Medtech Insight
Issue 1
medtech.pharmamedtechbi.com
Pharma Intelligence Informa
July 18, 2016

Photo credit: Kisan/Shutterstock.com

China Seeks Feedback On Priority-Review Designation For Devices

NEENA BRIZMOHUN neena.brizmohun@informa.com

The China Food and Drug Administration is planning to introduce yet another expedited-approval process for medical devices and has issued proposals for how the new procedure – called priority-review designation – will work in practice.

The priority-review process would apply to devices that fall under national priority areas or meet unmet clinical needs, according to a June 21 circular issued by the agency.

Priority-review designees would be eligible to take advantage of several features intended to expedite the review process, including frequent interactions with CFDA's Center for Medical Device Evaluation, said Katherine Wang, a partner in the Shanghai office of law firm Ropes & Gray.

> "The CFDA may exercise its discretion to determine whether a device application qualifies for priority review based on an expert panel's opinion, not just when priority review is requested by the applicant," Ropes & Gray's Katherine Wang says.

CFDA's proposals also include a mechanism for third parties to challenge priority-review eligibility decisions by the agency, Wang noted.

As for how priority review would work, Wang explained that the procedure would be available to applicants with devices that: 1) have been enrolled in the National Science and Technology Major Project, or the National Key Research and Development Plan; or 2) can provide significant clinical advantages in the diagnosis or treatment of the following areas of unmet need:

- Rare diseases;
- Malignant tumors; or
- Frequently occurring diseases in the elderly or in children.

Priority review would also apply to devices that address an urgent clinical need for which no predicate device exists on the Chinese market.

Applicants would be able to request priority review when submitting their device application to CFDA, Wang said. "The CMDE will assess whether a device is eligible for priority review, and decide the priority-review designation before the technical review process begins."

For those devices that fall under the National Science and Technology Major Project, or the National Key Research and Development Plan category, CFDA would evaluate prioritization requests with-

CONTINUED ON PAGE 5

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

WELCOME TO MEDTECH INSIGHT:
The Gray Sheet, Clinica And More, All In One Place

Medtech Insight
Pharma intelligence | informa

Welcome to Medtech Insight, where you will find all the content from The Gray Sheet and Clinica, together with our medical device news and insight from Scrip Regulatory Affairs, Medtech Insight Newsletter and Start Up. Now you have an unparalleled source of information on the medical device and diagnostics sectors in one place.

People have counted on The Gray Sheet and Clinica for many years as the go-to sources for in-depth news and analysis about medical devices and diagnostics. We are proud of our long-standing commitment to excellence, and that commitment includes evolving to meet our readers' needs. As part of this evolution, we are expanding the breadth and global reach of our content and re-launching on a new enhanced website, under a new name: **Medtech Insight**. From today, you have access to a truly unparalleled source of information on the medtech industry.

Our global team of editors and reporters will continue to do what they do best: provide in-depth analysis, expert tips and up-to-the-minute news, on the core issues impacting the device industry. Only now, under the Medtech Insight banner, there will be more for you. Content that is currently found in The Gray Sheet, Clinica, Medtech Insight Newsletter, Scrip Regulatory Affairs and Start-Up magazine will come together onto one platform. That means a detailed focus on regulatory, quality, reimbursement and policy issues from across the globe, from the US to Europe, from Brazil to China – and beyond. It also means invaluable datasets; global reporting on business and R&D developments and trends; regular coverage of start-up companies and the challenges they face; and in-depth analyses of the diverse markets that make up the broader device and diagnostic sectors.

In tandem with the expanded content, we are launching a new platform to improve online access. It will provide simplified navigation and search tools, ways to customize the site to help you find the information you need faster, a fully responsive design so you can access content anytime on your desktop, tablet and smartphone, use of a single name and password for customers subscribing to multiple publications, and access to more multimedia and interactive data.

You can use your current log-in details to obtain this wealth of information online. Your emails will continue uninterrupted. And we will continue to produce a weekly print publication under the Medtech Insight brand and downloadable pdf. You don't need to make any changes to access this more robust content and the new online tools.

The new Medtech Insight will establish a content resource we can build on to best respond to our readers' needs for the future. Thank you for counting on us as your source for industry insight.

We welcome your questions and comments. To discuss matters related to your subscription or product access, contact Customer Care at clientservices@pharmamedtechbi.com.

To discuss the editorial content of our combined publication, reach out to us.

Richard Faint
Head of Medtech
richard.faint@informa.com

Dave Filmore
Executive Editor, North America
david.filmore@informa.com

Tina Tan
Executive Editor, Europe and Asia
tina.tan@informa.com


5


9


14

explore more:

exclusive online content

Quality metrics
http://bit.ly/2acu5ae

An in-depth look at the US FDA's efforts, with the help of the Medical Device Innovation Consortium, to adopt quality metrics that will not only help determine which medical device facilities to inspect next, but to also raise firms' overall approach to quality above baseline.

Tax tips
http://bit.ly/29VbuQF

Medtech services and products are increasingly provided across different borders. So what does this mean when it comes to paying tax and VAT? Attorneys from Baker & McKenzie address these issue an expert guest column.

IPO still no-go
http://bit.ly/29zivFF

The medtech IPO scene looks to be livening up from Q1, but activity levels are still far behind those seen last year.

Nanotech in cancer
http://bit.ly/29zivFF

Following positive outcomes in its phase I/II trial, Nanobiotix is advancing its NanoXray technology designed to dramatically increase the effectiveness of radiotherapy and expects to get its first CE mark by the end of the year.

Latin America regs
http://bit.ly/29FGjfG

Akhila Krishnan reviews the different regulatory requirements for medical devices in five Latin American countries and discusses how harmonization initiatives will make things easier for manufacturers in this guest column.

www.medtech.pharmamedtechbi.com

inside:

POLICY & REGULATION

Medtech insight

DAVID FILMORE @MEDTECHDAVID
david.filmore@informa.com

TINA TAN @MEDTECHTINATAN
tina.tan@informa.com

SHAWN M. SCHMITT @MEDTECHSHAWN
shawn.schmitt@informa.com

REED MILLER @MEDTECHREED
reed.miller@informa.com

AMANDA MAXWELL @MEDTECHAMANDA
amanda.maxwell@informa.com

SUE DARCEY @MEDTECHINSIGHT
sue.darcey@informa.com

DANNY AL-FARUQUE @ALFARUQUE
danny.al-faruque@informausa.com

ELIZABETH ORR @ELIZABETHJORR
elizabeth.orr@informa.com

ASHLEY YEO @ASHLEYPYEO
ashley.yeo@informa.com

MAUREEN KENNY @SCRIPREGMAUREEN
maureen.kenny@informa.com

NEENA BRIZMOHUN @SCRIPREGNEENA
neena.brizmohun@informa.com

VIBHA SHARMA @SCRIPREGVIBHA
vibha.sharma@informa.com

JANET HANIAK SENIOR DESIGNER

GAYLE REMBOLD FURBERT DESIGN SUPERVISOR

RICHARD FAINT HEAD OF MEDTECH
richard.faint@informa.com

PHIL JARVIS MANAGING DIRECTOR

Editorial office:
52 Vanderbilt Avenue, 11th Floor, New York, NY 10017
phone 240-221-4500, fax 240-221-2561

CUSTOMER CARE:
1-888-670-8900 OR 1-908-547-2200
FAX 646-666-9878
clientservices@pharmamedtechbi.com

▶ join the conversation

We are tweeting, chatting, liking and sharing the latest industry news and insights from our global team of editors and analysts — join us!

@medtechinsight

COMPANIES

COMMERCIAL

R&D

START-UP SPOTLIGHT:

CONTINUED FROM 1

in five working days of accepting the submission, according to medical device consultancy company, Brandwood Biomedical.

For devices that fall under the category of products for addressing rare diseases, malignant tumors or diseases in the elderly or children, "CFDA proposes a monthly review panel to consider submissions and issue notifications after each panel meeting," said Brandwood's Senior Consultant and Head of China Operations, Steven Wen.

Wang noted that for any application that had passed the initial eligibility review, "a third party may submit an opposition to challenge the initial eligibility review result" during a public notification period. A device application that does not receive a priority-review designation will follow the standard review process.

"In some cases," Wang said, "the CFDA may exercise its discretion to determine whether a device application qualifies for priority review based on an expert panel's opinion, not just when priority review is requested by the applicant."

OTHER FAST-TRACK ROUTES IN CHINA

The priority-review designation is the third expedited-approval procedure that CFDA has developed for medical devices, according to Wang. The other two procedures comprise accelerated approval for devices applicable to emergency public-health incidents, and fast-track approval for innovative devices.

Brandwood's Wen commented that the priority-review procedure was "quite different from the innovative device pathway (also known as the Green Channel).

The innovative-device pathway, he said, "offers more" in terms of providing "specific technical and regulatory assistance to applicants, parallel classification reviews and a nominated internal champion to ensure smooth passage through the review."

That said, the priority-review procedure would be simpler. "There's no lengthy pre-qualification. Rather it's simply a matter of making the request as part of a traditional regulatory submission – which, if successful, results in priority processing," Wen explained.

The CFDA circular proposing the priority review designation scheme is open for public comment until July 20.

Published online 07/10/2016

India Takes Another Stab At Regulating Devices as Devices

VIBHA SHARMA vibha.sharma@informa.com

The Indian government is inviting stakeholder feedback on new draft rules that aim to introduce a risk-based approach to support the regulation of certain medical devices that are currently being regulated as drugs.

The proposed Medical Device Rules, 2016, represent an interim arrangement and will only apply to the 23 types of medical devices and IVDs that are currently being regulated as drugs, or to other medtech products as and when these are formally brought within the ambit of the country's medicines legislation.

The draft rules, when in place, will help the government test the waters on applying international standards to the regulation of these devices. In the long-term, the government intends to introduce separate legislation to formally regulate all types of devices/IVDs on the market.

The proposed rules are based on international norms and would introduce a risk-based four-tier system for classifying medical devices and IVDs. They would also permit sponsors of low- and medium-risk devices (Class A and B) to rely on inspections conducted by third-party certification bodies to support their regulatory applications.

The Association of Indian Medical Device Industry (AiMeD) has welcomed the proposed rules, even though it has serious reservations about certain sections – the most contentious one being the definition of the term "manufacturer". [See Sub-Head Below: Outstanding Issues]

Creation of a separate rule book to regulate medical devices has been a longstanding demand of the industry and "in essence, we welcome the [proposed rules] … There are, however, some challenges as these [proposed rules] need to be tweaked to enable the dual needs of [supporting] patient safety and ease of doing business," AiMeD's forum coordinator Rajiv Nath told *Medtech Insight*.

Photo credit: Alexandra Lande/shutterstock.com

Nath explained that the proposed rules, when finalized, would introduce new requirements for medical device and IVD companies, such as compliance with defined essential requirements for patient safety and ensuring that quality management systems conform to international QMS standard ISO 13485. Also, the proposed rules would help align the labeling of medtech products with the provisions of the Drug and Cosmetics Act and the Weights and Measures Act.

The proposed rules are part of the government's three-pronged approach to strengthening its oversight of the medtech sector without being caught up in legal wrangles in the short term. The government's three-part strategy, Nath explained, would work as follows:

1) The draft medical device rules would allow the regulatory authorities to "go through a learning curve [on applying internationally-acceptable device-specific standards] with a handful of devices".

The draft rules have been issued in place of the government's earlier plan to amend the current medicines legislation, i.e., the Drugs and Cosmetics Act (1940), in order to add a new chapter on the regulation of medical devices. The amendments were to be brought about through the Drugs and Cosmetics (Amendment) Bill, 2013, but the government scrapped that plan and withdrew the bill from the parliament in June.

While the process of amending legislation requires parliamentary approval, Nath explained that the government can frame rules much faster as it does not need parliament's endorsement. It therefore decided to go ahead with framing the rules and to start applying them, as soon as they are finalized, to the few device types that are already being regulated as drugs.

While the government could regulate more and more devices as drugs, this is not the best way forward. For this to happen, Nath explained, each device type has to be formally notified as being brought under the medicines legislation and this leads to "confusion of terminology and applicability [of requirements]".

2) To ensure oversight of all devices and IVDs on the market, the government is preparing a separate Medical Devices Bill, 2016. Nath explained that the new bill would most likely be based on the now-scrapped Drugs and Cosmetics (Amendment) Bill, 2013, "but hopefully [it would be] better drafted [and subjected to] wider consultation."

The proposed implementing rules for devices being regulated as drugs, Nath explained, have been drafted keeping in mind the regulatory framework that the government wants to introduce through the new bill. This, he said, would ensure that the implementing rules "need minimal tweaking or change" once the device-specific legislation is finalized.

For the medtech sector, the biggest impact of the device legislation, when enacted, "would be that all devices would get regulated at one go within a definite transition period" instead of the current approach of subjecting each device type to drug regulations on case-by-case basis.

Nath expects the draft bill to be ready by the next quarter, after which it will undergo stakeholder consultation and an extended legislative process, which could take two to three years.

3) The government has finalized new QMS requirements for devices and IVDs being regulated as drugs and these came into effect on June 29, 2016. The new requirements are based on the international QMS standard ISO 13485:2013 and will bring the regulation of these products in line with the current international practice.

The QMS requirements for medical devices are specified in an annex (Schedule M III) to the Drugs and Cosmetics Rules, 1945. Until now, Schedule M III was regarded as grossly inadequate, as a result of which device manufacturers were arbitrarily asked to comply with good manufacturing practice requirements for pharmaceuticals.

The finalization of device-specific manufacturing requirements marks an important first step toward ushering in regulatory reforms for the medtech sector. AiMeD is, however, disappointed that no transition period has been provided to help companies adjust their processes.

INDUSTRY PREFERS A MIX OF JAPANESE & EU MODEL

AiMeD has serious concerns regarding certain provisions of the draft Medical Device Rules. Among other things, it wants the government to adopt the EU system of relying on notified bodies to audit device manufacturers.

In the draft rules, the government has stated that it could rely on notified body audits for Class A and B devices, but it wants to send in its own medical device officers to inspect Class C and D devices before granting a manufacturing licence.

AiMeD, for its part, has been instrumental in launching a new voluntary scheme that allows notified bodies to be approved by India's national accreditation body so that they may assess and certify QMS and other essential requirements of medical device companies against international standards.

AiMeD will now lobby to ensure that certificates issued under the voluntary scheme find some sort of acceptance under the new rules. Nath's company, Hindustan Syringes & Medical Devices Ltd, is the first to obtain certification under the voluntary scheme.

Other issues that AiMeD has found contentious in the proposed rules are detailed in the following table.

DRAFT MEDICAL DEVICE RULES, 2016	AIMED'S PROPOSAL
The Central Licensing Authority (i.e., the Drugs Controller General of India) will regulate the manufacturer and the importer, while the regulation of the trading company will be delegated to the State Licensing Authority.	AiMeD prefers the Japanese model wherein the Central Licensing Authority regulates the importer, the manufacturer and the market access authorization holder (irrespective of whether the MAAH is the manufacturer or a marketing company or an authorized agent of the overseas manufacturer). It wants the State Licensing Authority to regulate domestic resellers, wholesale dealers, retailers and health care providers.
The definition of "manufacturer" includes any person who has marketed or promoted any medical device or used any other similar expression printed, written, embossed, stickered or put in any manner on the medical devices	AiMeD believes that the government's proposed definition would allow traders/marketing companies to be called and labeled as manufacturers, which is unfair. AiMeD points out that the government's proposed definition is based on the EU's definition of the term "legal manufacturer". AiMeD prefers the Japanese approach as it would boost and protect domestic manufacturers.

Source: AiMeD

Published online 07/12/2016

COMPLIANCE CORNER:

9 US FDA Inspection Questions Answered By Agency Officials, Abbott Quality VP

SHAWN M. SCHMITT shawn.schmitt@informa.com

Are US FDA investigators allowed to hunt through a messy filing cabinet for documents? Do low-risk class III recalls play into an inspection? And does a device firm have to respond to an FDA-483 inspection form?

FDA investigator Ben Dastoli from the agency's Cincinnati, Ohio, district office, Cincinnati compliance officer Gina Brackett, and Monica Wilkins, divisional VP of QA/RA for device-maker Abbott Laboratories, answered these queries and more from manufacturers at MedCon 2016.

Comments were edited for clarity by Medtech Insight.

"What can a manufacturer do if an investigator is fishing for issues by going through all files and financial accounts?"

Ben Dastoli: If you have your quality system records in one file cabinet, and maybe designs are in there or your complaints are in there, then an investigator is probably allowed to go fishing through that. You know what they're looking for. They don't have anything specific in mind, but you've set yourself up for this. If you put all your files in one place, they will look at that.

Now, what you don't expect is for that investigator to be walking through your office and going through your drawers. That's not acceptable. You should be able to at least understand what we're looking for, but depending on how you organize it, they might do some random fishing.

Gina Brackett: I remember inspecting a smaller firm and I asked about their complaint files, and they said, "We keep them by customer." That firm had huge file cabinets with all the sales information and everything else, and the complaints were mixed inside.

We're going to look at something like that. That manufacturer didn't keep things separated, and that's just how it was. Now, the firm did go through the file cabinets with me because we needed to see what the complaints looked like.

Dastoli: And we don't look at financial data. I think most companies understand that, that we don't have the right to look at your financial data.

"The FDA investigator wants to ensure that manufacturers are monitoring all of their supplier quality data and asks for evidence of such. Is it sufficient to document this in the management review notes?"

Dastoli: We have to be able to audit this data, so monitoring should be part of the corrective and preventive action [CAPA] system. We need to look at that data, so you can't really hide it in management reviews. It has to be accessible to us. That's part of the Quality System Regulation, which we have to confirm that you're following.

"Does FDA inspect makers of low-risk class I devices that don't have a 510(k)?"

Dastoli: A lot of firms think that because they make class I products that they're GMP-exempt, and that is not necessarily true. You need to look at the regulation to see if you're GMP-exempt, which most of you probably are not. The ones that are exempt, though, are still going to need recordkeeping and maintain complaint files. So we may go to those firms to inspect.

Remember, there are class I devices that aren't exempt from design controls, including automated software.

Brackett: Yes, don't forget about software. How many class I devices have automated computer software? Many. And those firms don't think they need to conduct design control. But they do.

Dastoli: And remember, the MDR [Medical Device Reporting] and corrections and removals regulations still apply if you make class I products.

"Some FDA investigators have been asking for data analysis reports that are generated and used only for management reviews. Do firms have to show these records to the investigator?"

Dastoli: A lot of times when we ask for some of this data, manufacturers say, "Well, we're just generating this data for management reviews, so you don't really have the right to look at it." But that's not really true. Data that's generated, we have the right to look at. We can't look at your meeting minutes during management reviews, but we look at the outcomes from a management review, which includes information on corrective actions.

Monica Wilkins: [However,] in our company [Abbott], we share a slide deck that has the data and the outputs. We will not show an investigator the meeting minutes and we will not show the agenda and any certifications. What we will do, though – and I think it's what industry should do as well – is before you share the data, make sure that you've gone through the deck and redacted any deliberation point, but not the data itself.

In other words, remove information that management made a decision or something like that because that's still protected under the meeting minutes. That's what we do. We don't say no; rather, we say we'll review it and we'll redact anything that is a management decision or a deliberation. But we will share the data because it is, in essence, CAPA data analyses.

"The FDA investigator is asking for copies of confidential and proprietary manufacturing methods. Does the firm have to comply?"

Dastoli: We do look at those records. We just ran into this recently where a manufacturer didn't think we were allowed to look because it was proprietary information in the manufacturing. Of course, we have to look at those. That's how we do our inspection.

"A manufacturer places all internal and external audit findings into its CAPA system and opens a CAPA for each finding. The investigator wants to review some CAPA files that resulted out of that. Can the firm remove all CAPAs associated with audit findings because investigators don't look at audit results?"

Brackett: We don't look at any audit findings. But the problem is when the manufacturer puts those findings in a CAPA, that gives us license to look at the investigation and corrective action. From our standpoint, that's what the audits are for. When I see those CAPAs and you've corrected that observation, or you're working on fixing that problem, and you've identified it yourself, that shows us that you're finding problems and that your audits are working.

"If a firm performs a health-hazard evaluation and determines that a recall meets the definition of a low-risk class III recall, should it not be reported to the FDA, and how does that affect the inspection?"

Dastoli: Part of what we do during our inspections is we collect information on class IIIs to add the reports to our database. We need to understand all the class IIIs that are out there. Or, a lot of times we're going to question firms and say, "It might look like a class II, so we might turn it in for FDA to classify it." Remember, FDA does the final classification, not the firms.

Brackett: When investigators go out and collect the recall information of a firm-indicated class III, the recall coordinator will send that information out for classification by the device center, and you will receive a letter about that.

If it comes back as class III, it is published in FDA's Enforcement Report. That's why you might have seen a recall that is two years old in the Enforcement Report because the firm didn't turn in the class III recall for classification. You need to be aware that the investigators collect that information, even if it comes back as a class III.

I've had firms call me and say, "We have hospitals calling us about this recall but it's closed out." It can be a little confusing to your customers because they don't understand that the recall is old. So you're doing a lot of explaining that the recall happened, say, two years ago. So be aware of that.

Wilkins: And from an industry perspective, often an investigator will come in and say, "Give us a list of your recalls, and not just the ones you reported, but those that you did not report." That's the mechanism because investigators have to verify all of that, so recalls are indirectly submitted that way.

"According to a firm's procedure, only the top three failure modes associated with complaints or nonconforming product is assessed for corrective actions. Is this acceptable?"

Dastoli: It's not acceptable. We do see this a lot. We see where people say, "We're going to look at the top five suppliers or the top five of this category." It's not done in a risk-based fashion. However, this is all about being risk-based. We have to understand that even though something is not occurring at a high level, it might be very significant.

Brackett: And if you're making 50 different products, your failure mode for the biggest seller is going to come up all the time. But you might have a small-selling device that's deemed to be high risk, yet it's not on a failure measurement chart because it's such a small seller. Again, be aware.

"If a manufacturer receives an FDA-483 at the completion of an inspection, is it required to send a response to FDA?"

Brackett: You are not required to respond. There is nothing in the law that says you have to respond. And I'm just going to say this: We have 2,000-plus investigators. Just like in your firms where you have some employees that may not do the right thing or don't understand, our investigators are no different. They might be new and not understand that a company doesn't have to respond.

Simply explain to the investigator that responding is voluntary. And if you feel like there's an issue, then you can go to the investigator's management. You have the right to do that.

Published online 07/12/2016

Take Compensation Pieces Out Of Stark Law, Legal Experts Tell Senators

SUE DARCEY sue.darcey@informa.com

Legal experts and the CEO of a large health care system in North Carolina told the Senate Finance Committee July 12 that the best way Congress could reform the Stark self-referral law would be to remove the elements of the statute restricting compensation arrangements.

"We need to keep the ownership prohibitions under Stark, but you should think about eliminating the compensation components of the law," said Troy Barsky, partner, Crowell & Moring LLP. Barsky is also the former director of technical payment policy of the Center for Medicare and Medicaid Services.

He added, "There are very clear anti-fraud statutes, the Anti-Kickback Statute and the False Claims Act, that protect against bribes and kickbacks in the health care marketplace. So there already are some protections that allow for some balancing [with the new alternative payment models] under Medicare."

Barsky also said with the new innovative payment models that "the incentives in those models are completely different from fee-for-service. So, there is no incentive, in those alternative payment models, to over-utilize care, and if you over-utilize care, health systems would not make as much money as they would if they provide high quality care."

"I agree with Mr. Barsky that getting rid of the compensation arrangement is the most important thing, and even Chairman Hatch wrote that the law's author, Pete Stark once said that on balance, the law may have done more harm, than good," noted Ronald Paulus, M.D., president and CEO of Mission Health, Ashville, N.C.

"And when you look at how much has changed in terms of payment models, we have to ask ourselves, how do we do more good, than harm? There are already other laws – the Anti-Kickback Statute – to protect us," Paulus remarked. The hospital system CEO said that he would go much further than Barsky, though, by eliminating the Stark Law completely, if Congress considers that option.

Photo credit: Crowell & Moring, LLP

Troy Barsky, Partner, Crowell & Moring LLP, and a former CMS payment official, testified at July 12 Senate Finance Panel hearing on Stark Law reforms

Photo credit: Mission Health, Asheville, NC

Ronald Paulus, M.D., CEO of Mission Health, favors a total repeal of the Stark Law.

FINANCE COMMITTEE WEIGHS OPTIONS

In a June 30 white paper prepared by the Senate Finance Committee, total repeal of Stark is raised as an option. The committee is also considering congressional authorization of more Stark Law waivers to accommodate accountable care organizations and other innovative value-based payment systems, including bundling. (*Also see "Senate Finance Hearing To Focus Stark Self-Referral Law Exceptions" - Medtech Insight, 7 Jul, 2016.*)

Barsky said that, in the past, Stark Law waivers "provided a safe space," for innovative payment models authorized under the Affordable Care Act to flourish. "The only danger I see that is now developing is that with every new program being developed a new waiver comes out," he added.

"I disagree with my colleague," Paulus responded. "I would note that the overlapping waivers, while undeniably helpful, still create a lot of uncertainty that permeates the process." Paulus added that for hospital system programs that add more quality to patient health care, such as those to reduce hospital- acquired infections, Stark Law waivers simply do not fit.

Another witness, Peter Mancino, deputy general counsel, The Johns Hopkins Health System, pointed out: "Given the MACRA deadline, I don't think the waiver process can be fast enough. Also, waivers don't cover enough, because they only cover Medicare; they don't cover Medicaid, commercial payers, etc., and certain physician specialties."

Hatch told the witnesses that it was his intent to move quickly on Stark Law reforms in the Finance Committee, saying, "We are going to try to do something about this before the end of this year."

Published online 07/13/2016

New EU Regs Set Fluid Deadlines for UDI/ Eudamed Compliance

AMANDA MAXWELL amanda.maxwell@informa.com

No one knows exactly how long it will take to set up the updated version of Eudamed, the European Union's medical devices database that will form the backbone of the new medical device regulatory system. Nor can anyone specify with certainty the deadlines for introducing in the EU the Unique Device Identification (UDI) system, which will be fundamental to communication within this system.

Because of these unknowns, the forthcoming Medical Device and IVD Regulations have been drafted to offer some leeway for manufacturers, and some of the requirements for medical devices will not be fully applicable until several years after the Regulations have been adopted.

Some of the requirements for medical devices will not be fully applicable until several years after the Regulations have been adopted.

The way in which the new regulations are drafted, with multiple cross-referencing, does not make it easy to understand when the deadlines are likely to occur.

As a reminder, Eudamed will include electronic systems on registration of devices; registration of economic operators; UDI; notified bodies and certificates; clinical investigations; vigilance and post-market surveillance; and market surveillance.

Because of the potential delay in getting Eudamed and UDI up and running, some allowances in relation to registration of economic operators and certificates have been built into the Eudamed system, as mentioned in the table below.

According to the text of the Medical Device Regulation, economic operators and certificates should be registered by early in the second half of 2022 as long as the necessary IT systems have been developed (including Eudamed and UDI). But, in the meantime, registration requirements under the current medical device directives continue to apply.

The table below aims to provide a clearer overview of the likely timelines for compliance with rules for inputting information into Eudamed, such as certificates, and for UDI compliance.

It is followed by details for the timelines for a variety of other tasks, including governance issues such as for the redesignation of notified bodies; for the setting up of the European Commission's Medical Device Coordination Group; for multi-centre clinical investigation arrangements; and for new formal cooperation arrangements for between the member states and the Commission.

Published online 07/10/2016

UDI AND EUDAMED

Q: How soon will the European Commission need to draw up its functional specifications for the European database, Eudamed, and the electronic Unique Device Identification system?

A: t must be drawn up, in collaboration with the Medical Devices Coordination Group, at the latest in early 2018.

Info: The plan must seek to ensure that Eudamed is fully functional at a date that allows the European Commission to publish a notice stating that the necessary conditions have been fulfilled at the latest two months before the full application of the Regulation in early 2020.

Q: What happens if the Eudamed database and the UDI system are not fully functional by early 2020?

A: The requirements to input information into the database will then apply six months after the Commission has published an official notice to state that these systems are fully functional.

Info: The official notice will be published in the Official Journal of the European Union.

Q: How soon will manufacturers need to assign to all higher levels of packaging a relevant unique device identifier before placing a device on the market, and have to register this on the UDI part of the Eudamed database?

A: This will need to be done 18 months after early 2020, i.e. in the early part of the second half of 2021, unless there are delays to setting up the Eudamed and UDI systems, in which case it seems that the six-month grace period after publication (as above) will apply.

Info: This rule does not apply to custom-made devices. Also, importers will need to ensure that the manufacturer or authorized representative has uploaded the UDI information to the database within two weeks of the device being placed on the market and add their details to the relevant entries.

Q: How soon will the UDI carrier need placing on the label of the device and on all higher levels of packaging?

A: For implantable devices and class III devices, the UDI carrier will have to be placed on the label of the device and on all higher levels of packaging by early 2021. In the case of class IIa and class IIb devices, manufacturers have until early 2023. For class I devices, they will have until 2025.

Info: Higher levels of packaging do not include shipping containers.

Q: How soon will notified bodies need to enter into the relevant part of Eudamed information on notified bodies and certificates?

A: This will need to be done 18 months by early in the second half of 2021, unless there are delays to setting up the Eudamed and UDI systems, in which case it seems that the six month grace period after publication (as above) will apply.

Info: There is no clause suggesting what would happen in the case of any delays here.

Q: What about reusable devices that need to bear the UDI carrier on the device itself?

A: The UDI carrier will need to be placed on the label of the device and on all higher levels of packaging by two years after the date applicable for its class of devices as stated above.

Info: This is likely to mean: for implantable devices and class III devices, the UDI carrier will have to be placed on the label of the device and on all higher levels of packaging by early 2023. In the case of class IIa and class IIb devices, manufacturers have until early 2025, For class I devices, they will have until 2027.

NOTIFIED BODIES

Q: When will the requirements regarding notified bodies and the redesignation of notified bodies begin to apply?

A: They will apply in the early part of the second half of 2017.

Info: This covers a wide range of activities related to the auditing, designation and supervision of notified bodies under the MDR.

Q: How soon will the Commission draw up a list of codes and corresponding types of devices to describe the scope of the designation of notified bodies which member states will indicate in their notification?

A: This will need to be done by the early second half of 2017.

Q: How long will conformity assessment certificates issued by notified bodies that decide to cease conformity assessment activities remain valid?

A: The certificates may remain valid for a temporary period of nine months after cessation of activities as long as another notified body has confirmed in writing that it will assume responsibilities for these products. The new notified body shall complete a full assessment of the devices affected by the end of that time period before issuing new certificates for those devices.

Info: Where a notified body decides to cease its conformity assesswment activities it must inform the national authority responsible for notified bodies and the manufacturers concerned as soon as possible and in case of a planned cessation one year before ceasing its activities.

Q: What happens when the national authority determines the notified body does not have the capability to support existing certificates?

A: If the designation of the notified body that issued the certification has been suspended or restricted, the certificate may still remain valid if:
a) The national authority responsible for notified bodies has confirmed, within one month of the suspension or restriction, that there is no safety issue for certificates affected by the suspension or restriction; and the national authority responsible for notified bodies has outlined a timeline and actions anticipated to remedy the suspension or restriction; or
b) The manufacturer gives the competent authority – within three months of the suspension or restriction – written confirmation that another qualified notified body is temporarily assuming the functions of the notified body to monitor and remain responsible for the certificates during the period of suspension or restriction.

Info: There is also a possibility for the competent authority in these circumstances to extend the provisional validity of the certificates for further periods which may not exceed 12 months.

GOVERNANCE

Q: When will the Medical Device Coordination Group need to be set up?

A: The clauses establishing the MDCG apply in the early part of the second half of 2017.

Q: What about countries that have opted out of the arrangements for multi-center clinical investigations where one member state takes on the coordinating role?

A: For seven years after early 2020, i.e., until early 2027, the procedure for clinical investigations carried out in more than one member state will only apply to the member states that have agreed to it.

Info: After 2027, the procedure will apply to all member states concerned by the submission of a single application by the sponsor.

Q: When will new formal cooperation between the member states and the European Commission under the MDR apply?

A: This will apply by early 2018.

Info: This also includes participation, where appropriate, in initiatives developed at international level.

COMMON SPECIFICATIONS

Q: How soon do common specifications need to be adopted for those medical devices for which CS's are considered necessary?

A: CS's, or detailed technical specifications, need to be adopted by early 2020. They will then apply six months after their entry into force, or from early 2020, whichever is the latest.

Info: Member state requirements for Annex XV devices (non-medical purpose devices) will remain valid until the CS for those groups of products are applied.

Wyden 2017 Chronic Care Bill Would Reward Telemedicine, Home-Use Devices

SUE DARCEY sue.darcey@informa.com

Sen. Ron Wyden, D-Oregon, plans to reintroduce a bill next year that he first sponsored with Sen. Johnny Isakson, R-Ga., in 2014. The measure seeks to reform Medicare reimbursement for technologies including telehealth and remote patient monitoring for elderly patients with chronic conditions.

"Right now, too many Medicare beneficiaries have to make long trips across town for doctors' appointments, and then, there is that co-pay [required for] care coordination in physician offices, or at hospitals. I think care coordination under Medicare ought to be free …and that also, it makes little sense to pull people out of their homes to treat chronic conditions," said Wyden, ranking member of the Senate Finance Committee. He spoke at a recent Brookings Institution event on chronic care in Washington, D.C.

The planned legislation would be very similar to the Wyden/Isakson "Better Care, Lower Cost Act" of 2014, emphasizing Medicare reimbursement for "Better Care Programs." The programs would be comprised of health plans designated for groups of providers and suppliers who devise individual, patient-centered chronic care plans for beneficiaries. A central tenet of the bill is that "the Medicare program should recognize the growing uses and benefits of health technology in delivering quality and cost-efficient care by encouraging the use of telemedicine and remote patient monitoring."

Under the measure, individual chronic care plans should "include the use of technologies that enhance communication between patients, providers and communities of care, such as telehealth, remote patient monitoring, Smartphone applications, and other such enabling technologies that promote patient engagement and self-care."

The 2014 measure also called on the HHS National Coordinator for Health Information Technology's office to develop a streamlined pathway for the use of mobile applications and communications devices that enhance the patient's experience – while maintaining patient safety and cost-effectiveness.

In February, the Senate Health, Education, Labor and Pensions Committee approved similar provisions in S. 2511, the Improving Health Information Technology Act, introduced by Chairman Lamar Alexander, R-Tenn., and five bipartisan cosponsors. (*Also see "Senate HELP Advances Device Review Reform Bills" - Medtech Insight, 9 Feb, 2016*) S. 2511 calls for mobile device inter-connectivity with electronic health records held in hospitals and physicians' offices, and is part of a package of medical innovation bills now being considered on the Senate floor.

> "It makes little sense to pull people out of their homes to treat chronic conditions," says Sen. Ron Wyden.

MEDICARE 'GUARANTEE' NEEDS UPDATING, SENATOR SAYS

Wyden talked about the need to update the "Medicare guarantee" to provide beneficiaries the comprehensive type of health care needed for today's elderly population "so that it can catch multiple conditions like heart disease, stroke and diabetes" – the chronic care conditions that now dominate Medicare reimbursements, Wyden said. "The days of a broken ankle and a nasty bout of the flu ...are over, in terms of their impact on Medicare … just a memory of yesterday," he noted.

He described, for example, a woman in his state named "Sharon" who is 68 years old and suffers from arthritis and Alzheimer's disease, and a retiree named "Philip" who has diabetes and heart disease, and is living off Social Security and a small pension from a factory job.

"It is painful for Sharon to get up and move around" to the bus stops she needs to get to, in order to make her doctors' appointments, the Senator said. And for Philip's diabetes care, "he needs to see a physical therapist, a primary care doctor, and a renal specialist, to maintain mobility," he added.

For Philip, "who is walking an economic tightrope," and for Sharon, who has a hard time getting around, "they need care at home," as well as Medicare-reimbursed care coordination "that should start right after your first wellness visit that you get under Medicare," Wyden said.

The Senator said he had proof that the Better Care Programs envisioned in his bill would work with seniors suffering from multiple chronic conditions: when the Affordable Care Act was approved in 2010, "we were able to get a program rammed into the … Act, called Independence at Home," Wyden said. "It's all about giving people better care at home, where they need it the most," he said.

"Early results on this [Independence at Home] pilot program shows it is bringing costs down, by $3,000 per older person, on average. So think about that."

Despite the success of the Independence at Home program, and Wyden's desire to scale up the pilot to make it a central feature of Medicare, he did not believe that "such a transformational bill" could be approved before the end of 2016. "For that reason, we could be well into 2017 – and maybe into 2018, before we could pass this Medicare update," he said.

Published online 07/12/2016

Assessing Patient Impact From Recalls Often A Judgment Call, US FDA Says

ELIZABETH ORR elizabeth.orr@informa.com

Recent US FDA draft guidance on benefit-risk considerations for enforcement actions doesn't give specific standards for how manufacturers should weigh the potential public impact of a recall. But that could change if comments on the draft ask for the information, a device center official said during a July 11 webinar discussing the draft document that was issued in June.

Multiple participants in the webinar asked for more information on how companies should evaluate what potential effect an enforcement action would have on patients. The guidance lists patient impact as a factor for FDA and industry to consider when weighing what kind of recall or field correction might be most appropriate. But that's "never incredibly black-and-white," explained Ann Ferriter, director of the Division of Analysis and Program Operations in FDA's device center.

"Public impact decisions are always going to call for judgment on the part of the agency and the manufacturer," Ferriter said. She recommended manufacturers facing such a decision email FDA's Division of Industry and Consumer Education (DICE) for advice.

However, she added, if enough comments on the guidance ask for clarification on the point, the final version might include more discussion of how to gauge public health metrics to support post-market decisions.

The webinar largely served as an overview of the draft guidance, which attempts to expand FDA's ongoing efforts to incorporate risk-benefit analysis into the pre-market process into the post-market setting (*"FDA, AAMI Explore How To Consider Benefits, Risks In Postmarket" - Medtech Insight, 16 Jun, 2016.*) The draft attempts to set a shared, benefit-risk framework for the agency, industry and other stakeholders; it also seeks to harmonize FDA's approach to weighing benefits and risks for medical device compliance and enforcement decisions with its benefit-risk framework for evaluating medical device pre-market applications.

If enough comments on the guidance ask for clarification, the final version might include more discussion of how to gauge public health metrics to support post-market decisions, an FDA official said.

FDA anticipates the guidance could help inform decisions and actions taken in response to device shortages and facility inspection observations. It also could help guide evaluation of recalls and petitions for variance from the Quality System Regulation. When finalized, the guidance should be "very impactful," said Robin Newman, director of the Office of Compliance within FDA's device center.

Newman noted that the guidance will allow the agency to evaluate patient input when making enforcement decisions. For example, she said, patients with a severe or chronic disease might highly value the benefits of a device that extends their lives, even if only for a few months. A situation like that might encourage FDA to allow patients to continue using the device or to grant a manufacturer's request for variance from QSR requirements, she said.

The agency also will consider a device-maker's regulatory history in making enforcement decisions, Newman said. She noted that FDA might take a harsher enforcement action if the manufacturer's communications with FDA have been missing or inadequate, or if the company has failed to meet regulatory requirements.

Comments on the draft guidance, under docket number FDA-2016-D-1495, will be accepted through Sept. 14.

Published online 07/12/2016

Metal-On-Metal Hip Class Actions Go To Trial In UK In 2017

AMANDA MAXWELL amanda.maxwell@informa.com

A date has now been set in the UK for two of the largest product liability class-action suits concerning injuries due to the early failure and removal of metal-on-metal prosthetic hips.

The UK High Court has set out a timetable that will progress cases related to the Pinnacle and Corin hip implants to trial beginning Oct. 9, 2017. These two class actions concern the Pinnacle Ultramet THR (total hip replacement) and the Corin Cormet THR and resurfacing devices. Some of leading orthopedic players are involved in this litigation, including Smith & Nephew, Zimmer, Corin Cormet and Depuy Synthes.

The Court ruled that all other metal-on-metal device litigation – such as those related to components manufactured by companies including Zimmer, Smith & Nephew, Biomet and Finsbury, for example – should be stayed pending the outcome of the Corin/Pinnacle trial.

Leigh Day, lead solicitors on a number of the metal-on-metal group actions before the UK Court commented: "It is the Court's intention that whilst the outcome in the Pinnacle/Corin trial will not be directly binding on other metal-on-metal litigation, it will provide an essential indicator, for those parties to actions now stayed, as to the merits of their respective cases and may hasten settlement discussions in other cases".

Photo credit: Denis Simonov/shutterstock.com

Some 600 individual cases are being represented in these class actions.

Published online 07/10/2016

NuVasive To Settle Medtronic Spinal Patent Suit

ELIZABETH ORR elizabeth.orr@informa.com

NuVasive Inc. is paying $45m settle a long-running patent suit with Medtronic PLC.

The settlement brings to a close a series of suits first filed in California in 2008, as well as related proceedings before the US Patent and Trademark Office. As part of the settlement, announced by NuVasive in a June 30 regulatory filing, both companies agreed to resolve any patent disputes over spinal implant or nerve monitoring patent via an arbitration process outside the court system for seven years.

In 2011, a jury found NuVasive's CoRoent XL implants, MaXcess II and III retractors, and Helix and Helix Mini anterior cervical plates infringed three Medtronic patents on implants for the thoracic and lumbar spine, a plate-and-screw system for the cervical spine and a tissue retractor. The court awarded $101.2m, including lost profit as well as back royalties.

The court also awarded $600,000 to NuVasive for Medtronic's infringement of a NuVasive patent on the use of neuromonitoring in a lateral approach to spine fusion surgery. (*See "Court Wants To Reassess Damages In NuVasive/Medtronic Patent Fight" - Medtech Insight, 5 Mar, 2015.*) Medtronic attempted to appeal that verdict to the US Supreme Court, but the justices declined to take the case.

But in 2015, the Federal Circuit Court of Appeals vacated the awards and sent the case back to the district court for review. The appeals court said the amount awarded to Medtronic seemed to represent more than a "reasonable royalty." Specifically, the court said the district court's judgment had incorrectly included an ongoing royalty rate as part of the lost-profits component. The retrial had not yet taken place when the companies reached a settlement.

Spokesmen for both companies signaled relief to put the disputes behind them.

"We are very pleased to have negotiated a mutually agreeable settlement that removes the ongoing burden of this litigation and provides for a framework for resolution of potential patent disputes in the future," said NuVasive CEO Gregory Lucier.

Medtronic spokesman Eric Epperson said, "We look forward to continue focusing our efforts on accelerating innovations that transform spine surgery and improve outcomes for more patients."

Published online 07/07/2016

M&A ANALYSIS:

Cardio And Ortho Billion-Buck Deals Headline Otherwise Slow Month

REED MILLER Reed.miller@informa.com

The medtech industry saw few mergers or acquisitions in June, but the summer slowdown included some noteworthy deals that could shake-up their respective industries.

The 12 deals appearing in *Medtech Insight*'s M&A Tracker in June represent a sharp decline in activity from the 18 deals recorded in May – and two fewer than June 2015. However, unlike May, June brought some billion-dollar deals (*see Figure 1*).

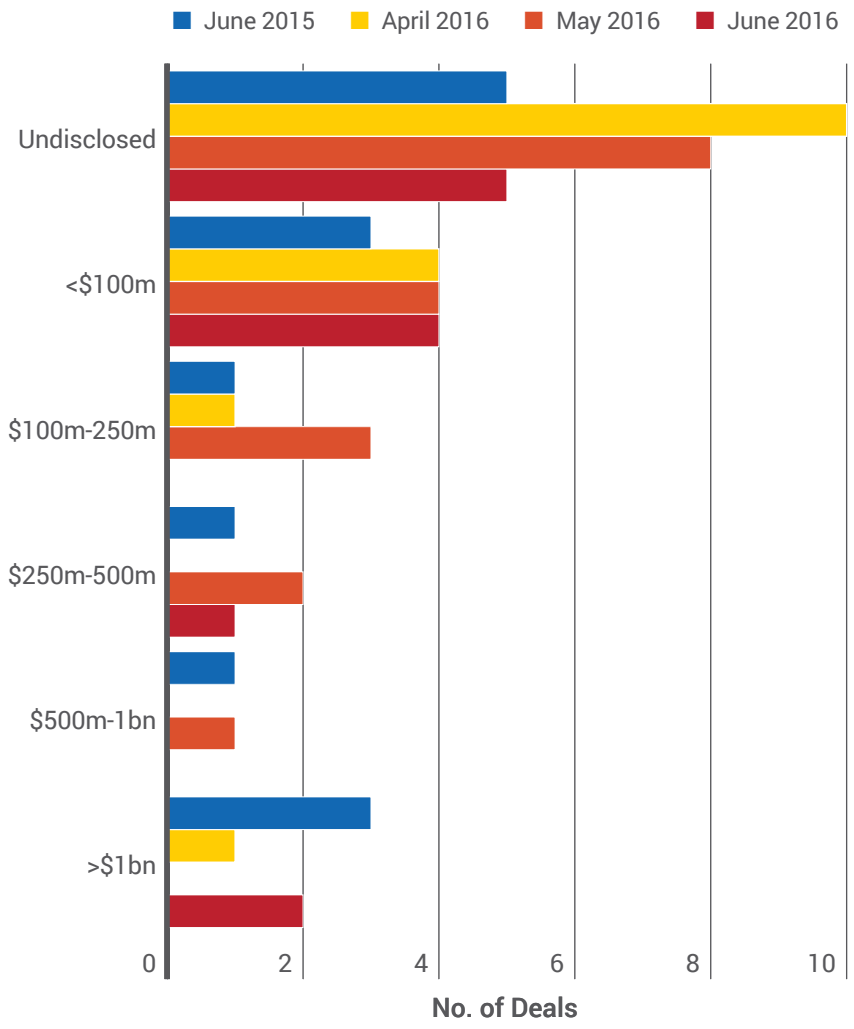
The biggest deal in June was Medtronic's $1.1bn deal for HeartWare, the number-two ventricular assist device maker behind St. Jude/Thoratec. The purchase price is about 4.6 times HeartWare's projected 2016 earnings and a 93% premium to its stock's closing price on June 23, but HeartWare shares were in the $90 range a year ago before problems in some of its clinical trials and competition with St. Jude/Thoratec deflated the share price. By comparison, St Jude paid $3.4bn for Thoratec about a year ago, a 40% premium over Thoratec's volume-weighted average stock price over the previous month and about five times the value of Thoratec's ventricular assist device annual revenues.

In the early 2000s, many small companies and researchers were trying to develop circulatory assist devices for heart failure patients unlikely to ever get a heart transplant. Now, most of those competitors are out of the race, and St. Jude's buy-out of Thoratec and Medtronic's acquisition of HeartWare means the VAD sector is securely in the control of big diversified medtech companies. And Thoratec is set to become part of an even bigger player when Abbott's $25bn acquisition of St. Jude is completed.

The other billion-dollar deal in June was Zimmer-Biomet's $1bn offer for spine-implant specialists LDR, announced June 7.

FIGURE 1

No. of M&A deals by transaction size June 2015 vs April-June 2016



The deal is Zimmer Biomet's biggest since Zimmer and Biomet merged in 2015 and Zimmer-Biomet's third acquisition in 2016. Zimmer-Biomet added a fourth 2016 deal later in the month when it announced the acquisition of its acquisition of Compression Therapy Concepts, Inc. a privately held New Jersey company that makes the VasoPress system, a non-invasive therapy for the prevention of deep vein thrombosis. Terms of that deal were not disclosed.

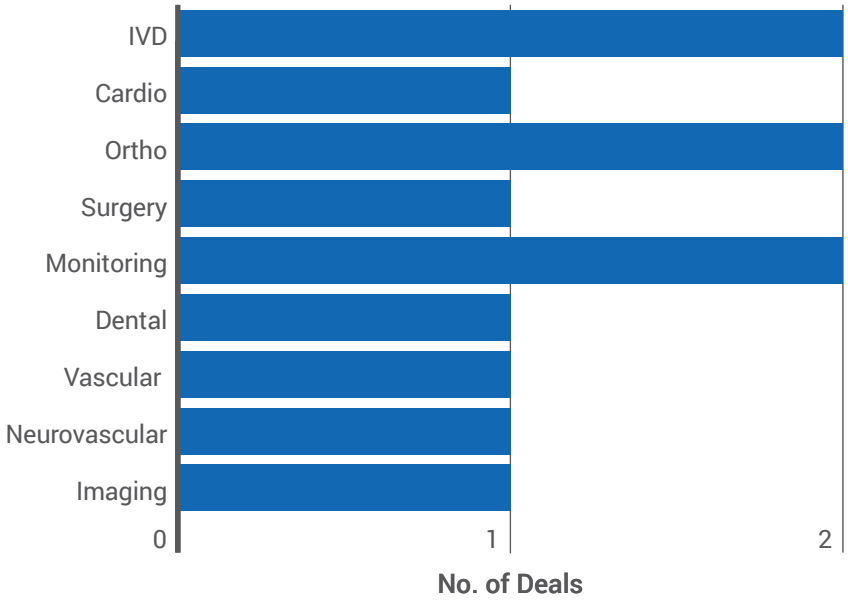
The LDR deal was one of two orthopedics mergers in June, putting that category in a three-way tie for largest industry category on June's list of medtech mergers and acquisitions (*see Figure 2*).

ANALYZE

To access Medtech Insight's database of M&A deals in 2016, go to http://bit.ly/29YxwVE

FIGURE 2

No. of M&A deals by product sector, June 2016



The other orthopedics deal in June was Medtronic's acquisition of Minneapolis-based Responsive Orthopedics for an undisclosed sum. Medtronic has been a minority investor and product-development partner with Responsive since 2014.

Responsive competes in the lower-cost subsegment of the knee and hip replacement industry. It's part of Medtronic's overall push into "value-based" healthcare. Medtronic previously moved into the value orthopedics business when it acquired Kanghui Medical, a Chinese developer of trauma and spine devices, in 2012. These two acquisitions in June pushes the number of M&A deals struck by Medtronic this year to five in total.

Published online 07/07/2016.

VC DEAL ANALYSIS:

Investor Interest Cools Off As Summer Sets In

TINA TAN Tina.tan@informa.com

While summer temperatures start to soar in some parts of the world, it looks like investor interest in medtech has cooled significantly as June recorded the lowest levels in venture financing, both in deal volume and value, this year so far.

Medtech Insight's VC deal tracker recorded 16 transactions of $1m and over in June, with just over $250m raised in total. This is a nosedive from the $585m raised from the 30 deals seen a year ago (*see Figure 1*), and also marks a downward trend that began last month in May.

While there were a number of large financings close to $50m and above, the majority were at the low end of the spectrum with a mere trickle of deals in the mid-sized ranges above $10m. Indeed, June had been a rather turbulent month for the financial markets, in the run-up to the UK vote on whether to stay or leave the EU and the subsequent Brexit outcome. The immediate impact of the Leave vote was not limited to the UK but had repercussions around the world's financial markets. While "uncertainty" has become the refrain of all post-Brexit discourse, one thing many seem to be sure of is that the UK's exit from the EU spells bad news for

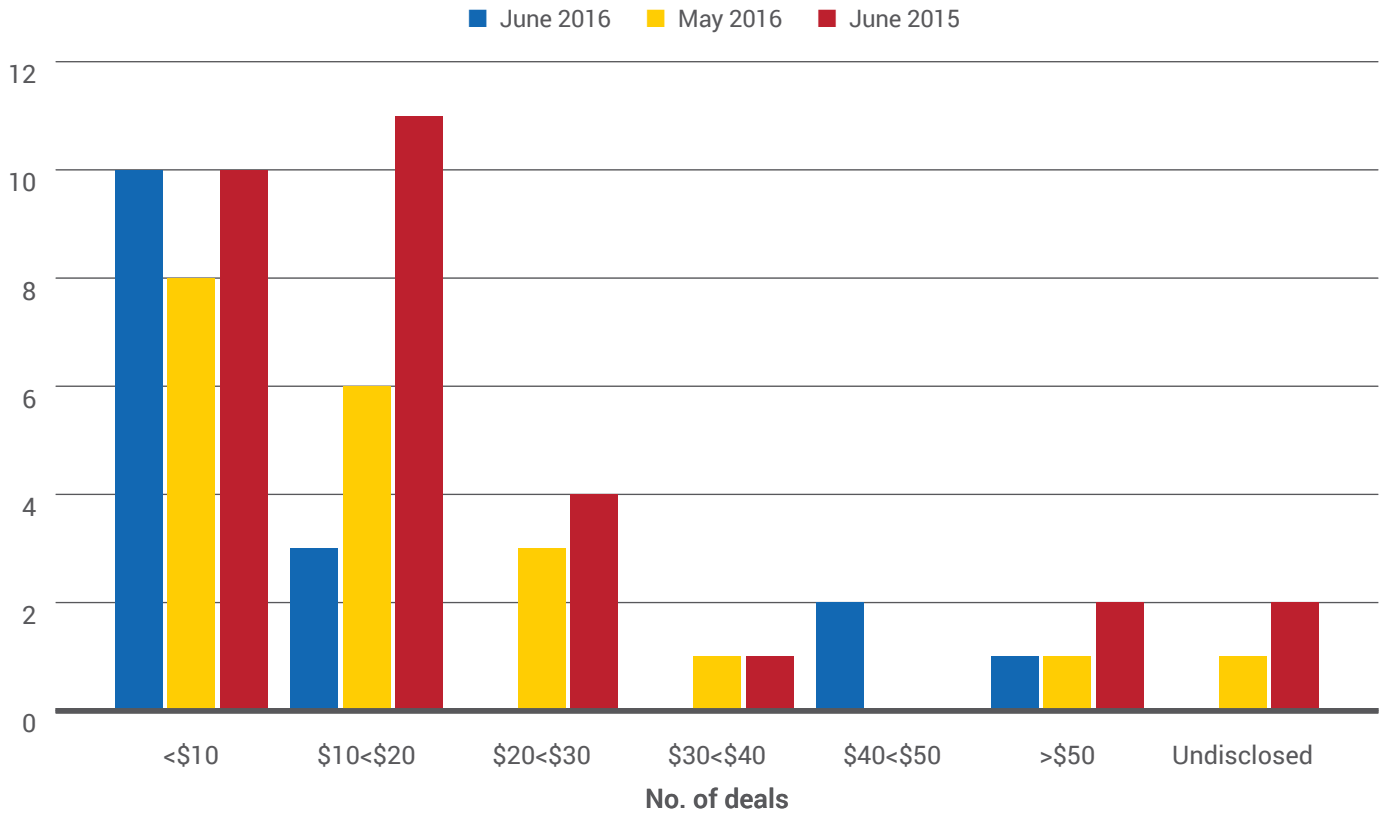
TABLE 1

Top 5 VC Deals By Amount Invested, June 2016

COMPANY	BASED IN	PRODUCT/ THERAPY SECTOR	AMOUNT RAISED	FINANCING ROUND	TOTAL INVESTMENT
EarLens	CA, US	ENT	$51m	First tranche of Series C	Undisclosed
Alcresta Therapeutics	MA, US	Gastroenterology	$49.4m	Series C	Undisclosed
CVRx	MN, US	Neuromodulation/Cardiology	$46.5m	Growth financing	Undisclosed
SI-Bone	CA, US	Orthopedics	$20m	Growth financing	Undisclosed
Reflexion Health	CA, US	Digital health	$18m	Series B	Undisclosed

FIGURE 1

Venture financing deals by amount raised, June 2016 vs May 2016 vs June 2015



future funding as UK companies would be less-attractive to European investors. Additionally, UK companies would unlikely be unable to access EU funding instruments such as those within the Horizon 2020 initiative to support innovation. Just how big a blow Brexit will really be for emerging companies in the longer term still remains to be seen.

But in spite of the poor performances in June and May, the bull-run between January and April means that the total takings for the first half of 2016 is still higher than that seen for the same period since 2013 (*see Figure 2*). That said, if the markets do not recover and investors remain nervous, 2016 will definitely lose the good headstart it had over the previous years and we may even see a decline in total venture investment this year.

ANALYZE

To access Medtech Insight's database of VC deals in 2016, go to http://bit.ly/29DUQZu

FIGURE 2

Total amount raised ($m), Jan-June 2016-2013

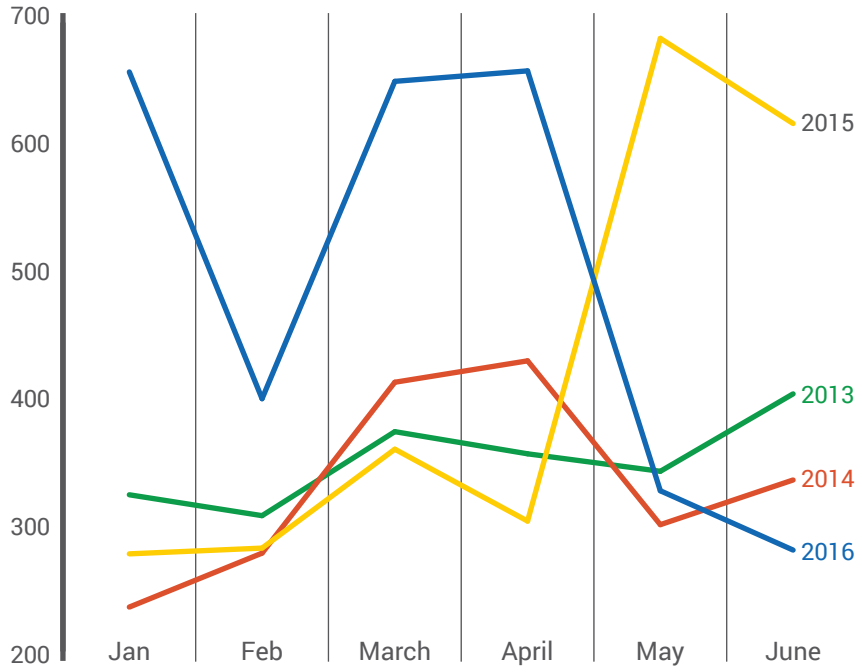
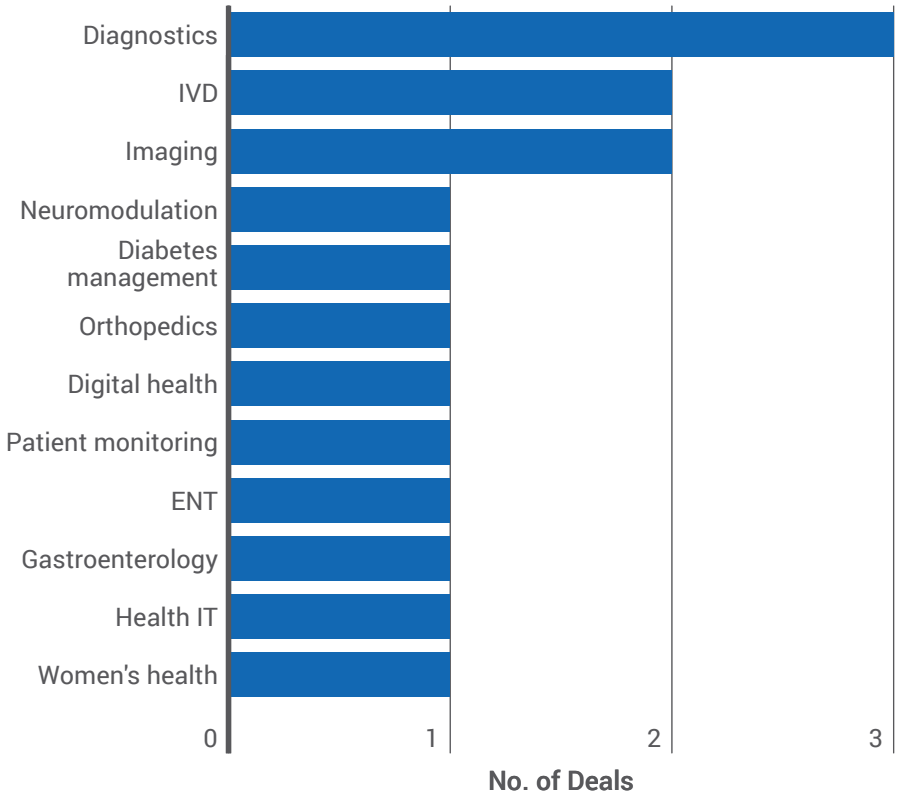


FIGURE 3

Venture financing deals by product/therapy type, June 2016



Institutional investors may have been more reticent last month to put their money into companies, but corporate investors on the other hand do not appear to share the same reservations. Medtronic – which has also been busy buying companies in June, not just investing – joined cochlear implant maker Cochlear and other private equity companies in a $51m series C round to support hearing aid maker Earlens. This was the largest deal of the month, while Chinese pharmaceutical firm Shanghai Fosun participated in the fifth largest deal, which was a $17.4m series B round by Spirometrix; the company has developed the Fenom PRO point-of-care breathalyzer for diagnosing and managing asthma. The device is digitally connected to receive data from the environment and other devices for better management (*see Table 1*).

The deals in June were spread across a diverse range of product and therapy sectors (*see Figure 3*), but diagnostic breathlyzers attracted the most investment interest. Aside from Spirometrix, two fledging companies are also developing similar technologies. Polish firm HealthUp got seed funding to advance development of MySpiroo, said to be the world's smallest personal, handheld, digitally connected medical spirometer for managing COPD and asthma patients, while new spin-out Owlstone Medical is developing a breathalyzer for diagnosing diseases beyond respiratory disorders, including cancer.

Published online 07/07/2016.

Medtronic's Prestige LP Joins LDR's Mob-C In Two-Level Cervical Disc Competition

REED MILLER reed.miller@informa.com

The US FDA has approved **Medtronic PLC's** *Prestige LP* artificial disc for two-level cervical reconstruction, putting it in direct competition with **LDR Holding Corp.'s** *Mobi-C* cervical disc.

According to FDA's online PMA database, the agency approved a PMA supplement for a labeling change for Prestige LP to include two-level reconstruction on July 7. During its fiscal fourth-quarter 2016 earnings call on May 31, Medtronic said it expected FDA to approve the new indication by October 2016, so the approval is slightly ahead of schedule.

FDA originally approved Prestige LP for treatment of single-level cervical disc disease in 2014. (*See "ANALYSIS: Boston bags four approvals in July" - Medtech Insight, 5 Aug, 2014.*) The new labeling indicates Prestige LP for treatment for reconstruction of the disc from c3-c7 following discectomy at one level or two contiguous levels in skeletally mature patients. The procedure is intended to relieve intractable arm pain and/or a neurological deficit or myelopathy due to an abnormality of the disc space and a herniated nucleus pulposus, spondylosis, and/or loss of disc height as compared to adjacent levels.

Unlike spinal fusion, implantation of Prestige LP, which has a ball-and-trough design, provides the patient with a range of spinal motion. The approval is based on results of the PRESTIGE LP Two-Level Study. Seven-year data from the trial, announced May 3 at the American Association of Neurological Surgeons meeting in Chicago, showed that the patients randomized to treatment with Prestige LP had a higher rate of overall procedural and neurological success compared patients randomized to traditional fusion.

The Prestige LP patients also had better patient-reported outcome scores and needed fewer follow-up surgeries than the fusion patients, with similar rates of adverse events. (*See "CLINICAL CORNER: Medtronic's Prestige LP Cervical Disc; Biotronik's Orsiro DES, More" - Medtech Insight, 16 May, 2016.*)

In a July 12 note, Wells Fargo analyst Larry Biegelsen writes, "The entry of market leader, Medtronic, into the two-level cervical-disk replacement market could put some competitive pressure on LDR's Mobi-C.". Mob-C, approved for two-level treatment since 2013,was one of the products **Zimmer Biomet Holdings Inc.** cited as motivation for agreeing to buy LDR for $1bn on June 7. That deal will likely close in the third quarter of 2016. (*Also see "Zimmer Biomet Buys LDR To Boost Spine Revenue Growth" - Medtech Insight, 7 Jun, 2016.*)

"The two-level cervical-disc replacement market has significant growth potential but adoption has been measured, primarily due to a lack of reimbursement coverage from private payers," Biegelsen writes. "Medtronic's clout as the global spine market leader could drive increased reimbursement coverage and spur market expansion, but it is difficult to predict the timing of increased payer coverage."

Published online 07/12/2016

APPROVALS ANALYSIS:

June Brings Uptick In Approvals Led By CE Marks

REED MILLER reed.miller@informa.com

Medtech Insight's Approvals Tracker recorded 63 medical device approvals worldwide, including five PMAs or noteworthy PMA supplements approved by the US FDA and 27 CE Marks or CE IVDs from Europe. There were also 27 510(k)s or other US FDA clearances and four approvals outside the US or Europe. The total beat last month's number by 6, due to the surge CE Mark activity, from 16 in May to 27 in June.

The June total means the first half of 2016 had a total of 334 approvals. If the second half could 54 fewer approvals than the first half and 2016 would still beat 2015's total of 613 (*see Figure 1*).

The full PMAs in June included Aspire Bariatrics Inc.'sAspireAssist stomach-draining device for long-term weight-loss therapy in obese patients with a body-mass index of 35 to 55. Aspire is pitching the stomach-draining device as a less-invasive alternative to bariatric surgery.

Also in June, the US FDA approved Medtronic/Minimed's iPro2Recorder continuous glucose monitoring system with Enlite sensor, approved June 17. According to the FDA's approval letter, iPro2 Recorder is intended to continuously record interstitial glucose levels in persons with diabetes to supplement, but not replace, blood glucose information obtained using a standard home glucose-monitoring device.

ANALYZE

To access Medtech Insight's database of product approvals in 2016, go to http://bit.ly/29QApYR

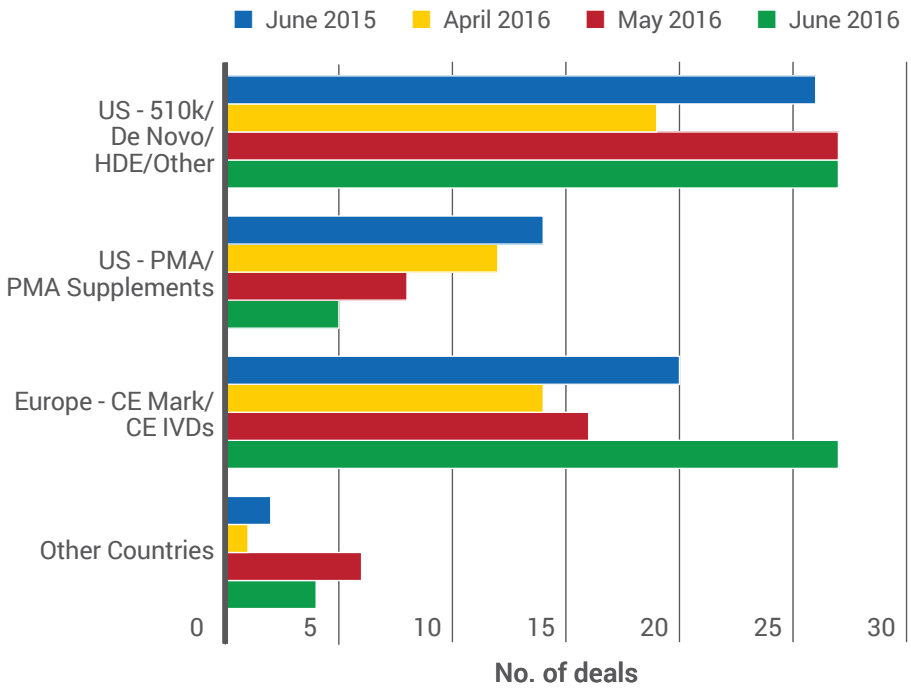
On June 1, the FDA approved Roche Molecular Diagnostic'scobas EGFR Mutation Test v2, a blood plasma test intended as a companion diagnostic for the non-small cell lung cancer (NSCLC) drug, Tarceva (erlotinib), a Roche/Astellas Pharma drug. The test is the first FDA-approved blood-based genetic test for detection of epidermal growth factor receptors genetic mutations that are associated with treatment response to Tarceva, according to Roche.

Roche's cobas EGFR Mutation Test v2 was one of 16 in-vitro diagnostic approvals in June, beating out cardiovascular by one to be the biggest product category of approvals during the month (*see Figure 2*).

On June 20, Roche announced the CE

FIGURE 1

Approvals by type, June 2015 vs April-June 2016



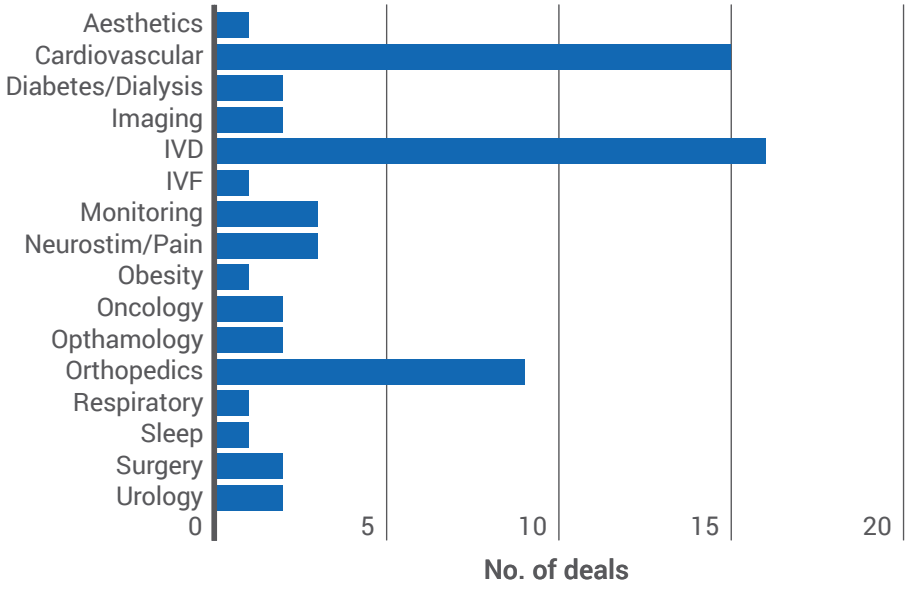
Mark and commercial availability of the LightMix Modular Zika Virus Assay for qualitative detection of the Zika virus in patients with signs and symptoms of infection living in areas where the Zika virus is known to be present. The test can be run on Roche's MagNA Pure 96 system for nucleic acid purification and LightCycler 480 or cobas z 480 instruments for real-time PCR system.

On the same day, the FDA approved Hologic'sProcleix Zika virus blood-screening assay for the Procleix Panther system under an Investigational New Drug (IND) study protocol. The approval allows major US blood centers to use the Procleix Zika virus assay to screen blood donated by people from potential endemic areas of the southern US. Testing may expand to other areas if the virus spreads, the company explains.

Published online 07/10/2016

FIGURE 2

Approvals by product sector



St. Jude's *SyncAV CRT* Pacing Software Launched

REED MILLER reed.miller@informa.com

St. Jude Medical Inc. has launched its *SyncAV CRT* software worldwide following US FDA approval of the resynchronization pacing-optimization platform July 11 and CE mark approval June 23.

SyncAV automatically adjusts pacing in real-time in response to changes in the heart's electrophysiology, according to St. Jude. It also allows the treating electrophysiologist to adjust and improve cardiac resynchronization therapy therapy, even in patients who have already responded well to traditional CRT.

SyncAV CRT is designed to optimize cardiac resynchronization therapy in concert with St. Jude's *MultiPoint* pacing technology, but the SyncAV software algorithm can also function independently. MultiPoint allows implanting electrophysiologists to activate more ventricular tissue immediately after implanting the CRT device, which improves the chances the patient will respond to the therapy. St. Jude launched the MultiPoint pacing technology on the *Quadra Assura M* cardiac defibrillator (CRT-D), the *Quadra Allure MP* CRT-pacemaker (CRT-P), and two new quadripolar *Quartet LV* leads in April. (*See "New Product Briefs" - Medtech Insight, 18 Feb, 2016.*)

The benefits of MultiPoint pacing are supported by more than 65 abstracts and publications, according to St. Jude, including the results of the MPP IDE trial, presented on May 5 at the Cardiostim-EHRA Europace 2016 meeting in Nice, France. The trial enrolled 506 patients with a standard CRT-D indication who were implanted with a St. Jude *Quadra* CRT-D capable of delivering either quadripolar biventricular pacing, activated at implant, or MultiPoint-pacing. The trial showed multi-point pacing to be safe and effective; it met the pre-specified hypothesis that the response to MultiPoint pacing is non-inferior to that of quadripolar biventricular pacing. The response to CRT was greatest (87%) and all previous non-responders were converted to responders when the MultiPoint pacing was programmed with cathode spacing of at least 30 mm and a 5-millisecond left-ventricular delay.

Results presented at the same meeting from a 507-patient registry (IRON-MPP) on MultiPoint left-ventricular pacing in CRT showed that MultiPoint pacing programming can improve heart failure patients' clinical status and ejection fraction. But, according to lead investigator Giovanni Forleo of the Tor Vergata University Hospital in Rome, there are many different programming practices among centers, and establishing the optimal programming to maximize the benefit of MultiPoint pacing "remains a challenging issue."

St Jude is also sponsoring the MORE CRT MPP clinical study, which is enrolling about 1,900 heart-failure patients who have not responded to six months of CRT therapy. The patients will be randomized to continued treatment with MultiPoint pacing turned on or off for an additional six months. The primary endpoint will be the percentage of non-responder patients converted to responders (left ventricular end systolic volume reduction of at least 15%) with MultiPoint pacing. The company expects to collect the primary outcome data by April 2017.

Published online 07/11/2016

Novel Essential-Tremor Treatment Gets US Green Light

ELIZABETH ORR elizabeth.orr@informa.com

Focused ultrasound has moved into the US neurological market with the FDA approval of InSightec Ltd.'s *ExAblate Neuro* for treatment-refractory essential tremor.

The *ExAblate Neuro*, which was developed by Israeli device manufacturer InSightec Ltd., uses MRI to deliver focused ultrasound to destroy tissue in a tremor-linked area of the brain called the thalamus.

"As with other treatments for essential tremor, this new device is not a cure but could help patients enjoy a better quality of life," said Carlos Peña, director of the division of neurological and physical medicine devices in the FDA's device center.

Insightec gained approval for its novel platform to treat uterine fibroids in 2004, but this is the first neurological application of the technology. Early research on use in the brain was funded by the Focused Ultrasound Foundation, which was created expressly to accelerate development of this type of technology for more indications. (*See "InSightec's Focused Ultrasound Shows Early, Positive Data For Disabling Tremor" - Medtech Insight, 6 May, 2013.*)

Several million Americans, most over age 40, experience tremors. The condition can be treated by beta blockers, or anti-convulsants. Currently, patients who do not respond to medication are typically treated by surgery or deep brain stimulation to remove the thalamus, FDA says.

Patients are first identified as candidates for ExAblate via MR and computerized tomography. Physicians then administer and incrementally increase transcranial-focused ultrasound energy until a reduction of tremor is achieved. The patient remains awake during the treatment, which requires no incisions or implants.

In a double-blind clinical trial of 76 patients with essential tremor who did not respond to medication, the treatment group experienced almost a 50% reduction in tremors and improvement in motor function after three months, while the control group saw no improvement. The treatment group maintained a 40% improvement at 12 months after the procedure.

InSightec submitted the PMA for ExAblate in October 2015.

The approval represents "a tipping point for non-invasive medical treatment," said InSightec CEO Maurice Ferré.

ExAblate was approved in May in Canada for essential tremor, and is also CE marked for essential tremor, tremor-dominant Parkinson's disease and neuropathic pain.

Trial Supports NeuroMetrix *Quell* For Lower-Back Pain

REED MILLER reed.miller@informa.com

Results of a clinical trial published in the *Journal of Pain Research* suggest NeuroMetrix Inc's *Quell* non-prescription wearable pain relief device is safe and effective in the treatment of low-back and lower-extremity pain.

"These results further motivate the use of [fixed-site transcutaneous electrical nerve stimulation] in development of wearable analgesic devices," the trial's primary investigator, NeuroMetrix CEO Shai Gozani, concludes. "The study results also support the hypothesis that the effects of [transcutaneous electrical nerve stimulation] can be widespread, most likely arising from activation of descending pain inhibition."

The trial enrolled 130 patients with chronic low-back and/or lower- extremity pain and gave them a Quell device to self-administer fixed-site high-frequency transcutaneous electrical nerve stimulation for 60 days. The primary outcome measure was the patients' "global impression of change" in pain as scored on the Brief Pain Inventory questionnaire. According to Gozani, this was the first trial to use patients' global impression of change to assess the benefit of transcutaneous electrical nerve stimulation in a diverse chronic pain cohort.

Of the 88 patients who completed the 60-day follow-up questionnaire, 80.7% of participants reported that their chronic pain had improved enough to count as therapy-responders. There were no apparent differences in baseline characteristics between the non-responders and responders.

Responders showed a trend toward reduced pain-interference with walking their ability and sleep, "These findings are particularly relevant to the design of future studies," Gozani writes in the *Journal of Pain Research*. "Most [transcutaneous electrical nerve stimulation] studies have used changes in pain intensity as the primary outcome measure. However, the current and other studies suggest that pain intensity may not efficiently represent the impact of [transcutaneous electrical nerve stimulation]. In fact, the focus on pain-intensity may have contributed to low-fidelity studies that have contributed to confusion regarding the clinical effectiveness of [transcutaneous electrical nerve stimulation]."

Also, 80.3% of responders reported using fewer pain drugs compared to 11.8% of the non-responders. "The design of this study as a series of online surveys made it challenging to monitor pain-medication use. We were therefore unable to determine if specific classes of analgesics were most likely to be affected or to quantify changes in medication use," Gozani explains. "Nevertheless, these results mirror [transcutaneous electrical nerve stimulation] associated reductions in post-surgical analgesic use."

The US FDA cleared Quell in 2014, and NeuroMetrix launched it in the US market in 2015. (*See "NeuroMetrix Brings TENS Pain Therapy To Over-The-Counter Market" - Medtech Insight, 20 Aug, 2015.*)

Published online 07/11/2016

BioDirection Inc.

BioDirection Inc. is poised to launch what it says is the first objective point-of-care test for diagnosing concussion and other traumatic brain injuries.

Traumatic brain injury took front and center stage in the recent movie Concussion, starring Will Smith in the role of forensic pathologist Bennet Omalu, whose research on brain damage among professional football players puts him at odds with the National Football League. To detect such injuries, patients either undergo a series of subjective cognitive tests that in many cases are inaccurate and inconsistent, leading often to misdiagnosis, or patients are sent to the hospital for a computed tomography (CT) scan, which is costly, time-consuming and exposes them to unnecessary radiation.

Omalu serves on the medical advisory board of BioDirection Inc., which is slated to launch what it says is the first objective point-of-care test for diagnosing concussion and other traumatic brain injury, according to president and CEO Eric Goorno. Based on proprietary nanotechnology, the company's Tbit device detects molecular levels of two crucial brain biomarkers that are released into the bloodstream immediately after a brain injury, from just a single drop of blood in less than two minutes.

The initial setting for Tbit will be a hospital emergency department to rapidly assess patients with traumatic brain injury, but the device is expected to move beyond the ER to ambulatory care centers, including walk-in pharma clinics and physician offices, and eventually to the field at the site of injury. Ultimately, the start-up thinks Tbit is applicable for all of the 10 million-plus concussions sustained a year in the US alone, representing an annual market opportunity of between $750,000 and $1 billion.

BioDirection was founded in 2010 by Brian McGlynn, who serves full time as the company's executive vice president and chief technology officer. Over the decades, McGlynn developed a passion for diagnosing and treating traumatic brain injury, due to casualties suffered by family and friends in the military. "Brian did the research and put the pieces of the puzzle together," Goorno says. "He focused on blood-based brain biomarkers as an ideal diagnostic tool. However, he also quickly recognized that there was a void in technology to detect these markers. Without a device, the biomarkers cannot be leveraged into clinical use, which is necessary to improve patient care."

BIODIRECTION INC.
10 Comstock Court
Ridgefield, CT 06877

Phone: +1 (508) 308-8592

Web Site: www.biodirection.com

Contact: Eric Goorno, President & CEO

Industry Segment: Neurodiagnostics

Business: Portable system measures brain biomarkers released following brain injury

Founded: September 2010

Founder: Brian McGlynn, EVP & CTO

Employees: 7

Financing To Date: $10m

Investors: Provident Healthcare Capital; Undisclosed medtech investors; High-net-worth individuals

Board Of Directors: James Wylie; Robert Mercier; Stephen Brackett; Brian McGlynn

Medical Advisory Board: Scott Parazinski, MD (University of Texas Medical Branch, Galveston); Bennet Omalu, MD (University of California, Davis); G. Alexander Hishaw, MD (University of Arizona, Tucson); John Michels, MD (University of California, Irvine)

Sports Advisory Board: M.L. Carr (retired Boston Celtics basketball player); Kristen Kuliga (K Sports & Entertainment LLC); Bob Sweeney (retired Boston Bruins hockey player); Brian Westbrook (retired Philadelphia Eagles and San Francisco 49ers football player)

As a result, McGlynn married the biomarker diagnostic capabilities with the enabling nanowire technology originating from the research lab of Charles Lieber, PhD, at Harvard University. A pioneer in the field of nanowire science, Lieber had developed the use of nanowires as biosensors to measure molecular levels of proteins. The core nanotechnology patents were licensed to BioDirection from Nanosys Inc., a joint venture between Harvard and Lieber. In total, the licensing package includes 14 issued and one pending patent.

Prior to joining BioDirection, Goorno was employed at Boston Scientific Corp. from 1996 to 2008, leaving as president of the urology and women's health divisions. Afterward, in 2009, he co-founded Pulse Veterinary Technologies LLC (orthopedic shockwave therapy for pets and horses), where he remained as CEO until 2014.

HOW IT WORKS

Tbit consists of two user elements: a battery-operated portable (either handheld or tabletop) analyzer with the footprint of an iPad; and a single-use, disposable cartridge containing a chip (nanosensor) that is placed in the analyzer. "Every biomarker that we measure has an associated nanochip, containing a nanowire which is functionalized with the antibody associated with the particular protein biomarker to be measured," Goorno states. Each nanochip is then placed onto a tiny circuit board. Next, the circuit board is encased in a plastic housing, which forms a cartridge about the size of a memory stick.

A nurse or laboratory technician will likely administer the test in the ER. After blood is collected from either a finger pinprick or through a venous draw, the blood is placed into the well (hole) of the cartridge itself. The cartridge is then pushed into the analyzer, which activates the system. Similar to a battery that measures resistance, each chip contains both a positive and negative pole. "The resistance measurement essentially correlates with the concentration of the protein biomarker that is in the bloodstream," Goorno explains.

At first, the analyzer will be limited to detecting the two most widely recognized proteins that correlate with TBI: glial fibrillary acidic protein (GFAP) and S100beta expression. "When you have a traumatic brain injury, the proteins themselves jump the blood-brain barrier and become present in the peripheral bloodstream," Goorno says.

The analyzer has a screen that will display numerically the quantitative level of the proteins. Above a certain threshold, brain injury is indicated. "This will also let the clinician know if a CT scan is recommended," Goorno says. "Today, about 80% of the time patients with suspected brain injury are given a CT scan, yet only 8% of the time is the CT positive, and only 1% of the time is surgical intervention required. These unnecessary scans cost both hospitals and the overall health care system a significant amount of money." Moreover, there are increased patient safety concerns with radiation emitted from CTs, particularly with head scans.

The company is targeting at least a 30% reduction in CT scans, based on existing clinical findings on the two selected proteins. "With our device, patients can be in and out of the ER "in a matter of minutes as opposed to hours," Goorno notes.

Competitor BrainScope Co. Inc.'s product (Ahead 200) records and analyzes a patient's electroencephalograph (EEG), "but with some real limitations in both the patient inclusion criteria (tiredness and alcohol consumption, for instance) and the physical environment for use," says Robert Reid, vice president of global marketing for BioDirection. "Measuring brain waves is not nearly as accurate as our device. We are biologically based, which at the end of the day is truly where you need to be."

THE COMPETITION

A second emerging rival, Quanterix Corp. (Simoa), uses a large, central-lab machine to detect biomarkers in a research-only setting. Not only can results take much longer with the Quanterix system, but also the capital expenditure is well over $150,000, and the cost per test is prohibitive compared with the cost for the Tbit system, which is a fraction of the price of Simoa, according to Reid.

CE mark is anticipated early next year, followed by 510(k) approval shortly thereafter. Tbit should begin selling in Europe in 2017 through distributors, while the US launch will likely start with a direct sales force. "Even without direct reimbursement initially, we will be saving hospitals money and improving patient care from the outset," Reid says.

The $10m raised to date by BioDirection constitutes three rounds of financing: a Series A common stock offering of $3.95m that closed May 2013 [See Deal] and a Series A convertible preferred stock of $1.6m that concluded December 2014, both of which were capitalized by numerous high-net-worth individuals; and a Series B convertible preferred stock of $4.3m that closed in January, with Provident Healthcare Capital as the lead institutional investor, plus several wealthy individuals. A Series C in the amount of $15m is expected to close this summer, funded by a combination of existing and new money sources.

Furthermore, BioDirection has been in early conversations with several strategic partners, both as investors and/or distributors of the product, that are either in the neurology/ER or the in vitro diagnostics (seeking point-of-care) space. The most likely exit strategy for the company is acquisition by a strategic partner or investor, perhaps as early as product launch.

BioDirection would also like to expand beyond diagnosing acute traumatic brain injury by providing prognosis and stratification of the injury, as well as indicating when the patient is ready to return to activity. Beyond traumatic brain injury, other neurological opportunities include stroke and Alzheimer's disease. "All of these future applications, however, depend on the evolving biomarker research," Goorno stresses. "Fortunately, the great news for BioDirection, as well as our customers and the general public, is that such research is exploding, as biomarkers promise to bring more accuracy and personalization to disease diagnosis."

Over 100 event types

Over 100 catalyst types

Over 5,000 products

Meddevicetracker
Pharma intelligence | informa

Double the Power

Meddevicetracker with Medtech Insight reports is a new interactive real-time source of in-depth medical technology market intelligence

Meddevicetracker brings you closer to the medtech market, helping you to:

- Identify upcoming device regulatory events/filings
- Search for medtech clinical trial starts and data
- Find historical and forecasted procedure volumes data
- Monitor drug delivery technologies and identify partnership opportunities
- Quantify the market size for devices or diseases
- Discover forecasted market share of devices by type
- Understand the device competitive landscape and identify unmet clinical needs

Request your free demo today:
please visit - **www.meddevicetracker.com**