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Medtronic Stands To Be Biggest Beneficiary Of J&J's Exit From Insulin Pump Market

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Johnson & Johnson's decision to pull the plug on its **Animas Corp.** business and get out of the insulin pump market completely will likely help **Medtronic PLC** build on its dominant position in that market while creating opportunities for smaller players – including **Insulet Corp.**, **Roche,** and **Tandem Diabetes Care Inc.**– a chance to build on their small market shares.

On Oct. 5, Animas, part of J&J's Diabetes Care division, announced that it will discontinue manufacturing and selling *Animas Vibe* and *OneTouch Ping* insulin pumps, close operations, and exit the insulin pump business. "With changing needs of customers, rapidly evolving market dynamics, and increased competitive pressures, it proved too difficult to sustain the insulin pump business and we decided to pursue an exit of the business," General Manager of Animas, Valerie Asbury said in a release. "This decision was extremely difficult and comes following the extensive exploration of all other viable options for the Animas business."

J&J's diabetes care device revenues have been declining over the past few years, which the company blamed partly on competitive pricing pressure. However, the company had been especially optimistic about the Animas Vibe as a new product would help offset the declines in the business overall. The FDA approved Animas Vibe in 2014 as only system available in the US for children as young as 2 years of age. *(Also see "Q1 EARNINGS: JnJ bullish in spite of device slump" - Medtech Insight, 15 Apr, 2015.)*

Clearly that optimism was not enough to ensure the survival of the business as part of J&J. At the beginning of 2017, J&J announced it was "evaluating strategic options" for its consumer medical device diabetes franchise including Animas and **LifeScan Inc.**, its blood glucose monitoring business. "We're assessing a wide range of options including strategic partnerships and joint ventures and have not set a definitive timeline to complete this review," J&J CEO Alex Gorsky said during a Jan. 27 earnings call. J&J's diabetes care device revenues dropped about 6% year-over-year in 2016 to $1,789bn.

In its second-quarter earnings report in July, the company announced it would record an impairment charge of approximately $125mm related to the process of seeking strategic alternatives for the diabetes busi-

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

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Brexit conundrum
http://bit.ly/2wNulHs

Nearly 16 months after the Brexit vote, uncertainty persists over whether the EU's Medical Device and IVD Regulations will be adopted by the UK. Sector player are looking to avoid the worst, and one strategy being taken is to move to other countries.

MDUFA IV makeover
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US FDA detailed new review performance goals and user-fee policies to mark the start of a new fiscal year and five-year user-fee program.

Hindsight 20/20
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In the third instalment of our CEO war stories series, Jon H. Hoem, current CEO of start-up CorFlow Therapeutics, reveals what he thinks is the best clinical strategy, what he would not skimp on when building a business, and more.

M&A goes steady
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September was a steady month for M&A deals in terms of deal volume. But there were several big-buck transactions to boost total value. What were they?

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Medtech insight

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ness. In the release announcing the closure of Animas, J&J says is continuing to evaluate potential strategic options for LifeScan.

According to a Meddevicetracker report on the global diabetes management device market released in March, the global insulin pump systems market is dominated by Medtronic and its *MiniMed* line of insulin pumps, with 62% of the market and $1.86bn in annual revenue. Johnson & Johnson/Animas was a distant second with 22% share and about $656m in revenue. The rest of the market includes Insulet (8% share; $227m); Roche (7% share; $213m), and Tandem Diabetes Care (more than 2% share; $73m), according to the report.

While price pressure has made it harder to make profits from diabetes devices, the overall market is growing. According to the Meddevicetracker report, global sales of glucose meters and continuous glucose monitors are set to expand from around $6bn in 2015 to $7bn in 2020, driven partly by both Type 1 and Type 2 diabetics using these devices in their daily glucose monitoring routine, compared to a smaller number of severe Type 1 diabetics relying just on insulin pumps.

Pricing pressures have hit the glucose meter segment, but the adoption of next-generation insulin pumps is expected to drive growth of this segment. Total insulin pump sales are expected to jump from $3bn in 2015 to nearly $4.2bn by 2020.

J&J GIVES MEDTRONIC A GOING-AWAY PRESENT

Medtronic is not only the dominant supplier of insulin pumps, but J&J is giving Medtronic an immediate opportunity to turn the roughly 90,000 Animas customers into Medtronic customers. Animas says it has selected Medtronic "as its partner-of-choice to facilitate a seamless transition for patients, caregivers and healthcare providers" and will offer patients using an Animas insulin pump the option to transfer to a Medtronic pump.

The smaller players in the insulin pump market will also have a chance to take some of the territory Animas is vacating. For example, Roche is a small player in the insulin pump global market, but the seventh largest medical device maker overall with extensive market reach and technological resources. Roche has reported especially strong revenue growth from its *Accu-ChekInsight* insulin pump system in Europe. *(Also see "Advent Of Artificial Pancreas Tech To Galvanize Fast-Growing Diabetes Market" - Medtech Insight, 26 Apr, 2017.)*

While price pressure has made it harder to make profits from diabetes devices, the overall market is growing, according to a recent report from Meddevicetracker.

Insulet's *Omnipod* is a small wearable, disposable, waterproof self-adhesive patch pump that provides 72 hours of continuous insulin delivery. In its Aug. 3 second-quarter 2017 earnings report, Insulet reported that US revenue from Omnipod was over $65m in the quarter, representing 16% year-over-year growth, and international sales grew about 60% to $27m.

Privately held Tandem boasts the only touchscreen insulin pump available in the US, recently launched the *t:slim X2* pump, which integrates the **Dexcom Inc.**'s *G5Mobile* continuous glucose monitoring system, following FDA-approval in late August. This approval represented Tandem's fifth new insulin pump launch in the last five years and the second featuring Dexcom technology, according to the company. *(Also see "Senseonics, TypeZero Join Forces On Artificial Pancreas" - Medtech Insight, 12 May, 2017.)*

ANIMAS WILL LIVE ON OVERSEAS, AT LEAST FOR A WHILE

Animas has discontinued the sale of all Animas Vibe and OneTouch Ping insulin pumps in the US and Canada immediately, but the timing to exit countries outside of the US and Canada is subject to completing consultation with relevant works councils, J&J said. Animas employs approximately 410 people globally. "Consistent with Our Credo, all affected employees will be treated with fairness and respect," J&J states in its press release.

Animas says it will continue to sell pumps and operate as usual outside the US until resolving the remaining labor issues in those countries and it will continue to provide customer service, training and warranty support, including providing pump supplies that are used with the Animas Vibe and OneTouch Ping insulin pumps, "through a transition period."

J&J says it remains committed to the prevention and treatment of diabetes and will continue to serve diabetes patients with medical devices, pharmaceuticals, and consumer products, including **Ethicon Inc.**'s bariatric surgery products and drugs like Invokana (canagliflozin) and Invokamet (canagliflozin/metformin HCl). *(Also see "J&J's Ethicon Calls For Game-Changing Holistic Approach To Obesity Care" - Medtech Insight, 5 Sep, 2017.)*

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OMB: US FDA Has Withdrawn At least 10 Regulations In Response To Trump 2-for-1 Order

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According to the White House, FDA has so far withdrawn at least 10 rules in response to the president's executive orders earlier this year calling for deregulation.

Deregulation has been one of President Trump's pet issues and back in January soon after taking office he issued a number of executive orders to promote his agenda. The executive orders included one to require federal agencies to withdraw two regulations for every regulation issued, known as the "2-for-1" order, and another requiring federal agencies to create Regulatory Reform Task Forces to promote deregulation. *(Also see "Trump's Two-For-One Reg Order Needs Agency Interpretation, Medtech Reg Experts Say" - Medtech Insight, 30 Jan, 2017.)*

"President Trump signed into law 14 Congressional Review Acts – blocking harmful Obama-era regulations from being implemented - and specific executive actions designed to roll back governmental overregulation," said Jacob Wood, a spokesman for the Office of Management and Budget. " As of right now, there have been 4 regulatory actions, and 10 deregulations actions [at FDA]. This number is preliminary, as the process is not finalized."

According to OMB, 860 regulations in total have been either outright withdrawn or removed from active status since the president issued his orders. That includes 469 completely withdrawn regulatory actions and 391 regulations were pulled from active status.

OMB did not respond to questions asking for more specificity on what regulations were withdrawn and whether the 2-for-1 order only applies to FDA rules or also includes agency guidances.

Based on the OMB's web site, however, 13 FDA rules are currently under consideration for approval or withdrawal for 2017 under its Spring 2017 Unified Agenda. Among them are seven proposed rules and six finalized rules. By comparison OMB noted there were 44 FDA rules that were under consideration in the fall of 2016, which is a significant drop in number of rules being examined.

However, several rules such as "Internal Agency Review of Decisions; Requests for Supervisory Review of Certain Decisions Made by the Center for Devices and Radiological Health," which would codify procedures and timeframes for applying supervisory review of significant decisions made by the device center, are still under consideration by FDA. Other rules such as "Electronic Submission of Labeling for Certain Home-Use Devices," which would require medical device establishments listing certain home-use medical devices to submit electronic-format labeling and package inserts, have been moved to long-term consideration by FDA.

The most recent list of rules under consideration are still not final, as the Office of Information and Regulatory Affairs at OMB is currently reviewing all regulations that have been proposed, approved or withdrawn over the past year. The list will be compiled in a report after the analysis is complete.

> "What we can say now is we expect agencies to have met or exceeded both of the goals established in the [executive order]: Less than zero incremental cost and more than two deregulatory actions for each regulatory action," says Jacob Wood, OMB.

"We expect the complete report along with the full Agenda and Regulatory Plan in late November," said Wood. "However, what we can say now is we expect agencies to have met or exceeded both of the goals established in the [executive order]]: less than zero incremental cost and more than two deregulatory actions for each regulatory action. It should be noted that since we are still compiling submissions, this is an anticipated but not final outcome."

"When OIRA releases the final Regulatory Agenda, the contents therein will reflect each agency's anticipated actions over the coming year," he added.

UNCERTAINTY AROUND DEREGULATION

It's been nine months since President Trump issued the 2-for-1 executive order requiring federal agencies to remove two old regulations for every new regulation issued. But since the order went out, there hasn't been a clear explanation from the White House or FDA on its practical impact.

There's been uncertainty about how it will affect guidance documents industry has been expecting from FDA. While the year started off with very few guidances coming out of the agency on medical devices, CDRH has accelerated its release of guidance documents in the past few months. However, the publication of new guidances has not answered how FDA and OMB have reconciled issuing new guidances in context of the president's executive order.

Recently, FDA issued notices through its centers asking for public input on what regulations the agency should consider updating or withdrawing. However, FDA Commissioner Scott Gottlieb seemed to indicate that while the requests for comment were related to the president's order, responding to the order was not their exclusive purpose. He also stated he would like to see a more systematic periodic review of regulations, in general, to ensure they are relevant to changing technology and aren't unduly

burdensome. *(Also see "Gottlieb Wants More Systematic Updates Of Regulations" - Medtech Insight, 12 Sep, 2017.)*

FDA spokesman Michael Felberbaum says the agency's 2017 unified agenda as presented by OMB focuses on its most immediate priorities and addresses the executive orders issued earlier this year, however, he states, it's important to note that just because a previously rule on the list is no longer on it does not mean the agency doesn't consider it a priority or that it won't consider implementing the rule at some point in the future.

"We anticipate that some of the items not included in the Spring Unified Agenda will appear on the Fall 2017 Unified Agenda," he added.

Felberbaum also noted while the agency has opened several federal register dockets to get input from the public about updating regulations, it is also exploring other opportunities to solicit input from stakeholders. *(Also see "US FDA To Public: Help Us Streamline Our Regs" - Medtech Insight, 7 Sep, 2017.)*

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Questions Answered On Device Submission Woes

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Manufacturers who notice competitors making misleading claims might get a faster reaction by writing to the other company rather than first alerting US FDA, attorney Jeffrey Gibbs said during a recent device submissions webinar sponsored by Massachusetts industry trade group MassMedic.

The tidbit was one bit of advice from Gibbs, who directs Hyman, Phelps & McNamara's medical devices practice, while responding to questions on everything from when to appeal an FDA verdict, to how to prepare for a 510(k) pre-submission meeting, to how closely manufacturers should follow guidance documents. A paraphrased summary of the question-and-answer sessions is below.

Jeffrey Gibbs
Hyman, Phelps & McNamara

Photo credit: Hyman, Phelps & McNamara

Medtech Insight: What should a manufacturer do when it believes an FDA decision is in error?

Jeffrey Gibbs: Appeal without hesitation – if the decision and the appeal meet certain criteria. Gibbs recommends manufacturers appeal when FDA was clearly wrong on a significant issue. Hold off if the product or issue isn't crucial. In addition, manufacturers should be certain they have a substantive argument, rather than just stating a matter of opinion. And appeals can't include new data that wasn't in the original submission.

"It's not something to do lightly," he said. "Don't go into it expecting to win. That's not a foregone conclusion at all." On the other hand, Gibbs says two typical concerns are overblown. Manufacturers shouldn't worry about FDA retaliation, he says. Also, changes to the law in recent years have accelerated appeals, so there's no need to fear that an appeal will tie up a product for years.

When does a guidance document become a rule?

While every guidance document includes a statement that the guidance isn't an official rule, that's not necessarily a statement to take literally. In general, guidance documents on submissions should be followed because the guidance lays out FDA expectations, Gibbs says. "Companies have to be aware that this is the way FDA expects it, and the burden will be on the company to show an alternate approach is suitable," he said. But guidance documents carry less weight if a dispute goes to court because they aren't considered legally binding.

Appeals are "not something to do lightly," Gibbs said. "Don't go into it expecting to win. That's not a foregone conclusion at all."

What are the best strategies for participating in physician-initiated studies?

Companies should have policies in place that allow them to support outside studies but also set some conditions, Gibbs says. For example, corporate research policies should require physician sponsors to obtain institutional review board (IRB) and other regulatory approvals, and ensure the research is in line with broader company goals. Assisting in a study without rules already in place can be considered a kickback.

How should a manufacture determine the best approach for approval of a medical mobile app?

Gibbs listed several options. It's possible to go to FDA informally to discuss the particulars. Alternately, manufacturers can determine the app's likely regulatory status internally with consultation from an outside attorney or regulatory expert, and do a pre-submission with the agency if they expect the app to qualify as a regulated device. Gibbs was less positive about the 513(g) device classification request process, noting that, in his experience, FDA may not respond to such requests in a timely manner.

When should a device sponsor who is getting repeated requests for additional information from different FDA reviewers escalate the issue to the branch chief?

"If you're getting contradictory advice, go now," Gibbs said. "FDA encourages that, and it's important not to be deterred by any fear of retaliation." Sometimes the only way out of a conflict with reviewers is to go to a higher level for intervention, he said

What can a firm do if a competitor is promoting its product as FDA cleared when it is not?

One first step is to have an attorney write a letter to the competitor company. The threat of legal action may lead the company to change its promotions even if their official response is to disagree, Gibbs says. Another option is to submit a trade complaint to FDA, though he noted that there's no assurance FDA will take any action. "If you want the matter within your own control, writing to FDA can be frustrating because no matter how well founded, the complaint may not be pursued," he says. "Writing to the company through a lawyer may be your best option."

The third and most expensive option, Gibbs says, is filing suit. Competitors can sue under the federal Lanham Act against unfair competition if the promotional claims are false and misleading, or take their complaint to a state attorney general or local prosecutor to see if any local laws are being violated.

Does a manufacturer have to have quality systems in place when submitting a de novo application or 510(k)?

Quality systems implementation are allowed to lag for submissions that aren't PMAs, Gibbs says. But a crucial element of the Quality System Regulation to have in place before pre-market submission is design controls – revising those procedures after approval could create enforcement risks, he warned. PMAs must have all quality systems elements in place pre-submission.

How should a manufacturer prepare for a pre-submission meeting for a 510(k)?

"In the old days, there was a lot more to do because you were expected to have a full presentation," Gibbs said. "Now you'll be in contact with FDA and get some feedback before the meeting." But FDA might not get its comments to the manufacturer until as little as two days before the meeting, so manufacturers should consider in advance what questions are likely and how they'll respond, he said.

How can a company's regulatory staff respond when the firm's marketing staff want to copy what competitors are doing, even if the regulatory teams says the competitors' actions are improper?

"You do get lot of pressure, but ultimately you have to comply with the law," Gibbs said. He recommended that the concerned staffers stress that the company's mission includes compliance and discuss the risks of FDA enforcement actions. He admitted those tactics might not be satisfactory to a marketer who feels compliance is costing the firm sales.

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Talking to US FDA? Here's How To Get It Right

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Manufacturers who need to talk to US FDA should keep two priorities in mind: maintaining common courtesy, and showing how a request aligns with FDA's goals. That was one key takeaway from a discussion on FDA communications at the recent Food & Drug Law Institute Advertising & Promotions Conference in Washington, DC.

In addition to treating FDA officials with respect, attorney Katlin Backfield recommended that a manufacturer explicitly lay out how its comments support FDA's mission to promote and protect the public health. Backfield was in FDA's chief counselor's office for nine years before launching the law firm Backfield PLLC in November 2016.

"FDA's staff is in meetings all day, and they have stacks of things on their desks that are not getting smaller," she said. "So when you're communicating with FDA,

really focus on why they should focus on your issue right now." Manufacturers can also help FDA by submitting questions in advance of meetings and effectively organizing written comments, she said.

It's also crucial to remember that FDA correspondence "is a documented record of their opinion," said Michele Sharp, senior director of global regulatory affairs – US, at **Eli Lilly & Co**. "Those can come back to haunt you later, particularly if you don't adequately resolve their comments, or you don't adequately document your thought process about the comments." A manufacturer doesn't necessarily need to agree with FDA, but should document its reaction because that may be requested in future inspections, she said.

COMPLIANCE COMMUNICATIONS ESPECIALLY FRAUGHT

Sharp also cautioned patience in explaining FDA correspondence. Business leaders who haven't dealt with FDA much may not be as skilled at understanding the nuances as an experienced regulatory professional, she said.

It's particularly important to be sure all of a firm's employees understand the importance of FDA warning letters, said Norma Skolnik, an independent consultant with EAS Consulting Group. While the significance may seem clear to regulatory professionals, "I've heard, 'Well, it's just a letter,'" Skolnik said. "Some marketers will view it as a small price to pay for increased product sales."

Only engaging the in-house marketing team that normally works with the ad agency in response to compliance citations is "like having the big fox tell the little fox how to guard the henhouse," consultant Norma Skolnik says.

If a manufacturer gets a warning letter, the letter should be read it closely to ensure all points are understood. The agency's comments should then be communicated to the relevant parties within a company, from executives to marketing to compliance. And they should all be involved in planning steps to respond and follow up, Skolnik said.

For warning letters that touch on marketing issues, it may be necessary to bring any outside advertising agency contractor into the internal discussions, even if they balk. Advertisers who don't work for the device manufacturer are often behind the most egregious misleading claims, Skolnik says. Only engaging the in-house marketing team that normally works with the ad agency in response to compliance citations isn't enough, she said. "It's like having the big fox tell the little fox how to guard the henhouse." And Skype and teleconferences offer a budget- and time-friendly alternative to in-person meetings, she noted.

A company that receives a warning letter should begin drafting a response immediately, Skolnik said. FDA's 15-day warning letter response deadline doesn't leave much time, especially since the letters will typically need to go through multiple levels of company revision and clearance before they are sent to the agency. If a firm believes an FDA observation is in error, company officials may want to reach out to the contact person identified in the warning letter to discuss it informally while drafting the response, she said.

While composing the response, manufacturers should also check for other advertising and promotional materials that might contain similar issues, including websites and postings to social media. Manufacturers should create a timeline to discontinue use of the materials and take further corrective action if needed, Skolnik said.

INFORMING ON A COMPETITOR

Another common reason to reach out to FDA is to report perceived regulatory violations by a competitor. That process should start with a phone call to the relevant office and be followed up by mail, said Sharp. If the violation involves promotional materials, the letter should include examples of the problematic ads. Don't expect to be kept in the loop by FDA investigators – while the agency generally acknowledges the complaint, manufacturers typically don't get an update until after an action has been taken.

"FDA's staff is in meetings all day, and they have stacks of things on their desks that are not getting smaller. So, when you're communicating with FDA, really focus on why they should focus on your issue right now," attorney Katlin Backfield says.

Manufacturers may also want to alert FDA to voluntary compliance actions, but that involves a calculated risk, Sharp said. On the one hand, coming to FDA shows that a company understands the relevant laws and regulations and has an active self-surveillance program. On the other, FDA may take further enforcement action, and there's the chance the company's alert will let FDA know about an issue that wouldn't have been on its radar screen. The level of concern raised by the problem may be the deciding factor, she said.

If a company decides to be proactive, any communication sent to FDA should describe the promotion, explain the company's concern, and state how widely the materials were circulated. The company should also state the actions already taken to rectify the issue, and any steps taken to prevent a recurrence.

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UK Medtech Adrift: Will US Lure Challenge UK Medtech's Regulatory Ethos?

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The US is ready and waiting to take advantage of the huge opportunities arising from the unique political and regulatory circumstances impacting the UK medtech sector. That was the message from Yvonne Puig, head of life sciences and health care at the US offices law firm Norton Rose Fulbright, in her keynote address at an Association of British Healthcare Industries (ABHI) meeting October 5.

Speaking to delegates at the ABHI conference, she said: "While you are struggling … we are watching you … with a lens of opportunity."

The US is "hoping more UK innovators will come to the US and invest in the US as a safe harbor from other regulatory guidance and restrictions that may be posed as a result of the [EU Medical Device Regulation.]"

The disruptive circumstances brought about by the hugely complex MDR, combined with Brexit and the pro-business and anti-regulation Trump administration, has brought unique opportunities for a closer relationship between UK medtech firms and the US, Puig noted.

Innovators are already facing more incentive to enter the US before the EU now, *Medtech Insight* notes, because of the increasingly stringent clinical data guidance in the EU that pre-empts the new, yet-to-be-enforced regulations. Some member states appear to be imposing on the clinical data expectations on their industries.

"The UK has no better friend than the US when it comes to technology and innovation… We are hungry to place our products in your market and we know there is a pent-up demand and hunger for you to place your products and innovation in the US," Puig said.

She also noted that the message being sent by the UK post-Brexit is that the UK is entering a period of self-governance and wants to negotiate new trade agreements.

This is a huge opportunity from a US perspective, Puig said, adding that this is the time to forge those relationships – while there is still some uncertainty.

UK MEDTECH: BETWEEN A ROCK AND A HARD PLACE?

Puig was speaking to some 200-plus medtech regulatory specialists, a large proportion of whom were UK citizens who had voted to stay in Europe and who have considerable reservations about President Trump.

Trump is telling the US government to get rid of two regulations for every one brought in, Puig told the meeting. And some in the FDA are spending more time, she said, "reviewing how to best to satisfy the one-in two-out rule than they are on other deeper and more important health and safety and regulatory issues."

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The US is "hoping more UK innovators will come to the US and invest in the US as a safe harbor from other regulatory guidance and restrictions that may be posed as a result of the MDR," attorney Puig says.

Against this background, it is hard to see how the established UK medtech industry would square the potential ethical issues around this US-style deregulation initiative with its own record on health and safety "to invest in the US as a safe harbor from other regulatory guidance and restrictions that may be posed as a result of MDR."

Indeed, despite the huge complexity of the new EU regulations and the struggle for companies to find sufficient resources to implement it, the UK medtech industry (supported by MedTech Europe) is actively campaigning for the UK government to fully implement the new EU Medical Device and IVD Regulations, which it firmly believes are critical for patient safety.

But if the government does not allow this – and many believe it will not, because of the timing problems with implementation of the regulation itself, plus the many delegated and implementing acts that will not be ready until well after the UK has left the EU – then what alternative regulatory route will UK be following?

Will any trade relationship with the US influence this choice? Might the UK be lured by less stringent regulation? And if it is, what might that mean in terms of trading with the then EU 27?

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Lack Of Device Identifiers On Recalled Cardiac Devices Cost Medicare 1.5bn, OIG Says

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The US Health and Human Services Department's Inspector General says that covering procedures to replace or repair damage caused by seven recalled or "prematurely failed" cardiac devices cost the Medicare program $1.5bn between 2004-2014, due to lack of information on claim forms about the devices' identity.

"The lack of information on the claim forms prevents the Centers for Medicare & Medicaid Services (CMS) from being able to fully understand and address the Medicare costs related to recalled or prematurely failed devices," according to an Oct. 2 report from OIG. In addition, OIG estimates that Medicare beneficiaries had to pay out $140m in copayments and deductibles related to the cardiac device replacements, and for related services and procedures.

OIG issued a preliminary report in October 2016, about the additional expenses that Medicare has to cover, when a device is recalled or failed, beyond the costs for the new replacement device. *(Also see "OIG Cardiac Implant Review Finds $1.5bn In Medicare Payments For Failed, Recalled Devices" - Medtech Insight, 5 Oct, 2016.)*

The report recommends that CMS should continue to work on getting its Accredited Standards Committee X12 to ensure that a space for Unique Device Identifier information is included on the next version of claim forms, although some device-makers, and hospital groups, have been opposed to this idea. *(Also see "UDIs Should Be Added To Insurance Claims, Panel Agrees" - Medtech Insight, 2 Feb, 2017.)*

The OIG report is titled, "Shortcomings of Device Claims Data Complicate and Potentially Increase Medicare Costs." It mentions that the devices included ICDs and pacemakers, came from three manufacturers, and were selected "because most of these devices have manufacturer warranties that establish a minimum useful life."

In describing the additional claims that Medicare had to cover, the OIG states in its report, "Approximately $1bn of the $1.5bn were Medicare payments for device replacement procedures, such as heart surgery to replace prematurely failed pacemakers or internal defibrillators." Another $500m, OIG said, were Medicare payments for post-device replacement services, such as imaging, post-acute care, and physician visits to monitor patients after the new devices were implanted.

Shutterstock: hywards

> OIG estimates that Medicare beneficiaries had to pay out $140m in copayments and deductibles related to the cardiac device replacements, and for related services and procedures.

MULTIPLE CRM RECALLS DURING THE PERIOD

The report doesn't name the specific cardiac device manufacturers, nor the ICDs or pacemakers that had to be replaced, but there have been a range of widespread recall actions in the cardiac rhythm management space during the study period that likely contributed to the Medicare costs, including for:

1. Medtronic's *Micro Jewel Model 7223 CX* and *GEM DR Model 7271* ICDs, due to problems with capacitor technology, recalled in April 2004. *(Also see "Class I Medtronic Defibrillator Recall Associated With Faulty Capacitor" - Medtech Insight, 26 Apr, 2004.)*
2. Medtronic's *Marquis VR/DR*, *Maximo VR/DR ICDs*, and the *InSync I, II*, and *III*, plus *InSync III Protect CRT-D ICDs*, recalled in February 2005, due to battery depletion issues. *(Also see "Doctors Discuss Strategies For Responding To Recent Medtronic ICD Recall" - Medtech Insight, 4 Apr, 2005.)*
3. Guidant's (acquired by Boston Scientific in 2006) *Ventak Prizm 2 DR* ICDs and *Contak Renewal CRT-D* ICDs, recalled due to short-outs in defective insulators. *(Also see "Boston Scientific Settles With States On Guidant ICD Investigations" - Medtech Insight, 3 Sep, 2007.)*
4. Guidant/Boston Scientific' *Pulsar Max*, *Pulsar*, *Discovery*, *Meridian*, *Pulsar Max II*, *Discovery II*, *Intelus II*, *Virtus Plus II* and *Contak TR* pacemakers, recall announced by FDA in July 2005, in which 69 failures of the devices occurred within 44 months of service. *(Also see "Guidant Issues Alert For Nine Pacemakers; Total Number Of Alerts Now 20" - Medtech Insight, 25 Jul, 2005.)*
5. Boston Scientific's June 2006, recalls of its Guidant *Insignia* and *Nexus* pacemakers, due to "foreign materials in the crystal components," making the pacemakers malfunction. *(Also see "Guidant's latest pacemaker alert "puzzling", says analyst" - Medtech Insight, 30 Sep, 2005.)*
6. Medtronic's October 2007, decision to halt distribution of its *Sprint Fidelis* defibrillator leads, due to fractures at the

distal portion, and anchoring sleeve tie-down of the implanted ICD leads. *(Also see "Fracture Data Spurs Medtronic To Suspend Sales Of Fidelis ICD Lead" - Medtech Insight, 22 Oct, 2007.)*

7. St. Jude Medical's December 2010 recall of its *Riata* and *Riata ST* ICD leads, due to "elevated risk of abrasion of the silicone outer insulation material," the company said. As a result, devices had a failure rate of 0.63%. *(Also see "Regulatory News In Brief" - Medtech Insight, 19 Dec, 2011.)*

CMS REVIEWING 'NEW ADMINISTRATION' RESPONSE

CMS received a copy of the OIG full report over the summer, and responded in late July: "Similar to other policies under review by the new administration, this policy is also under consideration," the agency said, adding that it "will carefully evaluate the potential that this policy will impose burdens on physicians unnecessarily." Last July, during the prior administration, the agency did signal support for adding UDIs to claims forms after a period of pushback. *(Also see "Medicare Agency Comes On Board With Adding UDIs To Claims Forms" - Medtech Insight, 18 Jul, 2016.)*

In addition, several physician groups, including the American College of Cardiology, as well as FDA and several lawmakers in Congress, support a proposal by CMS's X12 committee to add device identifiers to both Medicare and private payer insurance forms, Ben Moscovitch of The Pew Charitable Trust told *Medtech Insight*.

Moscovitch, who is manager, health information technology at Pew, added that having the device identifier information on Medicare claims forms would not only advance the accumulation of information about implanted cardiac devices on patients, but would also help physicians and researchers in the orthopedic space better track hip and knee replacement data.

"Hip and knee replacements are the most common procedures performed on Medicare beneficiaries, so no doubt, additional cost savings and safety precautions could be realized," he commented.

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Committees Vote To Secure Kid's Health Funding, But No Device Tax Relief In Sight

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Children's Health Insurance Program (CHIP) bills advanced through Senate and House committees Oct. 4 but with no device-tax repeal provisions.

CHIP reauthorization remains one the device industry's last few targets to carry a permanent device-tax repeal provision this year *(Also see "AdvaMed Still Wants Full Device-Tax Repeal, But Temporary Moratorium Is A Backup" - Medtech Insight, 25 Sep, 2017.)*, but a Republican Senate Finance Committee staffer told *Medtech Insight* that repeal would require a hefty "pay-for" provision that is difficult to find in the current tight budget climate amid other pressing priorities.

There was no device-tax repeal amendment among those prepared in advance of the Oct. 4 markups in the Senate Finance and House Energy & Commerce Committees.

CHAIRMAN HATCH ASKS, AND GETS 'CLEAN BILL' FOR FULL SENATE REVIEW

Senate Finance Chairman Orrin Hatch, R-Utah, said his goal was to extend the funding for CHIP for five years, gradually transitioning to a federal-state partnership program, and providing more protections for children in low-income families. Current CHIP funding technically expired on Sept. 30.

Hatch asked senators on the committee for a clean vote on the "Keep Kids' Insurance Dependable and Secure (KIDS) Act of 2017." He advised members to hold most of their amendments – including Medicare and Medicaid extenders – until the measure is taken up on the floor.

Panel members cooperated and held off from pursuing plans to try to amend the KIDS Act. For instance, Sen. John Cornyn, R-Texas, was poised to offer an amendment to repeal the Independent Payment Advisory Board (IPAB), but later withdrew it; and Sen. Ben Cardin, D-Md., was keen to amend the bill to eliminate the lifetime cap on dental benefits for impoverished children under CHIP, but agreed to stand down.

HOUSE PANEL PASSES CHIP, DEVICE BILLS

Similarly, House Energy and Commerce Health Subcommittee Chair Michael Burgess warned *Medtech Insight* just be-

fore the full committee's markup session that there were many other amendments directly affecting CHIP, and other bills and priorities, besides a device-tax repeal that the committee would have to address throughout the afternoon and evening. The full House committee was poised to first consider amendments directly germane to CHIP, followed slate of nine diagnostic, device, and electronic health record bills that passed through the Health subcommittee earlier this year. *(Also see "US House Bills Address Telemedicine, Prostate Cancer Tests, Diabetes Supplies" - Medtech Insight, 25 Sep, 2017.)*

The committee ultimately agreed to advance a Stroke Telemedicine Act (H.R. 1148), the Prostate Cancer Misdiagnosis Elimination Act (H.R. 2557), and the Protecting Access to Diabetes Supplies Act (H.R. 3271), along with bills on an "Independence at Home" project, one allowing for reimbursement for speech-generating devices, and an amendment on meaningful-use standards in the HITECH Act.

But complicating and delaying the House committee markup was a distress call from Rep. Jenniffer González-Colon, Puerto Rico's Republican non-voting representative in Congress, who came to the committee hearing to request an additional $1bn in funding through the CHIP program to help Medicaid recipients recover from damage caused by Hurricane Maria, which destroyed many hospitals and community health centers. Rep. Burgess said that the committee is trying to fund her request within the CHIP bill, but Democrats on the panel – including Rep. Ben Ray Lujan, D-N.M., wanted to give Puerto Rico $6bn more. Rep. Lujan argued that a supplemental spending bill released by the Trump administration Wednesday "would not be enough."

Lujan's comments touched off a lengthy debate on the additional Puerto Rico funding, and for additional funding to aid the US Virgin Islands, as well. In the final bill approved by the House committee, "close to $1bn was agreed to within this CHIP bill," chairman Walden said, and added that more funding for both territories would be taken care of, in a supplemental funding bill scheduled to be voted on, on the House floor this week.

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Gottlieb At The Medtech Conference: US FDA Commissioner Talks About CDRH Innovation, Puerto Rico, LDTs And More

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FDA Commissioner Scott Gottlieb gave the keynote address Sept. 26 at AdvaMed's Medtech Conference, and he also sat down with AdvaMed President and CEO Scott Whitaker for a public question-and-answer session.

During the conference, in San Jose, Calif., the commissioner touted the agency's device center as the spark of innovation across FDA. He also provided a key update in the agency's digital-health regulation plans, put his cards on the table regarding laboratory-developed-test policymaking, and made some substantive points on how industry should respond to the ongoing devastation in Puerto Rico from Hurricane Maria.

A some of Gottlieb's key comments and takeaways follows below, and check out a the video of the full speech and Q&A from The Medtech Conference online.

CDRH: FDA'S SEED OF INNOVATION?

"Some of the most creative and forward-leaning advances in regulatory policy are what we are doing on the medical device side of the FDA house," Gottlieb told meeting attendees.

He pointed out, as an example, that at a recent meeting he attended focusing on the use of real-word evidence for pharmaceuticals drew heavily on policies that are already in place on the device side of FDA. CDRH is also leading the way on a range of other issues, including in developing a benefit-risk framework, reshifting the balance of pre-market and post-market data, and creating to an overarching "Total Product Life Cycle" office, Gottlieb said.

"These policy advances, first engineered in CDRH, are going viral at FDA," he pronounced.

NAME-CHECKING BIG TECH

As previously reported by *Medtech Insight*, Gottlieb also announced the participants in FDA's nascent "Pre-Cert" pilot program, which is focused on establishing a pre-certification program for health software that could reduce or replace traditional pre-market device requirements. Apple, FitBit and Verily joined Johnson & Johnson and Roche among the nine companies that will be directly assisting FDA in the efforts. *(Also see "'Excellence' In Health-Software Design: US FDA Taps Nine Firms To Figure Out What That Means" - Medtech Insight, 26 Sep, 2017.)* "Our team will be spending the rest of the year working closely with these companies to deepen our understanding of their methodolo-

Scott Gottlieb

gies and how their technologies operate," Gottlieb said.

LDTS: A LEGISLATIVE PRIORITY?

During the Q&A with Whitaker, Gottlieb forcefully argued that new regulatory framework for laboratory-developed tests should be a priority and it should be Congress, and not FDA, that primarily makes it happen with legislation.

"I am working very hard toward that goal. I will have and have had conversations around Capitol Hill on these issues. I am going continue to speak out publicly," he said.

FDA has been working in fits and starts for decades to establish a framework to actively oversee tests that are produced and performed as services in the same laboratory, despite opposition from many in the lab community. A major effort to finalize such a framework fell apart in the 11th hour last November after the surprise election of Donald Trump to the White House. *(Also see "What's Next For LDTs? FDA May Be Eyeing A New Game Plan" - Medtech Insight, 25 Nov, 2016.)*

But Gottlieb still sees an opportunity to make something happen, pointing to better consensus on the issue than in the past, and to promising legislative vehicle that could pass within the year to authorize user-fee programs for over-the-counter drugs and animal drugs. "I think we have an opportunity to work on a framework on appropriate regulation of LDT tests for the long run as part of that legislative vehicle," Gottlieb said. "My view is it would be a missed opportunity if we didn't."

The commissioner also hinted at an approach to LDT regulation that he favors, specifically, modeling the Pre-Cert pilot program, where labs could be pre-certified based on their test-design process.

"This construct could form part of the framework for a modern legislative approach to laboratory-developed tests," he said.

PUERTO RICO: WORSE THAN PERCEIVED

Gottlieb has been very public and out front in recent weeks since Puerto Rico was devastated by Hurricane Maria, even traveling to the island last week. Drug and device manufacturing facilities make up a substantial part of the economic activity of Puerto Rico and part of Gottlieb's focus has been helping to facilitate operations getting back up and running to avoid shortages.

"I will tell you that the situation is a lot worse than what we perceive from the news on the island," Gottlieb told Whitaker. "The facilities themselves seem to be relatively intact. But it is a matter of getting supplies to facilities and getting people back into the facilities."

Asked for tips for companies that have local facilities that are responding to the disaster, Gottlieb recommended: "Make sure you are feeding up information to multiple channels. Just because you have a conversation with someone who works for the assistant secretary of emergency preparedness at HHS, [or] you talked to someone at DHS – made one contact – if I was a company with a critical issue, I would make sure I had that same conversation with as many touchpoints as possible, including with FDA. Don't be shy about that."

He emphasized that while the focus is "obviously on the people of Puerto Rico," that he is "not going to shy away in the coming weeks [to talk] about the need of providing relief to the facilities."

"What is going to be critical to the recovery of Puerto Rico is getting people working again, getting the economy restarted, and the medical-product-manufacturer base is a huge part of that economy," Gottlieb said. "The vast majority of that economy is driven by that. Puerto Rico's economic future is dependent upon us getting these facilities restarted and not seeing companies relocate their facility permanently. That would be the worst possible outcome. But that is a risk. We are all cognizant of that."

"What is going to be critical to the recovery of Puerto Rico is getting people working again, getting the economy restarted, and the medical-product-manufacturer base is a huge part of that economy," Gottlieb says.

WATCH

Find the video of Gottlieb's full speech and Q&A from The Medtech Conference online at http://bit.ly/2hPOFae.

CURES AS TEMPLATE FOR REFORM

Gottlieb also made some interesting comments about the implications of the 21st Century Cures Act. Enacted last December, the legislation includes a range of FDA reforms, including several impacting devices. *(Also see "21st Century Cures Implementation: Device Provision Updates" - Medtech Insight, 20 Jun, 2017.)* But the commissioner pointed out that he views the bill not just as a list of provisions to implement but also a "template upon which we can embed other policies."

"The ability to build around the Cures initiative with other policy effort that are very related to Cures, but not explicitly described in Cures, becomes very seductive," he said. "It is a very useful vehicle for things, where we have an expression of congressional intent. It is not just the agency trying to divine policy on its own, but we are following the intent of Congress and what they laid out in Cures."

Gottlieb seems to have taken this approach in the digital-health realm, where FDA is implementing specific Cures provisions to keep certain software types outside of the agency's jurisdiction, but infusing with it a host of additional deregulatory digital-health initiatives, including but not limited to Pre-Cert. *(Also see "US FDA's New Game Plan For Digital Health" - Medtech Insight, 15 Jun, 2017.)*

"I want to make sure we are not only implementing provisions in Cures efficiently and effectively… but we are looking for opportunities to embed other policy priorities," he said.

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From AI-Based IVDs To Precision Drug Dosing: Medtech Conference 2017 Gives Insight Into Tomorrow's Technologies

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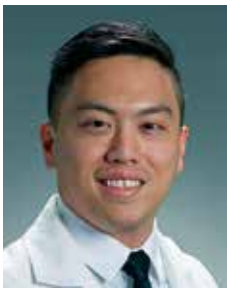
Veteran industry experts and the bright young minds they mentor were among the 2,700 attendees at the 11th annual Medtech Conference, organized by medtech trade association AdvaMed and held at the San Jose McEnery Convention Center on Sept. 25-27.

This year's meeting featured 50 companies showcasing a diverse range of early-stage technologies such as in-vitro diagnostics, orthopedic products, therapeutic dosing technologies, cardio- and peripheral vascular devices and surgical tools. The presentations also included the four finalists of the 2017 Medtech Innovator $500K Competition, who were whittled down from 600 companies.

This articles delves deeper into the technologies of five of these showcasing companies, three of which were the Medtech Innovator finalists. It also includes a table listing of the other up-and coming developers of tomorrow's technologies.

Jong Lee, CEO and co-founder Day Zero Diagnostics



Albert Huang, CEO and founder of Allotrope Medical

Bradley Messmer, founder and CEO of Abreos Biosciences

COMBATTING ANTIMICROBIAL RESISTANCE

Beating 600 other startups to win the $350,000 grand prize at the 2017 Medtech Innovator competition was Boston-based **Day Zero Diagnostics, Inc**., which is focused on developing IVDs for tackling antimicrobial resistance.

CEO and co-founder Jong Lee told the audience that had voted for the company to win that Day Zero is striving to be the dominant provider of data in the pathogen space.

The goal of the firm is to combine whole genome sequencing and machine learning *(Also see "Artificial Intelligence Brings Wave Of Future Health Care Innovation – Embrace it or be Left Behind" - Medtech Insight, 28 Jul, 2017.)* to develop a diagnostic to help accelerate the detection and identification of pathogens that are responsible for antibiotic resistance; and thus, help physicians triage patients with severe infections, in particular, sepsis, faster and more accurately.

"Our mission is to create a diagnostic that can take a clinical sample like blood, rather than blood culture, and give you a specific ID and resistance profile in five hours rather than five days, so that patients can be treated with the right therapeutic on the first day they are admitted to the hospital," Lee said.

Terry Harrison, attending physician, gynecology oncology at the Kaiser Permanente Medical Center in San Diego, California agreed that early diagnosis of these pathogens is often life-saving.

"It is critical to identify antibiotic susceptibility in critically ill patients with severe infections where minutes or hours may make a difference in terms of successful treatment and even survival," Harrison told *Medtech Insight*.

Thus far, the company has done proof-of-concept testing in more than 4,000 samples where they identified the species of the pathogen 100% of the time and achieved 95% accuracy on 39 classes of bug drug resistance, Lee said. The company has created a proprietary database through a licensing agreement with Boston-based Massachusetts General Hospital where they have collected 30,000 bacterial isolates that have different antibiotic susceptibility.

"We have all of their known phenotypic resistance profile and sequence the genomes of the pathogens," Lee said. What makes Day Zero Diagnostics different from other companies trying to identify bacterial susceptibility is the use of whole genome sequencing combined with machine learning *(Also see "Antimicrobial Susceptibility Test-Makers Seek Ways To Shorten FDA Clearance Process" - Medtech Insight, 19 Sep, 2017.)*.

"By using machine learning to do our algorithm, we can essentially identify any known pathogen that's available in our database and predict resistance even for things that have not previously been seen," Lee said.

He said a lot of molecular diagnostics that use technologies like PCR in trying to identify bacterial susceptibility are limited in that they identify a limited number of pathogens in a sample and only one or two resistance genes.

"But they are not agnostic, meaning they use biased detection methods and they tell you almost nothing about resistance," he said. The company focuses on sepsis, because it represents the biggest unmet clinical need in hospitals with the average patient treatment cost being $10,000-$50,000. It is also the biggest economic opportunity for saving hospital costs. He said inpatient infectious disease identification and susceptibility testing is an estimated $5bn market.

Under the business model, Day Zero Diagnostics may provide

Photo credit: Day Zero Diagnostics, Allotrope Medical and Abreos Biosciences

hospital clients with the analyzer and charge per disposable, single-use cartridge and offer lab testing in-house where clients would send samples to the company, Lee said. The company also has plans to offer future hospital clients access to its data analytics model on a subscription basis.

"Every time someone runs our diagnostic, they generate a genomic sequence which goes into our database," Lee explained. "The database is grown by customer usage. We'll be able to provide hospitals with investigative services for hospital-acquired infections and regional surveillance data and help discover new targets for antibiotics as a result of machine learning algorithms."

For now, the company is still in its earliest stages. The windfall from winning the Medtech Innovator competition comes just one month after Day Zero Diagnostics completed a $3m series seed financing led by Golden Seeds and Sands Capital Ventures. All these funds will be used to support prototype development of the company's diagnostic platform, Lee said.

He added that it was too soon to give a timeline on when the device would be fully developed. He said the ultimate goal is to develop an in-vitro diagnostic with US FDA clearance.

URETER DETECTION MADE EASIER

Innovations in surgical tools and planning continues to be a hot area in medtech and **Allotrope Medical**'s founder Albert Huang hopes to be on the cutting edge of this sector with *StimSite*, a hand-held device designed to assist surgeons to identify the ureter, a tube that carries urine from the kidney to the urinary bladder, more easily and quickly during a surgical procedure.

The technology was attractive enough for the company to be the runner-up in the Medtech Innovator competition, which translated into a $50,000 prize.

A general surgeon by training, Huang said he realized the need first-hand for a better instrument to aid surgeons in identifying the ureter back in 2014. "Current ways to identify the ureter fall short," Huang said.

He told *Medtech Insight* he spent the next two years developing a prototype during his limited free time, experimenting with spare parts from electronic stores and talking to experts. When Allotrope Medical raised $350,000 in seed funding from Houston, Texas-based angel investors and Houston Health Ventures last fall, Huang decided to trade in his OR scrubs for a business suit to grow his company and try to bring StimSite to market.

The two technology-based methods – ureteral stent placement and using fluorescent systems – are expensive and not reimbursed by insurance providers. Ureteral stent placement, which is used in 20-30% of surgery cases, costs about $1,200 per patient; and using fluorescent technology is even more costly and it subjects patients to chemical injections, he explained.

The target market for StimSite is general gynecologists who perform the majority of hysterectomies -- 1 in 3 women will undergo a hysterectomy by the age of 60 -- as well as general surgeons performing minimally invasive surgeries such as laparoscopic colon resections -- 1 in 20 Americans will have colon cancer, which leads to an operation in many cases, Huang noted.

Allotrope Medical's StimSite

Photo credit: Allotrope Medical

"Current ways to identify the ureter fall short," Huang said.

More than three million procedures are performed each year in the US where the ureter needs to be identified as a critical part of the operation. Injury to the ureter translates into a $3.2bn annual health-care burden in the US, Huang said during his presentation.

StimSite is safe, simple and easy to use and fits seamlessly into the surgeons' workflow, according to Huang. The battery-powered, single-use device generates a safe and brief electrical impulse with a push of a button that makes the ureter contract and easy to identify.

Though Huang feels the device meets an urgent need, not all surgeons would agree.

Harrison told *Medtech Insight* he feels that a device is only rarely helpful or necessary to identify the ureter.

"It is true that ureteral injury is a serious complication of pelvic surgery, occurring in about 1-2% of hysterectomies," he said. "Legal claims and lawsuits often follow cases of ureteral injury."

Huang said that it costs hospitals a significant amount of unnecessary dollars when surgeons spent up to 30-40% of their operating time trying to identify the ureter, referring, in particular to laparoscopic colon resection surgeries.

But Harrison and another Kaiser gynecologist both feel that this claim is exaggerated.

"It usually takes less than a minute (to identify the ureter)," Harrison said. "Furthermore, it's relatively straightforward to identify the ureter in most cases. It continually undergoes peristalsis, or contracts, on its own. When it does not show the characteristic peristalsis, it is easily stimulated to contract by touching it with any standard surgical instrument, without an electrical pulse."

"It takes us minutes to find the ureter," echoed Rene Perez, an OB-GYN at Kaiser Permanente Medical Center in San Diego, California, who said he has performed hundreds of hysterectomies.

Huang said the device isn't targeted at specialists who operate daily, but more toward gynecologists who operate on fewer days of the week.

He agreed with Harrison and Perez that the ureter will naturally contract on its own. But he argued that in some cases, waiting for the contraction to visually confirm the location of the ureter takes time and during the dissection process injuries can happen.

"Stimsite elicits contraction, which is safer and more efficient, if the ureter isn't immediately identifiable or during surgery when physicians can't locate it in a rapid way," he explained.

Huang is currently in the process of trying to raise $3m in a Series A funding to finance animal studies to show efficacy and safe-

ty of the device's power profile compared to existing devices.

This would put the device on track for FDA 510(k) premarket submission in Q1 2019. StimSite would qualify for reimbursement under the Diagnosis Related Code (DRG), which Huang noted would be a fraction of the cost compared to current ureteral stent placement or fluorescent technology used to identify the ureter. He is also talking to investor groups and companies that would be interested in integrating StimSite into their portfolio.

"Our device can be easily adapted in robotics, but because the technology is focused on a power profile and a tip design, we can see it integrated into existing instruments and plugged into current electrosurgical tools and build into endoscopic technologies," he explained.

ORTHOPEDICS: VR TRAINING PLATFORM

Two companies presenting at Medtech's orthopedic innovation showcase, though with entirely different technologies, were **Osso VR** and **Myovue**.

Justin Barad, a former game developer and practicing pediatric orthopedic surgeon, said he founded Osso VR to offer medical students and surgeons a training tool to perform "real" surgeries

TABLE 1

Ones To Watch: Other Promising Early-Stage Companies At The Medtech Conference

COMPANY	TECHNOLOGY	MILESTONES
Cardiovascular		
Access Vascular, Inc.	Platform of venous access devices using bulk-hydrophilic biomaterial technology that prevents thrombus.	FDA 510(k) pathway confirmed for HydroPICC
Advanced Prenatal Therapeutics	Technology targets removing blood components associated with symptoms of preeclampsia.	Commercial prototype under development, collaborating with University of New Mexico for clinical observatory study
Alleviant Medical	Transcatheter device that relieves pressure buildup within left atrium, a key driver of heart failure symptoms and hospitalizations.	Preclinical study initiated Q3 2017 at Houston Methodist Hospital; working prototypes successfully tested in swine models
Nanowear, Inc.	Cloth-based nanosensor technology to remotely monitor CHF by capturing vital data.	Received Class II FDA approval for nanosensors, mobile application & physician portal capturing and transmitting multichannel ECG, HRV & RR
VADovations, Inc.	Developed Angel Assist, a miniature VAD platform designed for the pediatric population.	Raised $30m to date
Orthopedics		
Evoke Medical	Developed spinal interbody fusion implant with built-in electrical stimulation properties to improve bone healing.	Proof of concept in animal study completed, showed advanced bone healing
Vertecore Technologies	Vertecore Lift decompresses the spine with a dual support harness and ratcheting system.	FDA approval in Q2 2016
Vascular/Neurovascular		
HemaFlo Therapeutics	Developed NephroFlow to treat acute kidney injury with a drag-reducing polymer that doubles blood flow without increasing blood pressure.	Secured FDA designation as device; completed animal study
Myonic Technologies Inc.	Develops wearable device to allow paralyzed users gain muscle control.	Beta test Q4 2017; direct-to-consumer sales planned for Q2 2019
Nexeon Medsystems Inc.	Developed closed-loop neurostimulation device to relieve chronic neurological disease. Requires one surgery vs. multiple surgeries, which is standard of care.	Acquired 100 patents from Siemens and Medtronic
PeriCor Therapeutics Inc.	PeriPath is an access tool for percutaneous epicardial procedures to replace open-chest surgery in pediatric patients.	Completed pre-submission meeting with FDA to establish 510(k) pathway
Voyager Biomedical	Developed technology to eliminate problems associated with venous access in dialysis patients.	Raised $225K to date; patent filed

(l) Leif Goranson, director of marketing, Osso VR; (r) Justin Barad, CEO and founder

Charles Allan, co-founder and CEO Myovue

Photo credit: Osso VR and Medtech Insight

in the virtual world, aiming to reduce complication rates, help surgeons learn complex procedures faster and safer, and improve patient outcomes.

Palo Alto, California-based Osso VR raised $400k in pre-seed funding, led by Presence Capital's Amitt Mahajan last September and another $2m in seed funding from Signalfire with participation from Anorak Ventures this June.

Barad said Osso VR's technology meets a real unmet need, citing data from the medical literature that shows surgeons who adopt a new technology typically need to do 50 to 100 cases to gain proficiency.

"Up to that point, the complication or revision rate is 300% higher than it should be," Barad said.

A study conducted at UCLA's David Geffen School of Medicine of eight medical student participants compared Osso's VR training with current training methods, using manuals and technique guides, showed that the VR group had twice the performance score vs. using traditional means when tested on a simulated bone model.

"For the first time, we're going to be able to shorten the learning curve and increase the adoption of newer medical technologies and surgical techniques," Barad said.

Osso VR is already being marketed to several top 10 orthopedic device companies, which Barad declined to name. Under the business model, Osso VR provides custom content for companies and a license that includes the hardware, analytics platform and support and training for the product, he explained.

Given that some $6.4bn is spent on training surgeons and sales reps, Barad said Osso VR's technology fills a significant need by improving patient outcomes and decreasing cost in this value-driven health-care environment *(Also see "Latest Mako Tech Fleshes Out Stryker's Robotic Joint Replacement Line But Cost Critics Still There" - Medtech Insight, 20 Mar, 2017.)*.

With VR and augmented reality (AR) being on the cutting edge of innovation, Osso VR is already exploring further applications of its technology to offer surgeons, Barad told *Medtech Insight (Also see "Virtual Reality: The New Game In Mental Health Care To Improve Outcomes" - Medtech Insight, 22 Jun, 2017.)*.

For instance, VR may be used by surgeons to perform "mission rehearsals," which encompasses using the exact anatomy of a patient to prepare for a specific case prior to the actual surgery.

"In the OR, there is a whole suite of technologies that can be enabled with frontier technologies such as AR and VR," Barad said. In the near future, surgeons may be using Osso VR's technology to interface with other technologies to do video proctoring, track instruments, navigate, and more.

"Some of them we are exploring right now and some are further out in the future," Barad said about his technology platform. "These all work together to accomplish the same goal, which is taking a device or technique and making sure the patient gets the maximum benefit and outcome at minimum cost and complications. We're really just getting started in the training space, but we're looking to expand to all of these frontier technologies that we're incredibly expert at."

ACS SENSOR

Meanwhile, Myovue's CEO, Charles Allan, hopes to break another frontier in the emergency department.

Allan co-founded Myovue with four partners in 2015 with licensed technology from McGill University in Montreal, Canada where he was a graduate student of bioelectrical engineering.

The device is designed for emergency department physicians to help diagnose Acute Compartment Syndrome (ACS).

Every year, some 500,000 trauma patients in the US are at risk for developing ACS, a potentially devastating diagnosis caused by high-energy trauma events, such as bone fractures. If undiagnosed, ACS that can lead to damaged nerves, muscles and vasculature. Compartment Syndrome can develop in several compartments throughout the body, but it is seen most commonly in the forearm and lower leg. If not undiagnosed and operated on within six hours, patients are at risk for permanent muscle and nerve damage; at 12 hours without diagnosis, it can lead to amputation, Allan told *Medtech Insight*.

If a patient presents with a fracture, the high-energy trauma that caused the fracture can cause swelling to build up in the adjacent muscle. Physical exams, such as the "pain out of proportion

"In the OR, there is a whole suite of technologies that can be enabled with frontier technologies such as AR and VR," Barad says. In the near future, surgeons may be using Osso VR's technology to interface with other technologies to do video proctoring, track instruments, navigate, and more.

"The sensor stays in the muscle, and thus, gives the surgeon a real-time number they can monitor continuously for up to 48 hours post-injury," Allan says.

exam", in addition to testing pain with passive stretching of the involved compartment have proven to be unreliable and are often insufficient to establish a proper diagnosis, he said.

Allan claims that *Myovue* can help diagnose ACS immediately or within hours.

The device measures perfusion pressure by placing a small sensor within the muscle, similar to the way an IV is applied. The sensor quantifies the amount of swelling and relays the data to a cloud-based mobile app, which gives the physician the information needed to decide if and when to intervene with a fasciotomy, an emergency surgical procedure that cuts open the affected muscle to relieve pressure. Clinical data shows that whereby using a threshold for intramuscular perfusion pressure sustained at <30mmHg for 2 hours or more, the calculated sensitivity based on performing fasciotomies is 94% with an estimated specificity of 98%.

What sets Myovue apart from currently available diagnostics testing is that it provides physicians with a continuous, reliable, real-time pressure measurement.

"The sensor stays in the muscle, and thus, gives the surgeon a real-time number they can monitor continuously for up to 48 hours post-injury," Allan explained.

That is critical, because if the pressure rises during that time, the doctor needs to perform fasciotomy immediately to allow the pressure to return to normal and to save the limb from amputation.

A test for ACS that is widely used by physicians today is **Stryker Corp.**'s *Intracompartmental Pressure Monitor System*, which uses a saline-filled needle that is inserted into the appropriate compartment to measure pressure, Allan said. But he feels that this test isn't as accurate as it could be.

"The water comes up to the sensor and the sensor is outside the body, so depending on the angle of the sensor, it changes the value you'll get, often significantly."

Myovue's sensor integrates MEMS technology to measure pressure from directly within the muscle, which he believes is significantly more accurate and independent of the angle at which doctors hold the device.

Allan said he plans to run a preliminary clinical feasibility study on Myovue comprising 50 patients at four sites across Canada this December and hopes to use the study results to apply for CE-marking in May 2018.

PRECISION MEDICINE: DRUG DOSING

Bradley Messmer, founder and CEO of **Abreos Biosciences**, finds in an era where so much focus is being given to precision medicine, it's unfortunate that precision drug dosing, or how much of a drug individual patients should receive to optimize treatment, doesn't get the same attention.

He is setting out to change that at Abreos.

Messmer first explored the critical need to optimize drug dosing as a faculty member at the Moores Cancer Center at UC San Diego. After realizing the potential for commercializing tests that would allow physicians to optimize how much of a biologics drug should be given to individual patients, he founded Abreos in October 2013. This June, he took on the CEO helm full-time and hopes to be on the market with a test next year.

Abreos was one of the four finalists in the Medtech Innovator competition.

Biologics, including antibody-based treatments for cancer and chronic autoimmune disorders such as multiple sclerosis, are far more expensive than their small molecule counterparts, Messmer told the audience at the event. A single dose can cost thousands of dollars, yet precise dosing and monitoring of biologics is still not a routine part in the clinic.

"When your drug costs as much as a Ferrari, it should at least come with a speedometer," Messmer said.

The company's core technology, *Veritope*, uses a proprietary reagent platform based on peptides to detect a given biologic or biosimilar drug by mimicking the natural drug target. That includes cell-membrane-bound proteins aiming to detect the biologic drug in serum or plasma. The tests are designed as both -- lab-based tests in hospitals and point-of-care tests, including at-home testing by consumers -- which Messmer said is the big differentiator between Abreos and other companies that offer precision dosing testing today.

Most companies focus on either POCT or lab tests, not both, which, he said, will give Abreos a competitive edge on the market *(Also see "Voyage Into Point-Of-Care Testing Gets Deeper" - Medtech Insight, 16 Aug, 2017.)*.

The company expects that the first test to hit the market will be a lab test to help physicians determine the correct dosing for Tysabri, an immunosuppressant commonly prescribed for multiple sclerosis patients. The drug costs roughly $5,000 per monthly dose and is known to put patients at risk of developing progressive multifocal leukoencephalopathy (PML), a viral infection of the brain that usually leads to severe disability or death.

"Tysabri is dosed in a one-dose fits-all fashion, so 100-pound Mary (a patient who was part of a clinical trial the company conducted) and a 300-pound football player are given the exact same dose," he said, adding that's "impersonal medicine" given that each individual absorbs a drug differently.

Abreos has been collaborating with Rocky Mountain Multiple Sclerosis Clinic in Salt Lake City using its technology to measure drug levels in 200 patients treated with Tysabri. Messmer hopes to be able to market this test as a CLIA-waived test in 2018. CLIA-waived status from the FDA allows non-laboratory personnel to perform this test. Another planned clinical trial for 2018 would be for a developed point-of-care test in 200-300 patients taking the drug Remicade for treating inflammatory bowel disease.

To date, Abreos has raised $2.8m in funding, predominantly from angel investors and NIH small business innovation research grants, Messmer told *Medtech Insight*. This May, current investors funneled another $1.2m into Abreo's coffers for hitting a milestone to hold a pre-submission meeting with the FDA to discuss a de novo 510(k) pathway for developed tests, he added.

Next summer, Messmer hopes to raise another $5m-8m in a Series A funding round, which would allow the company to launch the test to optimize dosing for Tysabri and fund clinical trials for point-of-care testing to optimize Remicade dosing in patients, which would require FDA 510(k) approval.

Asked about his short-term plans, the entrepreneur said he hopes to get market validation for their commercial products.

"We have gotten the feedback from pharma and payers that they see the value that we can bring," Messmer told *Medtech Insight*. Abreos has joined forces with unnamed pharmaceutical companies to use its tests in pre-clinical and clinical testing to optimize drug dosing.

The long-term vision calls for Abreos' tests to become the "gold standard for dose monitoring of biologic drugs."

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VC DEALS ANALYSIS:

Quarter-Billion Round Hikes September Takings To Five-Year High

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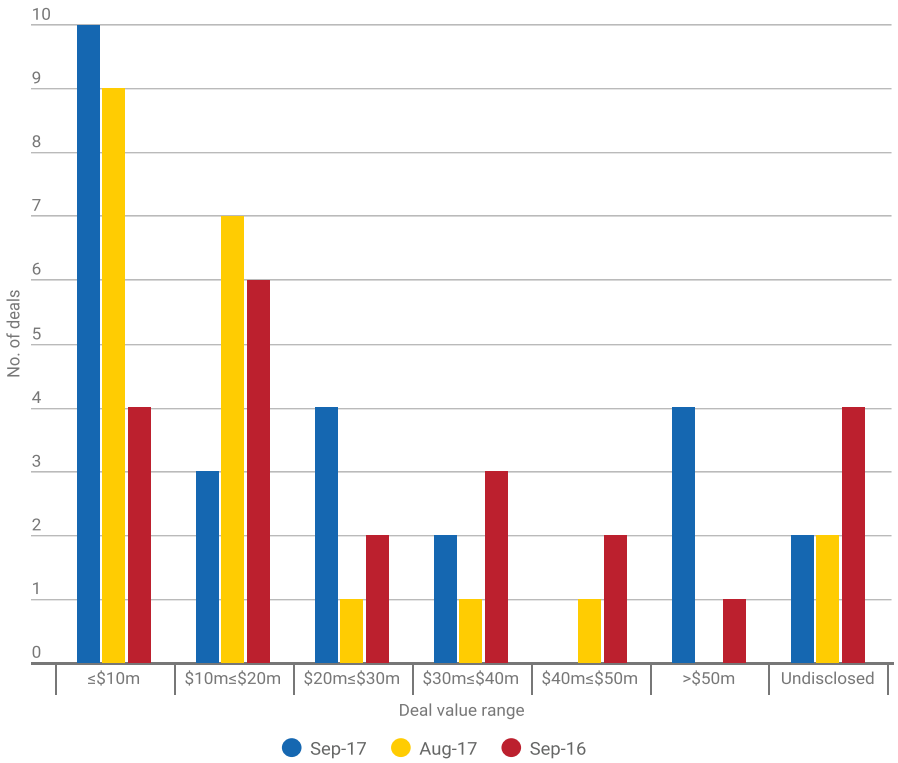
Only three months left till the end of the year but 2017 looks more likely than ever to outshine 2016 as a bumper year for medtech venture fundraising. September's takings of around $820.7m, raised from the 23 medtech-related deals that disclosed financial details (there were 25 transactions in all), brought the total takings for the nine months this year to $4.99bn, less than $200m away from 2016's haul of $5.14bn.

Giving a substantial leg up to September's recorded deal value were four big-buck rounds of more than $50m, including two transactions that surpassed $100m. (See Figure 1.) There was also a bigger deal volume in mid- to large-sized ranges of $20m≤$30m and $30m≤$40m compared to August and to September a year ago.

This September has proved to be the most bountiful over the last five years (See Figure 2), but it is not the biggest deal value this year. It falls just a bit short of May's $948.2m, and has some way to beat March's $1.34bn. *(Also see "VC Deals Analysis: From Famine To Feast, 2017 Bloats With May Haul" - Medtech Insight, 7 Jun, 2017.). (Also see "VC Deals Analysis: Big Boost From Bumper Round" - Medtech Insight, 6 Apr, 2017.)*. Nonetheless, the addition of September's harvest means that 2017 has so far had the highest peaks in deal value since 2013 and those three months should mitigate any impact from the other months that may not have fared as well, like February that had the lowest monthly takings across the last five years.

FIGURE 1

No. Of Deals, By Amount Raised, Sept 2017 Vs. Aug 2017 Vs. Sept 2017



Source: Medtech Insight's VC Deal Tracker

The biggest transaction of the month was a $250m growth equity financing raised by **23andMe Inc.**, one of the companies leading the charge for direct-to-consumer genetic test services. (See Table 1.)

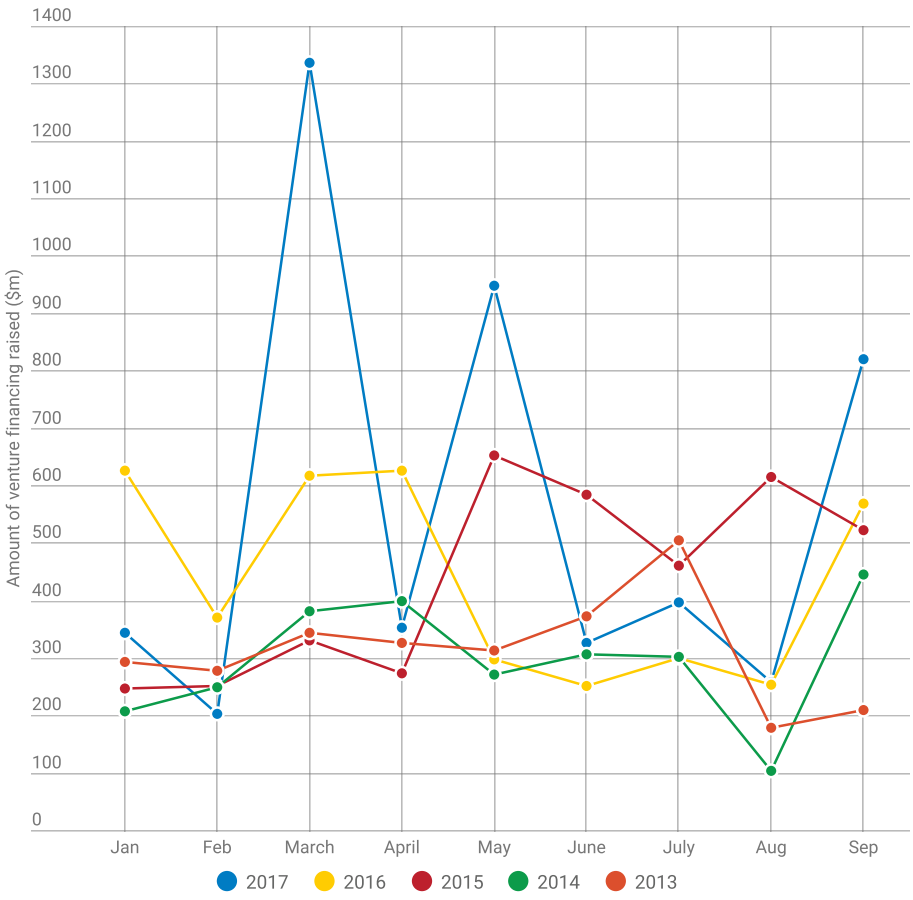
23andMe welcomed a number of new investors in this deal, including Sequoia Capital, which led this round, Euclidean Capital, Altimeter Capital and Wallenberg Foundation. Existing shareholders – Fidelity Management & Research Company and Casdin Capital – also chipped in.

This is the largest fundraising round to date for the California company and caps its achievements in this year, such as getting the first and only FDA authorization for over-the-counter genetic health risk reports. The investment also underlines the belief in the consumer genetic testing market; in a previous interview with *Medtech Insight*, Paula Dowdy, who oversees the EMEA operations of next-generation sequencing leader Illumina, said that the consumer genomics market in the US has been very successful for the likes of 23andMe and its rival, ancestry.com, and predicts that Europe will soon follow with an acceleration in adoption of these services. *(Also see "Illumina Enters Second Wave Of Growth As Genomics Demand Swells" - Medtech Insight, 27 Jul, 2017.)*.

WuXi NextCODE, another genomics

FIGURE 2

Five-Year Trend In Monthly Deal Value, Jan-Sep 2013-2017



Source: Medtech Insight's VC Deal Tracker

TABLE 1

September's Top 5 Medtech Venture Financing Deals

RANKING	COMPANY	BASED IN	PRODUCT/ THERAPY SECTOR	AMOUNT RAISED	FINANCING ROUND	TOTAL INVESTMENT
1	23andMe	CA, US	IVD	$250m	Undisclosed	$491m
2	WuXi NextCODE	Shanghai, China	IVD	$165m	Second tranche of a $240m Series B	Undisclosed
3	Tempus	IL, US	IVD	$70m	Undisclosed	$130m
4	Micell Technologies	Paris, France	Cardiology	$62m	Mix of debt and equity financing	Undisclosed
5	ElectroCore	NJ, US	Neuromodulation	$36m	Part of an expected $65m round	Undisclosed

Source: Medtech Insight's VC Deal Tracker

company, scored the second biggest deal in September by raising $165m, thus completing a Series B round that raked in $240m in total. Sequoia also has its finger in this pie, with its China arm being one of the investors in Shanghai-based WuXi, which is building a platform for genomic data, using NGS technologies. This data can then be applied to develop diagnostics and therapeutics. Other prominent Asian shareholders in WuXi include Singapore's Temasek and Yunfeng. Capital.

While the two biggest deals were in IVD, this product sector tied with cardiology/vascular for the top position as the most popular area of investment in September, each accruing six VC deals last month. (See Figure 3.)

Among the other notable VC deals in September was **Cambridge Medical Robotics**' $26m round, the biggest Series A of the month. CMR, based in the UK, is in the hot area of surgical robotics and it is developing a portable system. The robotic arms of this system sport a proprietary four-axis wrist joint which is designed to mimic the dexterity of the human wrist and allows the system to hold a surgical instrument the same way as a surgeon. This recent investment is the second tranche of a larger Series A transaction and brings the total raised in the round to $46m.

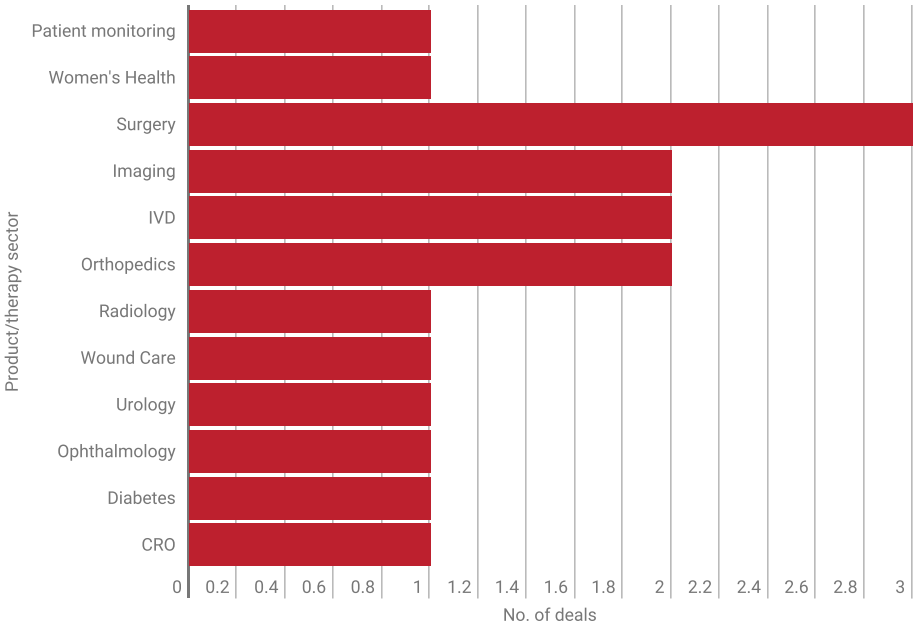
There were also multiple bits of funding news from Israel, which is a hotbed of innovation. Several of these came from the portfolio of Misgav-based innovation incubator Trendlines Group and they include:

- **Vensica Medical**, which is developing an ultrasound-based needle-free drug delivery system;
- **Elastimed**, which has developed a "smart' sock" that compresses and massages the legs to improve the circulation of peripheral vascular disease sufferers; and
- **Fidmi Medical**, which has developed a percutaneous endoscopic gastrostomy device, used in an enteral feeding. This device features a replaceable inner tube hat keeps the feeding line fresh and prevents clogging.

For more details about VC deals in 2017 and previous years, go to Medtech Insight's VC deal tracker: https://medtech.pharmamedtechbi.com/datasets/vc-funding.

FIGURE 3

No. Of Deals, By Product/Therapy Sector, Sept 2017



Source: Medtech Insight's VC Deal Tracker

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