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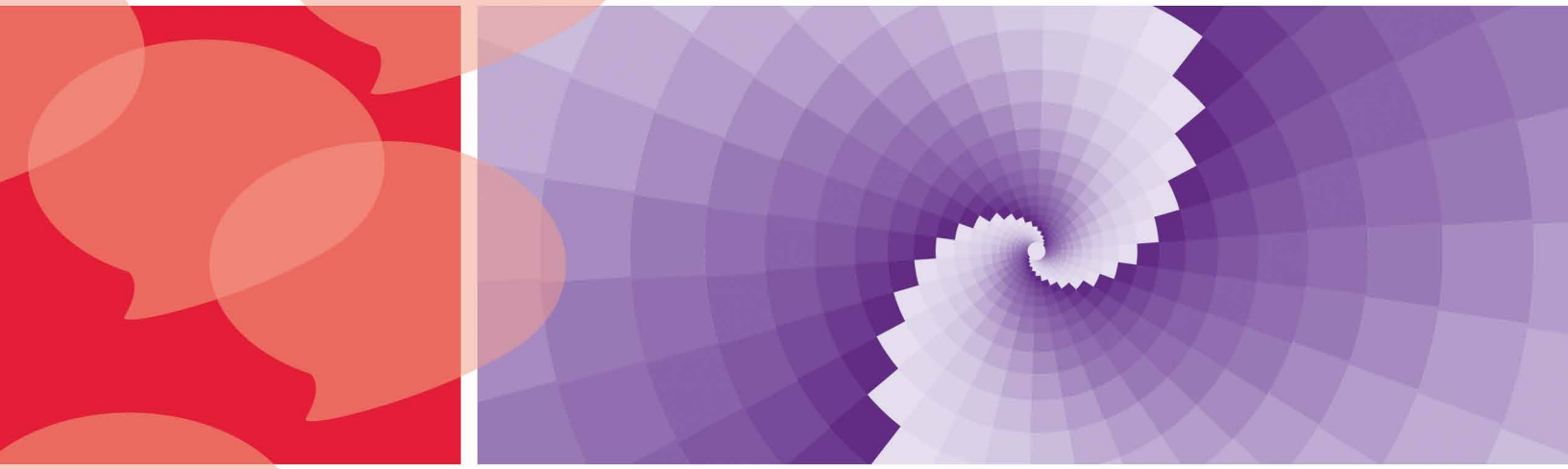
MEDTECH 2013 IN REVIEW



EvaluateMedTech™

MEDTECH IN 2013

Thirteen is an unlucky number, and 2013 has been an unlucky year in medtech. Caught between the Scylla and Charybdis of a downturn in M&A activity and a reluctance on the part of venture capitalists to part with cash, the medical device industry has had a tough year.

Though the wider economic conditions have been improving for some time, hospitals, insurers and other payers have learned the lessons of austerity well and see no reason to reduce the pressure they found it necessary to exert on costs during the financial crisis. Larger medtech firms are finding their customer base unwilling if not unable to pay, and insisting on evidence of cost-effectiveness of their products as well as of therapeutic effect.

With less money coming in, the large firms' attention turns to their own profitability, prompting them to conserve cash and shy away from the riskier acquisitions. The past year was not, in fact, the worst in a decade in terms of device maker acquisitions, but the total value of the pure medtech buys that closed in 2013 was less than half the total for 2012.

And with most exits for early investors coming in the shape of buyouts, venture funders have reacted to the lack of M&A activity by keeping their hands in their pockets. A tiny year-on-year

THE PAST YEAR WAS NOT, IN FACT, THE WORST IN A DECADE IN TERMS OF DEVICE MAKER ACQUISITIONS, BUT THE TOTAL VALUE OF THE PURE MEDTECH BUYS THAT CLOSED IN 2013 WAS LESS THAN HALF THE TOTAL FOR 2012.

increase in VC cash was seen, but early-stage medtech companies in particular found this source of cash difficult to tap. VC rounds are getting later as risk-averse investors seek to place their cash in companies that can provide a return in short order.

The number of premarket approvals awarded by the FDA fell 44% on 2012. Increasingly, acquirers and investors are waiting for a company to gain US approval for their products before stepping in, meaning that smaller companies can find themselves facing a catch-22 situation: they have no means of funding the development of their products unless their products are already fully developed.

It is to be hoped that the worst is over. Once larger companies come through the cost saving programmes they have put in place to deal with the slowdown their focus will turn towards growth, and they will surely seek out new technologies. The question is how long this will take; it cannot come soon enough.

ONCE LARGER COMPANIES COME THROUGH THE COST SAVING PROGRAMMES THEY HAVE PUT IN PLACE TO DEAL WITH THE SLOWDOWN THEIR FOCUS WILL TURN TOWARDS GROWTH, AND THEY WILL SURELY SEEK OUT NEW TECHNOLOGIES.

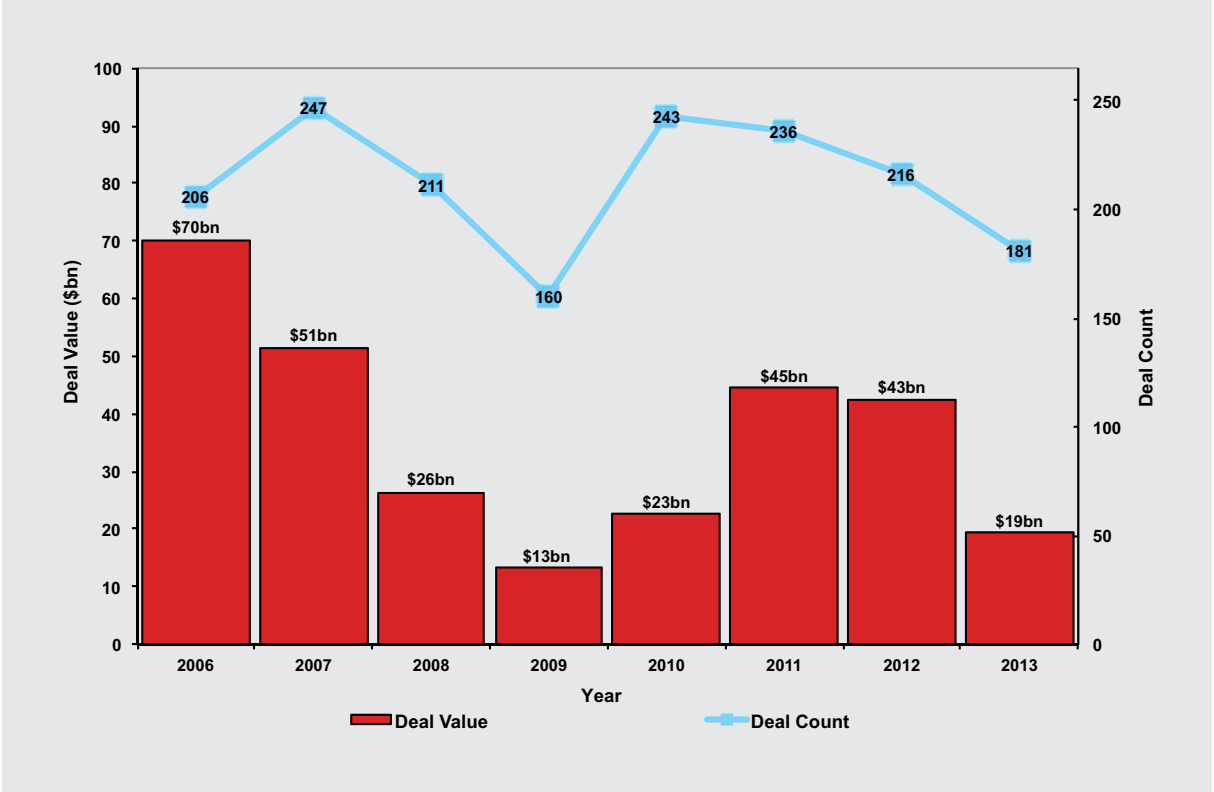
Unless stated, all data is sourced to EvaluateMedTech and was accessed in January 2014.

M&A PICKS UP BUT STILL DISAPPOINTS

2013 defied the most doom-laden predictions of being the worst year in a decade in terms of device maker acquisitions – but only just. With the pure medtech buys closed in 2013 worth less than half the 2012 total, the sector made a pretty dismal showing, despite two deals worth more than $1bn closing in the second half.

If the deal count is down – 16% on 2012 – the total value of medtech acquisitions has fallen even further. Just $19.3bn was spent in total last year, less than half 2012's total. It should be noted that this analysis excludes acquisition targets with both pharma and medtech operations; only those companies listed in EvaluateMedTech as pure medtech have been included.

Medtech M&A Activity



One factor that could explain the dearth of mergers is the lure of a public listing. Medtech shares have performed well over the past year – though not to the same extent as biotech shares – and device makers, most recently Lombard Medical Technologies, are starting to notice the potential benefits of a presence on Nasdaq.

The biggest spender of 2013 is Baxter International, whose purchase of Gambro launched it onto the hospital dialysis market and was by far the largest it has ever made. The company may have cause to regret entering this sector, though – cuts in US reimbursement for dialysis procedures could force the closure of some of Baxter's clinics.

Baxter is one of only two large-cap firms in the top 10, the other being Abbott Laboratories, which bought the laser cataract surgery specialist OptiMedica for nearly a tenth of the price of the sector's biggest deal. The rest are either private or mid-cap firms.

Stryker appears twice in the table with buys in the surgical and trauma areas worth $2.4bn in total. The larger deal, the acquisition of the robotics firm Mako Surgical, was particularly generous, with the buyer offering a massive 86% share price premium.

The surgical robotics sector still has a lot to prove, with some research suggesting that the technologies cannot offer an improvement over the performance of human surgeons; Stryker obviously feels that the techniques will be valuable in the future.

Its earlier purchase of Hong Kong's Trauson looks a safer bet, with the orthopaedics sector growing nicely. Furthermore, a base in an emerging market is unlikely to be a bad idea, particularly as Stryker has opted to buy a Chinese company that already knows the market; the recent woes of US and European healthcare companies as they try to make their way in China have been well publicised.

Top 10 M&A Deals in 2013

Rank	Acquiring Company	Target Company or Business Unit	Deal Value ($m)
1	Baxter International	Gambro	3,900
2	Stryker	MAKO Surgical	1,650
3	Bayer	Conceptus	1,100
4	Stryker	Trauson	764
5	Bausch + Lomb	Technolas Perfect Vision	645
6	CareFusion	Vital Signs – GE Healthcare division	500
7	Kinetic Concepts	Systagenix	485
8	Illumina	Verinata Health	450
9	Abbott Laboratories	OptiMedica	400
10	Argon Medical Devices	Angiotech Pharmaceuticals' Interventional Products division	363

The decline in M&A activity is particularly worrying for an industry built on takeovers. Even the largest medtech firms buy in technologies, and, rather than favouring the licensing deals common in pharma and biotech, the usual method is to purchase the company outright.

Ingeborg Øie, an analyst at Jefferies covering the European medtech sector, agrees that 2013 was not a good year for M&A. "The one thing which is challenging for the large companies in terms of making these acquisitions is that the valuations that the smaller companies are expecting are quite high, because of how well the share prices have done."

She says that the situation will improve in the coming year if the larger companies' belt-tightening pays off. "A number of successful cost-containment programmes have been initiated, and companies are becoming leaner, reducing their expenses. In general, they have better at containing costs than we expected.

"Those companies that have made cost savings will have more cash – in general the sector is cash-rich – and then focus will be more towards growth. In that case it's natural to look outside to see what new technologies are there," Ms Øie says.

Naturally the larger companies develop devices in-house, but this cannot compensate for the shortfall in bought-in innovations. An increase in the number of purchases in 2014 will be crucial for the future of the medtech sector.

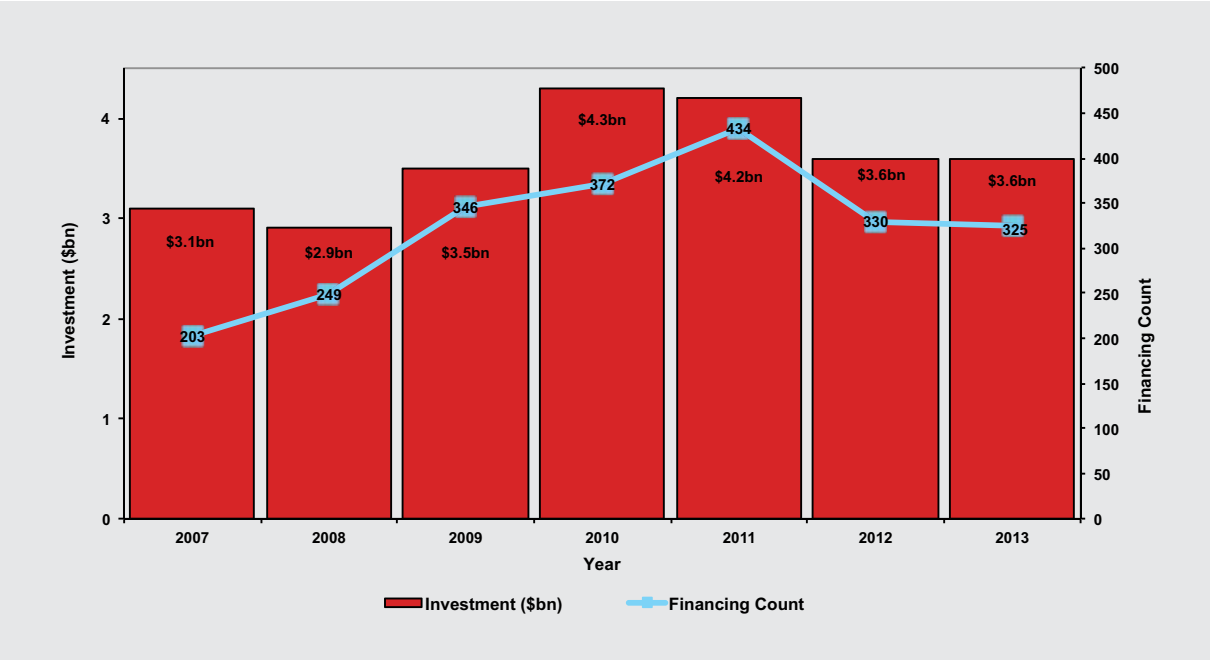
FEWEST VENTURE FINANCINGS FOR FIVE YEARS

The medtech venture capital landscape remains flat. Device makers managed to raise just over $3.6bn in total VC funding last year, only $42m more than the total the previous year. If this is a recovery it is a pretty pathetic one.

What funding is available is getting later and later. Coupled with the tough environment for M&A the medtech sector is also seeing, this means that early-stage businesses are being squeezed from both sides, potentially endangering the development of future technologies.

The total raised in 2013 might be slightly – very slightly – up on the previous year, but the number of deals has dropped. Just 325 funding rounds were completed last year, making 2013 the worst year since 2008 in terms of financing count.

Annual VC Investments



The reasons for the dearth of funding are well-rehearsed: increasingly stringent regulation lengthening the time to market, coupled with mounting pressure on pricing from payers, makes these firms higher risk propositions. Those investors who switched to medtech from biotech in pursuit of a faster return have found that the sector is not as speedy as they had hoped, and are returning to biotech.

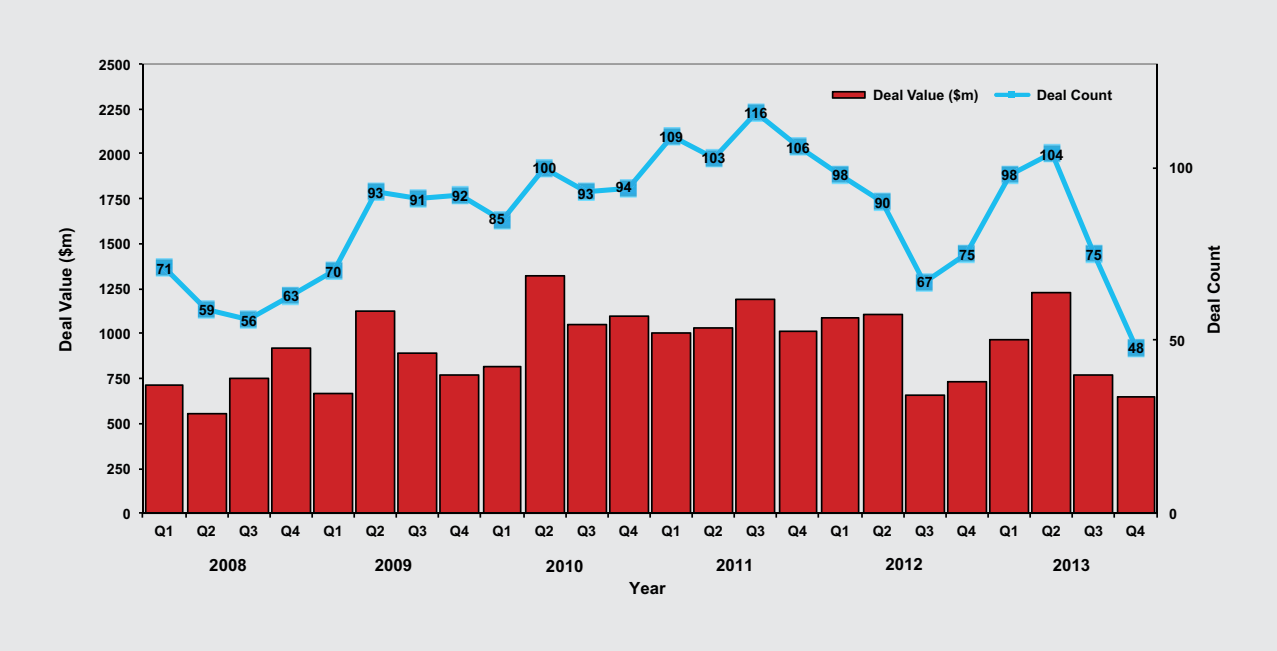
"The returns in medtech are not good on an absolute basis, and are even less good in a comparative basis to biotech. The average time to a medtech exit is eight or nine years, and biotech is probably around six," Tim Haines, a partner at VC fund Abingworth, says.

Most medtech exits are, as they have always been, company acquisitions, and these are happening ever later if they happen at all. Often a company must have not just CE mark and US approval for their product but reimbursement as well before purchasers even consider them.

"Things have got tougher for medtech companies in that, at one time, a medtech company could turn up to a VC and gain funding if the device was easier to use or had a marginal difference over a predicate device," Allan Marchington of Apposite Capital says. "Now, VCs are much more savvy about what is required to get reimbursement, what the market looks like and true differentiation. It has got harder and harder to get funding."

This is exemplified by some of the top rounds so far this year. ConforMIS's knee replacement system, iTotal, is already approved in both the US and Europe, but no buyer has yet materialised. Similarly, JenaValve Technology closed a $62.5m round in July; the company's heart valve technology is CE marked but not yet approved in the US. JenaValve may have to wait some time before it is bought.

Quarterly VC Investments



And the year has ended on a low. The fourth quarter saw just $650m raised through 48 deals, making the third quarter, previously thought of as poor with 75 deals worth a total of $773m, look good by comparison.

One of the fourth-quarter rounds did make it into the year's top five, but it was not a typical one. Oxford Nanopore Technologies raised $64m to fund development of its molecular analysis systems, but the money came not from a classical VC round but through a private placement of ordinary shares.

New and existing investors participated, but the only new shareholder named by Oxford Nanopore was Odey Asset Management – a London-based hedge fund. Still, Oxford Nanopore's funding was by far the largest of the fourth quarter, perhaps thanks to its unorthodox nature.

Biggest Rounds of 2013

Company	Financing Round	Investment ($m)
ConforMIS	Series E	78.7
TearScience	Series Undisclosed	70.0
Oxford Nanopore Technologies	Series F	64.0
Proteus Digital Health	Series F	62.5
JenaValve Technology	Series C	62.5

The trend towards later rounds is here to stay, Mr Marchington says, thanks to the tricky regulatory climate. "It's becoming more difficult at the FDA to get approval – we're definitely seeing that. It's getting longer and longer. And it's not until companies have got to the US that [VCs are] interested."

Tighter regulation and lower prices are the new reality in medtech. Start-ups and multinationals alike are dependent on venture investment. If investors continue to stay away from the sector, larger device companies may have to step in to fill the gap themselves through their corporate VC wings.

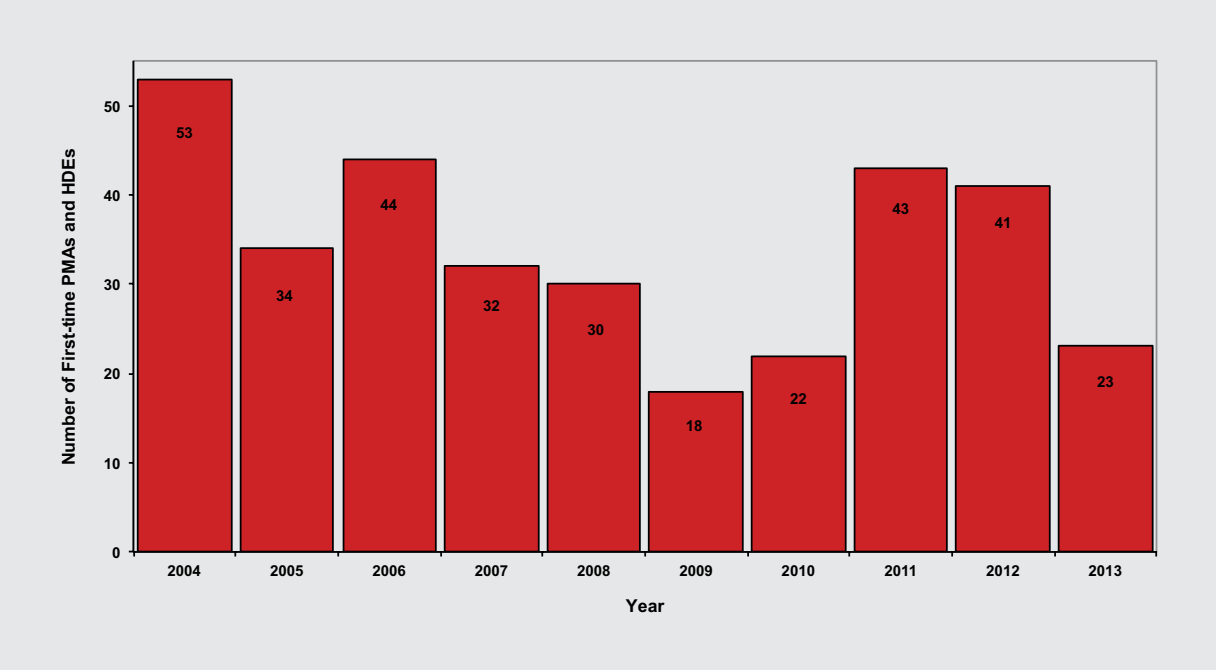
It is to be hoped that 2014 brings an improvement in both M&A and venture funding. Without either, far fewer new medical technologies will reach market.

US APPROVALS SLASHED ALMOST IN HALF

If the worryingly low numbers of mergers and financing events in medtech could contribute to a lack of innovative 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.

The increasingly stringent FDA approval process means that devices tend to gain European approval around three to five years before they reach the US market. 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 premarket approval (PMA), a longer and more expensive procedure.

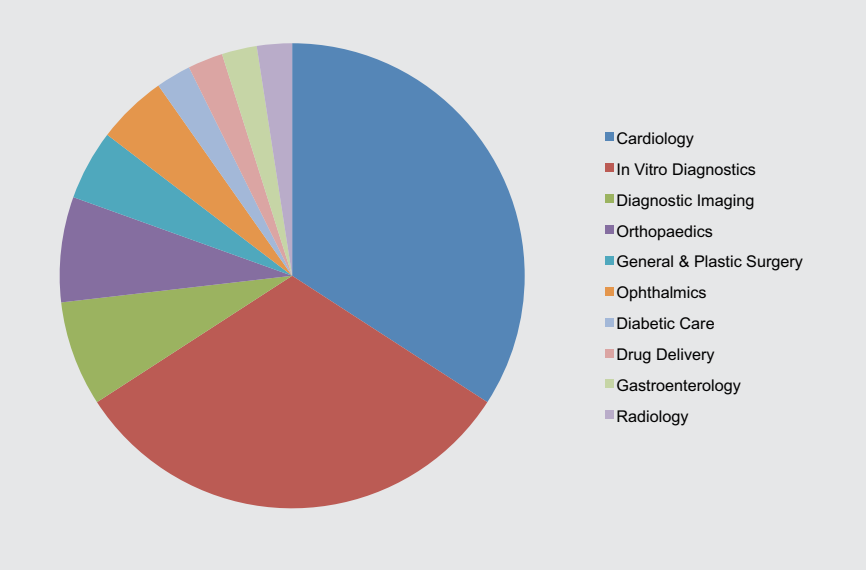
FDA Approval Activity



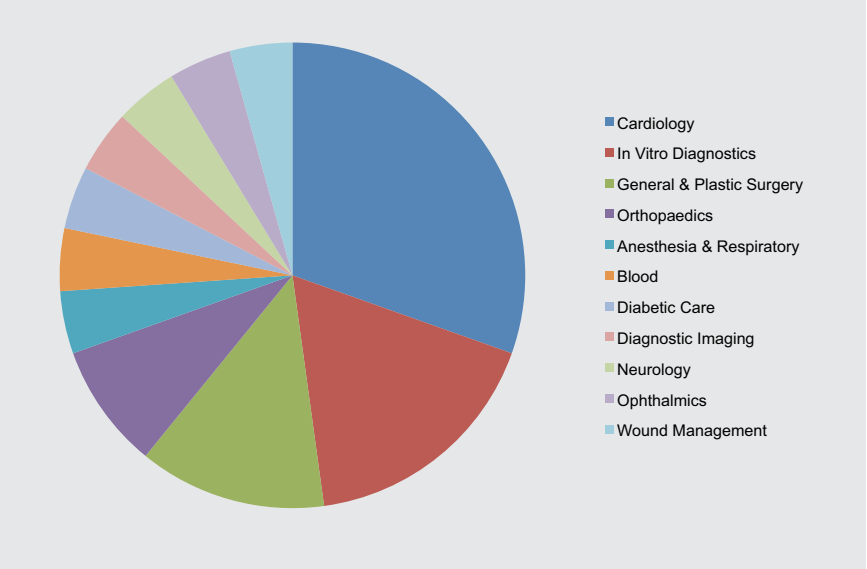
EP Vantage's analysis includes first-time PMAs plus humanitarian device exemptions (HDEs). An HDE can be awarded to a device that is intended to treat or diagnose a condition that affects fewer than 4,000 individuals in the US each year. A lower burden of proof of efficacy is required compared with a 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.

First-time PMAs are hard to obtain, calling for stricter trials than either 510(k)s or CE marking – and they 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.

First-time Premarket Approvals (PMAs) by Therapy Area, 2012



First-time Premarket Approvals (PMAs) by Therapy Area, 2013



With US approval now almost a prerequisite for a smaller company seeking to sell itself or obtain venture funding, and the FDA raising its bar, it is difficult to see how smaller companies can move forward.

Jefferies's Ingeborg Øie suggests that the European market may come to have greater significance. "Maybe demonstrating the product's worth on the European market will become more important as a way of getting validation. A buyer may be willing to acquire the product – and the company – before FDA approval if it's shown to be very effective in Europe."

Ms Øie points out that a similar situation has worked for less established companies working on transcatheter heart valves, at least when it comes to coaxing venture investment. "The smaller companies that don't have approval in the US yet are already attractive [to VCs] because they have done well, capturing market share in Europe and helping the European market expand.

"If your product has done well in Europe it's a much lower risk for bigger companies to take it on and try to get it through the FDA approval," Ms Øie says.

First-time PMAs Granted by the FDA in 2013

Device Name	Company	EvaluateMedTech Device Classification Level 1	EvaluateMedTech Device Classification Level 3	Number	Decision Date
Vascade	Cardiva Medical	Cardiology	Vascular Closure Devices	P120016	January 31
Aorfix	Lombard Medical Technologies	Cardiology	Abdominal Aortic Stent Grafts	P110032	February 14
Natrelle	Allergan	General & Plastic Surgery	Breast Prosthesis	P040046	February 20
ArterX	Tenaxis Medical	Wound Management	Surgical Sealants	P100030	March 1
Sedasys	Johnson & Johnson	Anesthesia & Respiratory	Other Anesthesia & Respiratory Therapeutic Devices	P080009	May 3
cobas EGFR	Roche	In Vitro Diagnostics	Oncology Molecular Diagnostics	P120019	May 14
THxIDTM-BRAF assay	bioMérieux	In Vitro Diagnostics	Oncology Molecular Diagnostics	P120014	May 29
Mentor CPG	Johnson & Johnson	General & Plastic Surgery	Breast Prosthesis	P060028	June 14
RealTime HCV Genotype II	Abbott Laboratories	In Vitro Diagnostics	Infectious Disease Molecular Diagnostics	P120012	June 20
Therascreen EGFR	QIAGEN	In Vitro Diagnostics	Oncology Molecular Diagnostics	P120022	July 12
Mobi-C (one-level indication)	LDR	Orthopaedics	Artificial Discs	P110002	August 7
Nit-Occlud	Pfm Medical	Cardiology	Interventional Catheters & Guidewires	P120009	August 16
AccuDetect 6.1.0	Parascript	Diagnostic Imaging	Image Analyser Systems	P120004	August 22
Mobi-C (two-level indication)	LDR	Orthopaedics	Artificial Discs	P110009	August 23
Complete SE	Medtronic	Cardiology	Peripheral Vascular Devices	P110040	September 19
MiniMed 530G	Medtronic	Diabetic Care	Artificial Pancreas	P120010	September 26
Diamondback 360	Cardiovascular Systems	Cardiology	Atherectomy Devices	P130005	October 21
Juvederm Voluma XC	Allergan	General & Plastic Surgery	Dermal Fillers	P110033	October 22
MitraClip	Abbott Laboratories	Cardiology	Heart Valve Accessories	P100009	October 24
RNS	NeuroPace	Neurology	Deep Brain Stimulation Devices	P100026	November 14
Viabahn	W. L. Gore & Associates	Cardiology	Graft Prosthesis	P130006	December 5

HDEs Granted by the FDA in 2013

Device Name	Company	EvaluateMedTech Device Classification Level 1	EvaluateMedTech Device Classification Level 3	Number	Decision Date
Argus II	Second Sight Medical Products	Ophthalmics	Other Ophthalmic Prosthetic Devices	H110002	February 13
Liposorber LA-15	Kaneka	Blood	LDL Therapeutic Devices	H120005	October 10

Changes are afoot in Europe as well. The CE mark system, generally far quicker and easier to negotiate than the FDA's approval paths, is to change significantly in the latter part of this decade.

The proposed changes in their current form would see some notified bodies – independent agencies empowered by national governments to award the CE mark – specially designated by the EMA as able to certify the more complex and high-risk devices. An entirely new body, composed of around 600 medical personnel divided into 21 committees, will also be formed. Overseen by the European Commission, these committees will scrutinise some, but not all, approval applications, decided case by case, adding another layer of regulatory assessment.

If gaining European approval of medical devices becomes a longer, more arduous and more expensive procedure, pressure on the FDA to look with favour on applications will grow. There is of course a balance to be struck between unnecessary standoffishness and simply waving devices through without proper oversight, and the FDA's caution has served it well in the past. Nonetheless, a more cooperative approach to approvals would help to ease the gridlock that has characterised 2013.

SHARE MOVEMENTS IN THE SECOND HALF OF 2013

While the medtech arena has not seen the same exuberance as biotech, the second half of 2013 has brought large cap device makers sizeable share price gains – and not a single one of them has suffered a fall. The top three risers can be loosely grouped as diagnostics specialists, so it is possible that they have benefited from the biotech boom as their fortunes are closely linked with those of drug makers.

The share price indices covering medical technology companies have put in a similar performance, on average, in the second half of last year as in the first; that is steady, measured growth. The large cap medtech firms have outpaced them handily.

Percentage Change in Medtech Stock Indices Over the Second Half of 2013

Stock Index	% change in H2 2013
Thomson Reuters Europe Healthcare	15%
Dow Jones U.S. Medical Equipment Index	15%
S&P Composite 1500 HealthCare Equipment & Supplies (US)	12%

The medtech sector "has recovered better than the market as a whole, but there is certainly an element of a recovery from the past," says Ingeborg Øie of Jefferies. She estimates that around half of the medtech companies she covers are currently trading at peak share price.

Top of the list is Thermo Fisher Scientific, still enjoying the fruits of its takeover of Life Technologies, announced in April. Buying into the red-hot area of advanced genetic sequencing could hardly fail, and the company has gone from strength to strength since. As well as the high-end bioinformatics capabilities, the company manufactures simple hand-held devices designed for use by the layperson, such as tests for illegal drugs.

To facilitate the Life buy, Thermo Fisher sold its drug development operations to the third-highest riser, General Electric's healthcare business. GE Healthcare has faced tricky headwinds this past year; imaging specialists have suffered particularly thanks to pricing pressure from hospitals and ongoing austerity measures that mean their equipment is simply not being replaced quickly enough. But the firm has a well-defined strategy to adapt to the tricky market conditions, and this appears to be meeting with some success.

Large Cap ($30bn+) Top Risers and Worst Performer in H2 2013

	Share Price (Local Currency)			Market Capitalisation ($bn)	
Top Risers	**30-Jun-13**	**31-Dec-13**	**Change**	**30-Jun-13**	**31-Dec-13**
Thermo Fisher Scientific ($)	84.63	111.35	32%	30.48	40.24
Danaher ($)	63.30	77.20	22%	43.85	53.82
General Electric ($)	23.19	28.03	21%	239.79	283.59
Worst Performer					
Baxter International ($)	69.27	69.55	0.4%	37.64	37.74

The large-cap group was devoid of fallers in the second half of 2013. The worst performer in the $30bn+ group, Baxter International, posted a share price increase of 0.4%. Investors could be fearing the effects of the forthcoming clawback in US Medicare reimbursement of dialysis procedures. If the cut is not reduced, the company could be forced to close some of its clinics.

That the stock of medtech firms has remained buoyant is overall a good thing, but it is acting as a brake on acquisitions.

The picture is more mixed for the smaller-cap players, though many more companies have gained than lost, and by much wider margins. The winners here include broad-based companies such as Omron, perhaps pointing to the intentions of the more specialised companies that have moved towards diversification in the second half.

Other Significant Risers and Fallers in H2 2013 (Ranked on Market Cap.)

	Share Price (Local Currency)			Market Capitalisation ($m)	
Risers	**30-Jun-13**	**31-Dec-13**	**Change**	**30-Jun-13**	**31-Dec-13**
OMRON (¥)	2,979.00	4,645.00	56%	6,920	10,788
Align Technology ($)	37.04	57.14	54%	3,021	4,589
Mako Surgical ($)	12.05	29.99	149%	565.7	1,544.7
Given Imaging ($)	14.01	30.08	115%	439.5	957.8
Pacific Edge (NZ$)	0.59	1.33	125%	139.4	353.1
Fallers					
Intuitive Surgical ($)	506.13	384.08	(24%)	20,327	14,620
Quest Diagnostics ($)	60.63	53.54	(12%)	9,581	7,786
Sequenom ($)	4.21	2.34	(44%)	484.8	270.8
Merge Healthcare ($)	3.6	2.32	(36%)	336.5	218.3
Baxano Surgical ($)	2.4	1.01	(58%)	108.4	45.6

In Omron's case its range of products spans blood pressure and weight monitors as well as respiratory devices and neurostimulation technology. Medtronic, Fresenius and Boston Scientific, inter alia, have all widened their focus in 2013; companies with a range of products and services seem likely to continue to do well, so this trend can be expected to persist into 2014 and beyond.

The other discernible pattern in the mid cap risers is growth in areas that are to a large degree elective. As the US job market as a whole picks up, albeit slowly, more people find themselves with health insurance – or simply with more cash in their pockets. The advent of the Affordable Care Act in the US has also contributed to this.

It is to be hoped that employment continues to grow, and an improvement in European economies would also provide a welcome boost.

It is no surprise to see Intuitive Surgical in the fallers. The robotic surgery company has lurched from disaster to disaster during 2013 and, while its shareholders held faith for a remarkably long time, a collapse was inevitable.

There is some cause for hope that the moribund medtech sector could begin to improve in the coming year as companies continue to alter their strategies to adapt to harsh conditions of cost containment. Many have wondered whether the astonishing growth of the biotech sector is setting that market up for a crash. With more modest growth, and tiny glimmers of improvement, medtech could be the tortoise to biotech's hare.

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