Evaluate Vantage

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Downturn in US premarket approvals for devices continues

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If the worryingly low numbers of mergers and financing events in medtech could contribute to a lack of devices reaching patients in future, there is also a block on new products in the present: the US FDA. Just 23 innovative devices were granted FDA approvals last year, down 44% from the 41 in 2012 (see tables).

The stringent FDA approval process means that devices tend to gain European approval around three to five years before they reach the US market. But with the efficacy of Medtronic's Symplicity renal denervation system, sold in Europe but not yet available in the US, recently called into question, perhaps the agency's scepticism is not entirely unjustified.

EP Vantage's analysis includes first-time premarket approvals (PMAs) plus humanitarian device exemptions (HDEs).

First-time PMAs and HDEs by therapy area, 2012 and 2013

EvaluateMedTech device classification - L1	Number of first premarket approvals (PMAs) FY 2012	Number of first premarket approvals (PMAs) FY 2013
Anesthesia & respiratory	0	1
Blood	0	1
Cardiology	14	7
Diabetic care	1	1
Diagnostic imaging	3	1
Drug delivery	1	0
Gastroenterology	1	0
General & plastic surgery	2	3
In vitro diagnostics (IVD)	13	4
Neurology	0	1
Ophthalmics	2	1
Orthopaedics	3	2
Radiology	1	0
Wound management	0	1
Total	**41**	**23**

Unlike the CE marking system under which medical devices are approved in Europe, the US system is stratified. Devices that can measure themselves against a predicate are granted 510(k) market clearance, whereas the most innovative or risky products must seek a PMA, a longer and more expensive procedure.

PMAs call for stricter trials than either 510(k)s or CE marking. This was Symplicity's undoing; it was the sham-control group – required in the pivotal US trial but avoided in all previous trials of Symplicity and indeed all other trials of renal denervation devices – that showed the product up (*Failure of Medtronic's Symplicity trial exacerbates concerns over renal denervation, January 9, 2014*).

First-time PMAs are hard to obtain, then, and appear to be getting harder. To its credit, the FDA is aware of this and is weighing options to combat it. These include the new de novo pathway, a swifter review process for low-risk devices intended for unmet needs, such as Luminex's xTAG Gastrointestinal Pathogen Panel, a molecular diagnostic for gastrointestinal bugs (*Luminex's five-hour gastroenteritis test impresses FDA, January 17, 2013*).

Lucky 13

At least the second half of 2013 is heading in the right direction, with 12 PMAs compared with just nine in the first six months (*US approvals of innovative devices halve, July 29, 2013*).

Of the PMAs awarded in the second half, five were for use in cardiology, making it, as so often, the most-represented category. These include Abbott's MitraClip device for repairing the mitral heart valve, approval of which once seemed unlikely. The FDA's greenlighting of it despite a lacklustre panel vote shows that the agency can take patient demand into account (*MitraClip approved in US but reimbursement could limit sales, October 28, 2013*).

First-time PMAs and HDEs granted by the FDA in the second half of 2013						
Device Name	**Company**	**EvaluateMedTech device classification - L1**	**EvaluateMedTech device classification - L3**	**Type of approval**	**Number**	**Decision date**
Therascreen EGFR RGQ PCR kit	Qiagen	In vitro diagnostics (IVD)	Oncology molecular diagnostics	PMA	P120022	July 12, 2013
Mobi-C cervical disc prosthesis (one-level indication)	LDR	Orthopaedics	Other Spinal Devices	PMA	P110002	August 7, 2013
Nit-Occlud PDA	Pfm Medical	Cardiology	Interventional catheters & guidewires	PMA	P120009	August 16 2013
Parascript AccuDetect 6.1.0	Parascript	Diagnostic imaging	Image analyser systems	PMA	P120004	August 22 2013
Mobi-C cervical disc prosthesis (two-level indication)	LDR	Orthopaedics	Other spinal devices	PMA	P110009	August 23 2013
Complete SE vascular stent system	Medtronic	Cardiology	Peripheral vascular devices	PMA	P110040	Septembe 19, 2013
MiniMed 530G system	Medtronic	Diabetic care	Insulin pumps	PMA	P120010	Septembe 26, 2013
Diamondback 360 coronary orbital atherectomy system	Cardiovascular Systems	Cardiology	Interventional catheters & guidewires	PMA	P130005	October 21, 2013
Juvederm Voluma XC	Allergan	General & plastic surgery	Dermal fillers	PMA	P110033	October 22, 2013
MitraClip delivery system	Abbott Laboratories	Cardiology	Heart valve accessories	PMA	P100009	October 24, 2013
Neuropace RNS system	NeuroPace	Neurology	Neuromodulation devices	PMA	P100026	Novembe 14, 2013
Gore Viabahn endoprosthesis and endoprosthesis with heparin bioactive surface	W. L. Gore & Associates	Cardiology	Graft prosthesis	PMA	P130006	Decembe 5, 2013
Liposorber LA-15 system	Kaneka	Blood	LDL therapeutic devices	HDE	H120005	October 10, 2013

Unexpectedly, only one IVD was approved in the second half, though predictably it is a molecular diagnostic for use in oncology. Qiagen’s Therascreen EGFR RGQ PCR kit is a companion diagnostic used to select non-small cell lung cancer patients eligible for treatment with Boehringer Ingelheim’s Gilotrif. The drug's US labelling requires the use of an FDA-approved diagnostic to select EGFR mutation-positive patients, and Therascreen EGFR is the only such test.

Two companies scored more than one PMA in the second half: Medtronic, for its Complete SE stent and MiniMed 530G insulin pump, and LDR, which, uniquely, saw two PMAs awarded for a single device.

The company's Mobi-C spinal implant, a prosthetic cervical disc, was approved on August 7 for one-level use – that is, to replace the cartilage between adjacent vertebrae – and two weeks later, it received a further PMA for two-level use. Two Mobi-C implants can now be used either side of a single vertebra, the first and only such approval to be granted in the US.

Last year was a big one for LDR, as in addition to these approvals it listed on Nasdaq (*CardioDx yanks float as medtech market fails to pick up, November 18, 2013*).

Humanitarian

As well as the de novo pathway, the FDA has another way to expedite the approvals of innovative devices: the humanitarian device exemption (HDE). This can be awarded to a device that is intended to treat or diagnose a condition that affects fewer than 4,000 individuals in the US each year. A lower burden of proof of efficacy is required compared with a PMA, though the company must show that the probable benefit to health outweighs any risk posed by the device and that no other therapy exists.

The only device to have gained an HDE in the second half of 2013 was the Liposorber LA-15 system developed by Kaneka, approved in October for the treatment of paediatric patients with primary focal segmental glomerulosclerosis. The device is a filtration and processing system that removes lipoproteins from the patient's blood.

There is of course a balance to be struck between unnecessary severity and simply waving devices through without proper oversight, and the FDA's caution has perhaps served it well in the case of Symplicity. But 2013 has been a disappointing year all round for the medtech sector. It is to be hoped that the picture grows brighter next year.

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