Sept. 30.

Source: FDA MDUFA III Performance Report, Nov. 3, 2017

OCTOBER APPROVALS

Notable devices approved by FDA last month include Respicardia's *Remede* implanted phrenic nerve stimulator for moderate to severe central sleep apnea, approved via an original PMA on Oct. 6. Remede is designed to work automatically and continuously during every hour of sleep and does not depend on patient adherence, which has been a major limitation of continuous positive airway pressure therapy. The firm reported positive data from its 151-patient randomized pivotal trial that was published last year. *(Also see "Respicardia's remedē Neurostimulator Improves Sleep Apnea Symptoms In Pivotal Trial" - Medtech Insight, 2 Sep, 2016.)*

FDA also OK'd a panel-track supplement Oct. 24 for NuMED Inc.'s *Cheatham Platinum* stent system, including new sizes and for use in a new indication: for use in the right ventricular outflow tract during conduit pre-dilatation procedures performed in preparation for transcatheter pulmonary valve replacements.

510(K) ACTIVITY IS UP

The 290 510(k) clearances in October, meanwhile, was somewhat above average. FDA has cleared an average of about 253 510(k) s per month over the past three years, and it cleared 249 applications in September.

The number of 510(k)s coming into FDA from industry sponsors is also at a high. According to the FY 2017 performance review data that the agency posted Nov. 6, FDA received 4,047 510(k) submissions in FY 2017, up from 3,633 in FY 2016, an 11.4% increase.

Noteworthy examples of devices that gained a 510(k) clearance last month include:

- IntraFuse LLC's *Flex-Thread* Fibula Pin System, cleared Oct. 30 for percutaneous fixation of distal fibula fractures, primarily Danis-Weber B type fractures, or trans-syndesmotic fractures.
- **Acutus Medical Inc.**'s AcQMap high-resolution imaging and mapping system and the AcQMap 3D imaging and mapping catheter, both cleared Oct. 16 as ultrasound cardiac mapping tools to guide ablation for complex arrhythmias.
- **OptiScan Biomedical Corp.**'s *OptiScanner 5000* automate glucose monitoring system, cleared Oct. 16 for monitoring plasma glucose levels and determining dysglycemia in surgical intensive care unit patients.

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CONTINUED FROM PAGE 1

Also, there is a question of where the resources to carry out all this new work will come from. Most of the efforts must be completed by representatives of the national medtech authorities in their roles on the Commission's working groups. It is already well known how stretched these individuals are in terms of time and how short-staffed many of the authorities are.

GUIDANCES DOCUMENTS AND PRIORITIES

That said, the industry is still at a landmark juncture. The roadmap document was issued several months later than had been expected, but it now provides clear signposting to the work that needs to be done.

A glance through the tables, shows that the intended outcome of much of the work will be in the form of guidance documents.

While the work items are currently assigned a generic priority of high, medium or low, these priorities are due to become more defined and specific by the individual working groups tasked with each activity.

CAMD says in an introduction, that it is important to note that, although the MDR and IVDR have specified implementing acts (some 118 in total, *Medtech Insight* notes), additional guidance and information will

"High-Priority" Roadmap Work Stream Items

	WORK STREAM	HIGH PRIORITY WORK ITEMS			
1	**Clinical Evaluation & Clinical Investigation (medical device); Performance Evaluation & Performance Studies (IVDs)**	**Clinical evaluation work package, including:** • Guidance on equivalence, well established technologies, clinical evidence • Gap analysis of MEDDEV 2.7/1 (EU clinical evaluation guidance) • Contribution to relevant Implementing Acts • Work on interface between various documents/ reports • Contribution to guidance on performance evaluation and clinical evidence for IVDs (The priority level of clinical evaluation-related template document development is marked as "medium/high.")			
2	**Scope & Classification**	Classification guidance for IVDs around classification rules and scope, giving practical examples		Common Specifications for annex XVI products (non-medical/aesthetic)	
3	**Notified Bodies**	Implementing act(s) with list(s) of codes/ corresponding types of devices to describe the scope of the designation	Guidance to be issued on re-designation process for joint assessments under the new regulations	Capacity and expertise of assessors – training based on a gap analysis	Conformity assessment – clarity over procedures for notified bodies and the meaning of technical documentation assessments on a representative sampling basis
4	**Post-Market Surveillance & Vigilance**	Guidance on requirements for vigilance reporting • Identify gaps between the current MEDDEV guidance and the MDR and IVDR – issue as an interim guidance via CAMD website with a view to updating a MEDDEV guidance in due course; • Details on how vigilance should be reviewed in clinical evaluation for device and performance evaluation for IVDs as well as the required detail of the investigations undertaken; and • Focus on new manufacturer incident report (MIR) form, what vigilance looks like for member states, flag areas that are law rather than guidance and where MEDDEV needs to be updated to reflect the new regulations.		Develop and agree on terminology for device/IVD Adverse Nomenclature and patient harm: defining AE nomenclature to be defined and identifying patient harm nomenclature, including problem and cause investigation. **Terminology already underway at the International Medical Device Regulators Forum, completion expected by 2018**	
5	**Eudamed & UDI**	Uniform input into the design/ development of a functioning Eudamed medical device database	Guidelines for manufacturers on Unique Device Identification assignments	Guidelines on UDI carriers and UDI marking	
6	**Market Surveillance**	This entire area has been given a "medium" priority level. Some work is already underway at the competent authority level on market surveillance as part of the second tranche of implementation of the "Dalli action plan" in reaction to the PIP breast implant scandal. *(Also see "Will EU's New Market Surveillance Project Hit As Hard As Notified Body Action?" - Medtech Insight, 17 Nov, 2016.)*			
7	**IVD-Specific Issues**	Information to support the prompt designation of EU reference labs		Guidance on how class D IVDs can be assessed in the absence of Common Specifications	
8	**Over-Arching & Cross-cutting Priorities**	This relates to transitional problems & uncertainties, and risks to continued supply of safe devices. *(Also see "New 'Transitional Measures' Taskforce To Answer EU's Most Critical Questions" - Medtech Insight, 8 Nov, 2017.)*			

An additional, eighth work stream has been added to the newly released roadmap that addresses "overarching and cross-cutting priorities." In conjunction, an "EU Transitional Measures Taskforce" has been established to help ensure the new regulations are carried out uniformly. For more, see: New 'Transitional Measures' Taskforce To Answer EU's Most Critical Questions.

be needed in advance to fully define how certain provisions are to be applied.

What form the guidance documents will take and how they will be issued still needs to be worked out in future discussions on specific topics, CAMD says.

The newly finalized document notes that, while such guidance will not have a legal basis, they are intended to be valuable tools to assisting a harmonized approach to implementation.

IVDs generally have been incorporated into the work streams of the roadmap, but the IVD-specific work stream has also been retained to allow issues specific to IVDs to be addressed.

One particularly important and heavy work stream is the one that relates to the development of the new Eudamed medical device database. Within this stream, there are three high-priority work items:

- Uniform input into the design/development of a functioning Eudamed medical device database;
- Guidelines for manufacturers on Unique Device Identification assignments (e.g., when is a new UDI or basic UDI-Device Identifier necessary); and
- Guidelines on UDI carriers and UDI marking.

This last item is one of only two areas in the document where industry is mentioned – it is given co-ownership of the work with the UDI taskforce within the Commission's UDI working group and will be evaluating issues including: how to control UDI labeling inside the manufacturer's quality management system; where to put the UID carrier in case of implants; and where to put the barcode on the device or parts of a device system.

Meanwhile, its noteworthy that the entire "market surveillance" work stream has been labeled as a "medium" priority. Some may question whether a high priority should have been given to the production of general high-level guidance and infographics for economic operators (EOs) clarifying expectations around: EO obligations; responsible persons; liability; interaction with Eudamed; and registration requirements.

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New 'Transitional Measures' Taskforce To Answer EU's Most Critical Questions

AMANDA MAXWELL amanda.maxwell@informa.com

An EU Transitional Measures Taskforce has been established to ensure that implementation of the new Medical Device and IVD Regulations is carried out uniformly during the ongoing transition period and that there is no interruption to the supply of safe products

This is one highlight to emerge from the near-final version of the official road map for implementation of new regulations, which *Medtech Insight* has now seen.

This latest version was discussed at a stakeholder meeting on October 18, organized by the European Commission and the Competent Authorities for Medical Devices group, which have been drafting the text. The version that has been made available takes into account views and feedback submitted by stakeholders to an earlier draft version.

Public release of the final version of the road map has been anticipated over the last several weeks and is still understood to be due imminently.

Under this near final version of the road map reviewed by *Medtech Insight*, a new, eighth, work stream has been added. The work stream, titled "Over-arching & Cross-Cutting Priorities," includes six work items, including one (work item 8.1) focused on "transitional problems and uncertainties, and risks to continued supply of safe devices" that has been marked as high priority.

Given this is a last-minute, but very comprehensive work stream, it will demand a great deal in terms of time and resources.

With respect to the newly added work item, the EU Transitional Measures Taskforce task force is being advised to obtain legal input and to liaise with stakeholders – good news for industry, to ensure all relevant issues are identified.

Road Map Work Streams

This article focuses on a newly added eighth work stream. The full list of work streams, to be confirmed with the publication of the final road map, is below:

1. Clinical Evaluation & Clinical Investigation (MDs); Performance Evaluation & Performance Studies (IVD)
2. Scope & Classification
3. Notified Bodies
4. Post-Market Surveillance & Vigilance
5. Eudamed & UDI
6. Market Surveillance
7. IVD-Specific Issues
8. Over-Arching & Cross-cutting Priorities

EU ROAD MAP: Work Items 8.2-8.6

WORK ITEM	ACTIVITY	WHAT IS INVOLVED	PRIORITY LEVEL
8.2	Stakeholder engagement	Central coordination of information during implementation to ensure engagement with all affected stakeholders and mechanism to discuss challenges of regulation and outputs with stakeholders	Ongoing: specific guidance targeting new stakeholders needed by 18 months into transition
8.3	Resource requirements	Identify where there is a lack of expertise and resources needed for implementation issues and identify areas for peer training to help	High
8.4	Contributing to ensure the Eudamed database is fit for purpose, for audit and from go-live	All competent authorities to liaise though the Eudamed Steering committee and other involved groups.	Target: 2020
8.5	Clarifying role of Medical Devices Coordination Group in the governance of the regulations	Publish guidance outlining MDCG roles and responsibilities	High
8.6	Expert panels and expert laboratories	Define governance structure and information to support prompt designation of EU expert panels and expert labs	High

URGENT ITEMS IDENTIFIED

According to near-final text, issues that urgently need tackling within work item 8.1 in the period before application of the new regulations (before May 26, 2020, for the MDR and before May 26, 2022 for the IVDR) are:

- How products can comply during the transition period? – Interpreting MDR Article 120 (5) & IVDR 110 (5)
- Legal status of clinical investigations being conducted within the transition period: What happens if a trial begins according to the legacy EU directives before the date of application but finishes after?
- What are the legal enforcement powers during the transition period?
- What are the obligations of economic operators?
- How will this work in practice without the latest version of the Eudamed medical device database and what is expected of the authorities?
- How do statutory reporting deadlines apply in the absence of the updated Eudamed medical device database?

According to the work item, issues that need clarifying that relate to the period after the date of application of the regulations include:

- The status of devices that are placed on the market for a limited period after the transition period under a certificate that was issued in line with the directives (including aspects of notified body changes and reclassification of devices).
- Eudamed derogations around registration, reporting and clinical investigations.

When it comes to ensuring the continued availability of medical devices during the transitional period – where there are concerns about the capacity of the sector to deal with the implementation of the new regulations and staffing levels – the work item recognizes three risk areas that are particularly in need of contingency planning:

- Availability of notified bodies designated under MDR/IVDR.
- Availability of authorized representatives, and other market actors with capability of fulfilling the legal requirements.
- Risks of increased regulatory burden leading to supply issues of low-volume products, including IVDs.

The other five work items (8.2-8.6) in the new road map work stream, on overarching and cross-cutting priorities, are also significant. Overall, the workload that has been brought into this work stream is quite enormous and will demand significant resources multiple parties, especially the European Commission, the Medical Devices Coordination Group and the competent authorities throughout Europe.

Work item 8.3., on resource requirements for implementation of the regulations, arguably should be made the top priority because the Commission and most medical device competent authorities are known to be significantly short-staffed. Performing an effective job on implementation will be a difficult prospect for the relatively small numbers in these organizations, staff who are also currently expected to maintain the ongoing Medical Device Directives.

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'Program Alignment' Snaps Together: What's Next For US FDA's Inspection Scheme

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Nearly six months after US FDA rolled out the most sweeping changes ever to its approach to facility inspections, the agency's "program alignment" initiative continues to gain its sea legs.

Program alignment is "only five-plus months old, so it's not going to be perfect yet, but we're getting there," said Ellen Morrison, associate commissioner for operations within FDA's Office of Regulatory Affairs, and head of ORA's new Office of Medical Products and Tobacco Operations (OMPTO).

Under program alignment, which began on May 15, inspections performed by ORA – the office that conducts all of the agency's field activities – are structured along commodity-specific product lines to make audits more predictable and consistent for investigators and manufacturers. *(Also see "'Program Alignment' Falls Into Place: Everything You Need To Know About US FDA's New Inspectional Approach" - Medtech Insight, 8 May, 2017.)*

Program alignment restructured the agency's five regional offices – Pacific, Central, Northeast, Southwest, Southeast – into seven specialized programs: medical devices and radiological health; biological products; bioresearch monitoring; human and animal food; pharmaceutical quality; tobacco; and imports.

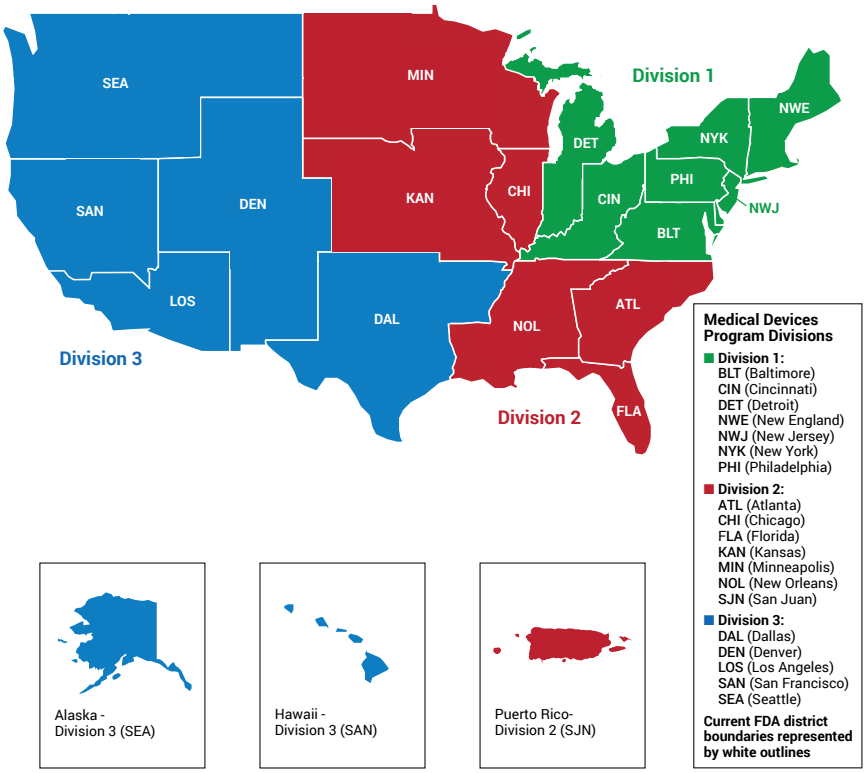
"Staffing [program alignment] has been tricky," Morrison conceded on Nov. 2 at FDAnews' 12th Annual FDA Inspections Summit in Bethesda, Md. "We had a federal freeze on hiring when we stood this program up, and had only 60 people on detail at the time – not the ideal situation for an organization."

The hiring freeze at FDA – put in place by the Trump administration last January – was lifted 10 days after program alignment began, on May 25. Since then, the agency has hired dozens for investigator and supervisory roles, although the vast majority are being used for inspections of drug-makers.

FIGURE 1

Office Of Medical Device And Radiological Health Operations

This map shows where the three medical device divisions are located.



Source: US FDA

For program alignment, "we have the challenge of having new managers, and we're continuing to hire a number of permanent managers," Morrison said, noting that the growing pains will be worth it in the end. "We believe that [program alignment] will drive efficiency across each commodity, and enhance coordination between ORA and our agency partners."

Morrison's OMPTO office was born out of program alignment restructuring. OMPTO's leadership team includes four office directors, including longtime agency staffer Jan Welch, who is director of the Office of Medical Devices and Radiological Health Operations (OMDRHO).

The OMDRHO office is split into three divisions, in the northeast, central/southern, and western areas of the country, encompassing all 20 former district offices. (See Figure 1.)

Moving forward, "it's important that we bring the best specialists that we can into the agency for these very complicated products. The programs of the future, the products of the future and the production of the future is going to be very challenging," Morrison said.

To help increase specialized training for investigators, Morrison said ORA should consider putting in place a program wherein investigators could visit manufacturers in good standing with the agency to

learn more about the products they make. That would "let our investigators see the technology of the future" and lead to better auditor job performance, she said.

Morrison likened her suggestion to that of the FDA device center's Experiential Learning Program (ELP), wherein agency staff can learn about specific device-related issues in the manufacturing field. Currently, through ELP, FDA wants its staff to gain more insight into combination products, software and clinical trials. *(Also see "FDA Calling: US Agency Again Asks Companies To Open Doors For Educational Purposes" - Medtech Insight, 17 Oct, 2017.)*

FDA is also determining the best ways to give specialized investigators the tools they need to establish a good-paying career path at the agency without having to advance to management positions to gain a higher salary. "Our [pay] structure has been lower than I think it should be for specialized investigators," Morrison said.

The agency is also looking at other incentives to offer investigators, including more specialized training on, say, emerging technology trends in medical devices, or the continuous manufacturing of pharmaceuticals.

Investigators are also being trained on how to most effectively inspect foreign firms, with Morrison pointing out that "our future is foreign inspections." But gone are the days of plum overseas assignments, she said, and auditors must be prepared for that. "The first foreign inspection I conducted was in France," she said, but that was in the 1970s. "Today, investigators will likely go to India or China. It would not be France."

The bottom line? "We need to do a lot more on the training side for the investigators, and do more to retain them," Morrison said.

Plans are also in the works to upgrade investigator technology. Device-makers shouldn't be surprised to see handheld devices such as tablets being used by auditors during inspections and for generating inspection report findings, rather than relying on old-school written notes. "It's easier to take a tablet out and write on it, and it becomes a part of your Establishment Inspection Report, instead of the green notebooks that investigators typically carry," Morrison said.

USING GIS TO TRACK INVESTIGATORS

The agency also plans to enhance the use of geographic information system (GIS) tools to help keep track of investigators in the field.

Morrison said she first purchased GIS for FDA in the early 2000s after she was named director of the agency's Office of Crisis Management. GIS is used by that office during, for example, natural disasters to determine whether particular manufacturing sites might be impacted.

"The mapping capability that exists is pretty powerful in terms of getting data and looking real-time at where all of your staff is," Morrison said. By letting ORA use GIS, "we can, in real time, look at every firm in our inventory and map them. We can then say, 'What firms are we inspecting right now? Where are those investigators?' And in real time, be able to see where everybody is working."

While she said using GIS might sound like "Big Brother" has arrived, Morrison claims the tool will simply help ORA better determine where to send investigators.

"Geographic information can help you manage better, and seeing things in real-time is a great advantage. Our program directors have embraced this and are using it for looking at the current inspections that are going on," she said. "Obviously, I'm a big fan" of GIS.

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COMPLIANCE CORNER:

20 Things You Should Never Say To An FDA Investigator

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When being inspected by US FDA, a medical device manufacturer might be tempted to defend itself. But one longtime industry insider says there are certain things that shouldn't be said to agency investigators.

In a Nov. 3 presentation at FDAnews' 12th Annual FDA Inspections Summit in Bethesda, Md., Steve Niedelman ticked off a list of 20 things that firms should never say.

Niedelman – lead quality systems and compliance consultant at the law firm King & Spalding – is a familiar face in the medical device arena, working at FDA for 34 years in both its Office of Regulatory Affairs and Center for Devices and Radiological Health.

"You always want to present your company in a very positive way during an inspection. You want to be very confident. You want to be able to present and represent your firm in a productive and constructive way," Niedelman said. "So, here are 20 things never to say to an investigator so you can present yourself in the best fashion possible."

1. "I think…"

"Don't ever say this. That just opens the door, just opens the Pandora's box, to an opportunity for the agency."

2. "I am not sure."

"If you're not sure, then you're not confident. It's the same thing. If you provide the investigator information and say, 'I'm not sure of this,' then you're suggesting to them that they have an opportunity to really dig in and start pushing further."

3. "I told them not to do it this way."

"Don't throw your firm under the bus. If you say, 'I told them not to do it this way' – well, then why'd they do it? You're responsible for what your firm has in its possession, so if you think it's going to get you any brownie points from an FDA investigator

perspective, it's not. It's just going to show that you acknowledge that things were done incorrectly. That's not a good thing."

4. "You are wrong about this … you don't know what you are talking about."

"When you tell the investigator this, that's really not a good sign. There could be differences of opinion. You might not think they know what they're doing. You may be able to say, 'Well, we respect your opinion, but we also respectfully disagree, and we went down this road,' versus saying, 'You guys have no idea what you're talking about.'"

5. "During the last inspection, the FDA investigator saw the same thing and did not put it on the FDA-483 form."

"If you say this, then you just acknowledged that this problem has been ongoing for longer than the investigator may have been aware. And quite frankly, inspections are a snapshot in time. Investigators might not look at the same thing. Different investigators have different sweet spots. They have different areas that they're more familiar with. And, not everybody is perfect. And so, first of all, you just threw another investigator under the bus, and that's not the best thing in the world to do. And by saying that this has been going on for a longer period of time, well, you just indicted your own firm again."

6. "The last investigator to inspect was crazy," or, "The last investigator to inspect did not know what he/she was doing."

"That doesn't bode well. Again, there's nothing to be gained by trashing a former on-site investigator."

7. "How would you recommend that we fix this deficiency?"

"FDA is not there to be your consultant. It just indicates to them that you really don't know how to deal with your problems. They're not going to give you an answer, so there's nothing to be gained by asking this."

8. "That is the way we have always done it."

"Having bad practices doesn't mean that it's good. And sometimes, quite frankly, teaching an old dog new tricks is not easy, either. So, by saying, 'That's the way we've always done it,' you've just incriminated yourself for quite some time."

9. "I probably shouldn't say this, but…"

"Well, you know, if you probably shouldn't say it, then don't. If you're going to be sharing information that you're going to have a tough time corroborating later or that may come back upon re-inspection, or will be memorialized in an Establishment Inspection Report that you will have to defend later, then you probably should just keep it to yourself. You might want to share it with someone else in your organization, but not the investigator."

10. "If we followed those procedures we would never get anything done."

"Well, you know what? If your procedures are deficient, fix them. But you're expected to follow your procedures. If you don't, not only is the problem not having procedures, but not following them is just as bad. And I can tell you as somebody who signed off on every enforcement action at FDA for about a decade, whether it was a device or drug or food, or whatever, most of the firms, probably 80% of the time, their procedures might not have been the gold standard, but if they were followed, the firms would have been fine. In most of the cases, they didn't execute their own procedures, and it resulted in enforcement actions such as seizures, warning letters and injunctions resulting in consent decrees."

11. "We don't have enough people or time to review all of those complaints."

"Well, that's a problem, but it's also a double-whammy, because it also says management has not given appropriate resources to the quality department to be able to handle those complaints. If there aren't adequate resources, that's a management control problem, and in the medical device quality system, that's the center hub of their quality system. So, you now have late complaints, improperly investigated complaints, and a management control problem because the resources aren't there."

12. "The management of this firm is only concerned with profits and does not take quality seriously."

"That's probably true in many situations, quite frankly. Let's be honest. Management is concerned with profits. If they don't have profits, they won't be in business. But management needs to be made aware of what the cost of poor quality is, and what the consequences of that are. I understand it's sometimes difficult to push that message up, but the best goal is always for a quality mindset to cascade down from the very top."

13. "I do it this way because our procedure does not make any sense."

"Well, have you made anybody aware of that? What are you doing to change the procedures so they work? What changes need to be made? Are you just living with them or are you even following them? If that is the case, whatever you do, don't make FDA aware of that.

14. "I will change the procedure right away."

"Well, you should have change procedures to handle that. Don't say to the investigator, 'Oh, we'll have that changed by tomorrow' just to make a pen-and-ink change, or whatever is necessary. You have to be able to establish that you're following your procedures, and that your procedures are not just ad hoc decisions that anybody could make willy-nilly, even if an investigator points out a problem. Instead, say, 'Thank you for pointing that out. We will review it. It will go through our change process as we feel it's appropriate."

15. "If you think that's bad, you should see this…"

"That's not a good situation. The investigator found something bad; don't point them to other things that are bad. Instead, take your lumps on the one thing that's bad and don't open the kimono for everything else that's going on. Because if you do, that inspection will just grow. What may have started as what was intended as a week inspection, well, FDA could now be in there for six months. You want to avoid that."

16. "We fixed the problem by firing the person."

"There are certain situations where firing certain personnel is a good thing. It may

change the culture of an organization. But chances are, firing the person wasn't the problem. The inadequate procedures were; the quality system in place was. And if the new person is going to follow those same procedures, then you didn't gain anything. It's important to keep that in mind."

17. "That's not my fault. It was the previous person who did that."

"Well, quite frankly, you're the person. You've been in that job. You knew there was a problem. You had an obligation to fix the problem, or at least take steps to fix it."

18. "That's not my problem … that is quality assurance's problem."

"You know what? Quality is everyone's business. If an investigator is pointing out a quality issue to you, then you need to make it your business. You need to make sure that the appropriate people in your firm are aware of the problem that was identified, as well. Quality's everybody's job; everybody has a role. Everybody contributes to it, and you can't just say, 'Ignore it, because it's not within my bailiwick.'"

19. "Write it on the FDA-483 form because that is the only way we will correct it."

"There are firms that, if it doesn't appear on the FDA-483, then it doesn't get anybody's attention. Of course, you don't want to tell the investigator you do that, but again, that's a quality culture issue within your firm that desperately needs to be addressed."

20. "Are you going to shut us down, or are we going to get a warning letter?"

"Don't ask investigators that because they don't make that decision. They're just the eyes and ears. They collect the information, and it's reviewed by their supervisors and compliance officers, and perhaps at the senior level beyond that."

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FDA To Cut Regs on Sharps Disposal Devices

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Manufacturers of devices used to destroy needles and other sharp medical waste would no longer need to submit PMAs under a Nov. 7 proposed order from US FDA that would move sharps disposal devices from risk class III to class II.

The disposal devices are typically electric, and destroy sharps via grinding, incineration or other methods. They may be stationary or portable. FDA says it approved the first sharps disposal device in 1997. Since then, it has approved 15 PMAs for the device type. A guidance document issued in 2001 laid out FDA's expectations for sharps disposal device PMAs.

The agency reviewed the classification for sharps disposal devices as part of a 2014-2015 initiative to determine whether PMA devices were appropriately classified. On Aug. 8, 2016, FDA included the devices on a list of products slated for reclassification because the agency believed special and general controls were enough to ensure device safety and effectiveness.

The new proposal would regulate sharps disposal devices as a class II prescription device that require 510(k) submissions.

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The proposed special controls focus on ensuring the devices perform their function safely. For example, sponsors must demonstrate that sharps disposal devices can contain or safely ventilate hazardous fumes such as ozone that might be generated during device operation. The performance testing should also show that heat from device operation won't harm users or affect the device's functional life, and that there's no risk of user injury from incompletely destroyed sharps. In addition, the device should be stable within the use environment despite any motions or vibrations, and sponsors must demonstrate the device can be safely cleaned and disinfected to avoid cross-contamination.

Other proposed special controls are less product-specific and include electromagnetic compatibility testing; electrical safety testing; software validation and hazard analysis; and appropriate warning labels.

FDA doesn't expect clinical trial data will be necessary for most 510(k)s in the category, but may request it if the manufacturer includes new indications for use, "such as indications for disease prevention or organism destruction."

Comments are due to docket number FDA-2017-N-6216 by Jan. 8, 2018. The docket can be viewed on regulations.gov.

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