COMPARATIVE EFFECTIVENESS HITS MEDICAL DEVICES

Converging provider, payor and regulatory forces are making comparative effectiveness and evidence of value top priority issues for device companies. Here are several principles and best practices designed to help companies succeed in this future environment.

- Evidence of value and comparative effectiveness (clinical proof of efficacy, safety and/or cost benefits vs. alternative therapies) should be a top priority for device companies as a result of converging provider, payor and regulatory forces.
- The current business model built on rapid incremental innovation and strong physician preference will no longer suffice as health systems focus on containing growth in medical products spend.
- Over time, these forces will reshape the medical device business model – in some cases, leading to dramatic increases in spend on clinical evidence and longer product development cycle times.
- While the pace of change is uncertain, the direction is clear, as are the actions that medical products companies should take.

BY JOHN LIN, MD, HOWARD HORN AND JAKE HENRY

The global economic crisis and the ever rising share of global output spent on health care products and services have pushed governments and payors to critically examine the value they are receiving for their health care dollar. This trend has prominently played out for over a decade in pharmaceuticals, where the large global bill (>$600 billion) and the availability of low-cost alternatives (generic versions of highly effective blockbuster medications from the 1990s) provide national health systems and large payors with ample incentive to examine their medical spend. In its simplest form this has played out as generic substitution: the automatic replacement of a branded medication with a cheap, generic equivalent. In more complex forms this takes the form of comparative effectiveness calculations: quantifying the incremental benefit created by a branded drug vs. another branded or generic drug, a device, or a procedure – whether in terms of efficacy (e.g., reduced mortality), safety (e.g., lower liver toxicity), convenience (e.g., once-a-day dosing) or downstream cost savings (e.g., reduced hospitalizations) – and then using this calculation to shape drug coverage and reimbursement policies.

Historically, medical device companies have largely escaped this scrutiny. The reasons are diverse: medical products represent a smaller share of the health care spend (~$200 billion); this spend is spread across a much broader and diverse range of products, with few individual products that can compare to blockbuster branded drugs; and product development cycle times are very rapid compared to pharma (18 vs. 120 months), thus making it more difficult to study the comparative effectiveness of an individual product. Furthermore, device companies have historically enjoyed streamlined regulatory pathways in the US (through the 510(k) process) and Europe (by obtaining CE mark approval), whereby fairly sophisticated devices (e.g., coated orthopedic implants, hemodialysis devices) can secure marketing approval with only rudimentary clinical evidence if they are able to claim material similarity to a predicate device. The situation for device companies is changing. Consider as examples the following three recent trends in the US market.

Over the past several years both public (Centers for Medicare and Medicaid Services [CMS]) and private (Aetna, Wellpoint, Blue Cross Blue Shield) payors have been using lack of clinical evidence as justification to refuse reimbursement coverage of new device technologies. As an illustration, consider **Johnson & Johnson**'s *Charité* artificial disc (for spinal surgeries): widely expected by sell-side analysts to be a blockbuster, it fizzled in the market following CMS' negative national coverage determination based on insufficient evidence of clinical benefit. This trend also extends beyond the therapeutic implantable class of devices. For example, CT virtual colonography was widely believed by

radiologists to be a safer screening alternative to invasive colonoscopies. Upon review of actual studies, however, both CMS and private payors concluded that evidence of value was lacking – and by refusing coverage, have taken away a vital growth avenue for CT imaging.

Since March 2009, the 510(k) regulatory approval pathway has been loudly and publicly criticized as lax and unsafe by the media, legislators, the Congressional Budget Office, and even the new FDA leadership itself. Consider the controversy over the *dETlogix* mitral valve ring from **Edwards Lifesciences Corp.**, which was not submitted for 510(k) review prior to human use. Facing questions, company officials' initial response was that the device was a trivial modification of an approved device (reshaping an oval annulus into a triangular shape), not requiring IRB review or a formal IDE. Meanwhile, critics point to the fact that the device innovators published a case series on its effectiveness as proof that implanting this device constituted human experimentation, and should be regulated as such.

The American Recovery and Reinvestment Act (aka President Obama's stimulus package) has injected $1.1 billion of funds through 2010 to fund comparative effectiveness research. To put this in perspective, this amount is more than ten times greater than the total annual funding of the four major global Health Technology Assessment (HTA) bodies (UK, Germany, Canada and Australia). President Obama's recently proposed budget, as well as the most recently endorsed versions of the House and Senate health reform bills, would sustain funding at approximately $300 million annually, or about three times today's total HTA spend. (*See Exhibit 1.*) A number of medical product categories have been included on the list of priority topics for CE evaluation.

At its core, these trends highlight two fundamental questions that payors and providers are now asking about medical technologies: Does it work? And if so, how much better is it then the cheaper alternative?

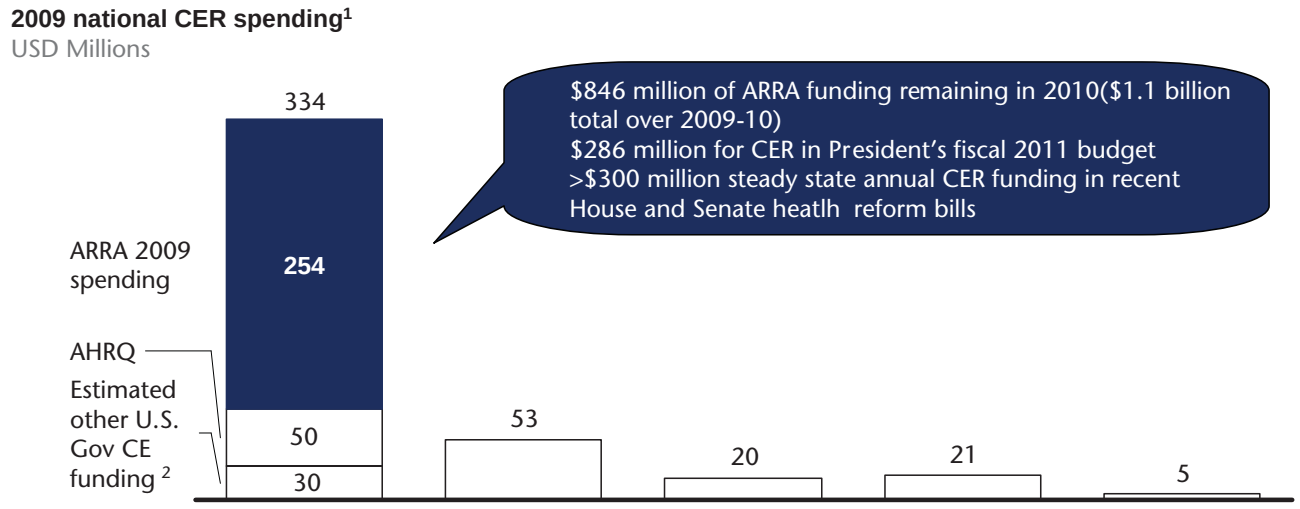
Defenders of the status quo highlight the broad range of issues that make answering these questions difficult – insensitive outcome measures (e.g., functional improvements post-spinal surgery), high user-to-user variability, and the impracticality and cost of conducting clinical trials in low volume patient populations. While each of these has merit, payors' and providers' desire to slow down (or reverse) their spend growth will create inexorable pressures to understand whether or not a given medical product does, in fact, create value for their patients.

WINNING IN THE NEW ENVIRONMENT

In our experience working with the majority of the large medical device companies, we have observed that they often

Exhibit 1

The US Stimulus Package Passage Represents The Start Of A Major Push To Conduct And Disseminate More CE Research In The US



	U.S. – H.R.2184	UK (NICE)	Canada (CADTH)	Germany (IQWIG)	Australia (PBAC)
Total health care spending	2,472,000	160,000	151,000	369,000[3]	100,000[4]
Nat. CER/Total	0.014%	0.033%	0.013%	0.006%	0.005%

1 Based on January 2009 exchange rates
2 Includes estimates for NIH, VA TAP, VA PBMSHG, DOD, CMS, and CDC funding
3 Based on 2007 spend using December 31, 2007 exhange rate
4 Based on 2007-2008 fiscal year spend using June 30, 2008 exchange rate

SOURCE: THOMAS (Library of Congress); US agency web sites

have a strong engineering culture and mindset. Therefore, product development is typically driven by engineering milestones (customer requirements, prototyping, validation, marketing authorization), and not health care milestones (clinical indications, target product profile, reimbursement). To win in the new evidence environment, medical product companies will need to make the transition from focusing on engineering targets to instead concentrate on health care milestones, and systematically elevate the role of evidence of value in their R&D efforts. Device companies should follow three principles to make this shift:

Defend against externally generated comparative effectiveness research (*CER*): monitor what products are targeted by health technology assessment (HTA) reviews, and intervene early (e.g., get involved in protocol design, launch your own "counter-research").

Invest in evidence of value to drive growth: assess what products will benefit most from evidence of comparative effectiveness, and launch the most efficient portfolio of studies to generate it.

Organize to win: embed evidence of value in your product development and commercial operating models, and resource accordingly – both in head count and funds. Simply creating a Health Economics or Payor/Reimbursement function is insufficient; success requires systematic inclusion of evidence of value principles in the operating model.

While medical products is a diverse sector (ranging from retinal implants to medical clinic disposables), these principles are relevant to any manufacturer of a differentiated product. The most obvious applications are in the therapeutic implantables segment, where the decision of which device to use is important from both clinical (life-preserving indications; difficulty of explants) and economic standpoints (unit prices in the thousands or tens of thousands of dollars). These principles are also relevant, however, to large- and small-box capital equipment manufacturers. Here the question applies to specific procedures and applications of the underlying equipment: is it a cost-effective screening tool? Is it clinically superior to alternatives (e.g., drug-only regimens, lower-tech imaging modalities, standard infusion pumps)? Finally, among commodity segments, innovating features that have tangible evidence of value can be a powerful driver of premium pricing and returns (e.g., antimicrobial vascular catheters and surgical drapes).

DEFEND AGAINST EXTERNALLY GENERATED CER

Payors' and providers' desire to use CER in their medical device decision-making processes is hampered by the current lack of adequate evidence for most products/

Exhibit 2

Medical Products Are Impacted By 24 Of The Top 100 "Initial National Priorities" Laid Out By The Institute Of Medicine

Top quartile (out of 100)	2nd quartile	3rd quartile	Bottom quartile (out of 100)
Atrial fibrillation therapies (comparison vs. pharmacologic treatment)	**Catheter-based treatment of vascular claudication** vs. other strategies (e.g., lifestyle interventions)	**Coronary stenting** vs. aggressive medical management	**CT angiography** vs. conventional angiography
Proton-beam radiotherapy for prostate cancer	**Robotic assistance surgery** vs. conventional surgery (e.g., for prostatectomies)	Innovative **CHF therapies**, including CRT and remote monitoring	**Minimally invasive vs. open abdominal surgery**
Prospective registry **treatment strategies of low back pain** (without neurological deficit or spinal deformity)	**Remote patient monitoring and management technologies** (e.g., telemedicine, remote sensing) vs. usual care, especially in rural settings	Treatment options (including lasers) for **retinal diseases and open-angle glaucoma**	**Diagnostic imaging** performed by radiologists vs. non-radiologists
Imaging technologies for cancer, including PET, MRI, & CT	**Renal replacement therapies** (e.g., HHD, ICHD, CAPD, transplant)	"Effectiveness of **formulary management practices and practices in controlling hospital expenditures** for products other than drugs including medical devices"	Surgical strategies for **symptomatic cervical disc herniation**
Effectiveness of **genetic and biomarker testing** for several cancers	New **colorectal cancer screening technologies** (e.g., CT colonography)	Traditional vs. newer **imaging modalities** for neuro and ortho indications	**Liver metastases: ablation vs. other therapies (e.g., resection, observation)**
	Psoriasis treatment (including UV light therapies)	Obesity treatment strategies (including **bariatric surgery**)	
	Use of **ultrasound in normal pregnancies**	Systemic therapies (e.g., **NPWT**) vs. topical treatments in chronic lower extremity wounds	

SOURCE: Institute of Medicine report (June 2009)

therapies. The US government's vast increase in CER investments through both stimulus funds ($1.1 billion) and proposed health reform legislation attempt to remedy this situation. As CER research and infrastructure levels improve this could create sufficient legitimacy to catalyze payor and provider efforts to utilize CE research in their decision-making processes.

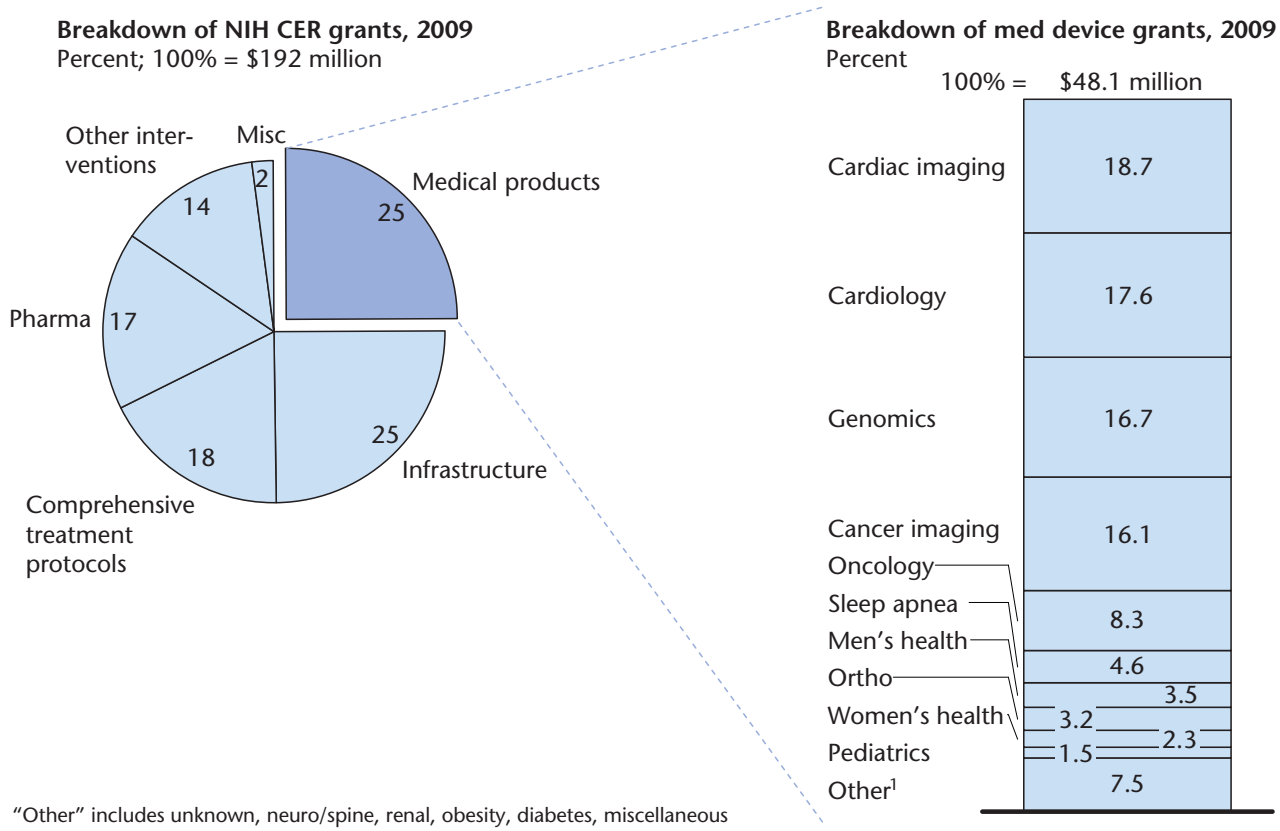
The proposed CER priorities will touch a broad swathe of the device industry. The Institute of Medicine's consensus list of the top 100 CER priorities include 24 that address therapies that use medical products and affect almost all large device players. (*See Exhibits 2 and 3.*) We estimate that $40 billion of global medical products revenue are associated with therapies targeted by these IOM CER priorities. (*See Exhibit 4.*) Most of these studies will study the effectiveness of a medical product therapy vs. alternatives (e.g., medical therapy; doing nothing) that are often cheaper, with the ultimate goal of eliminating unnecessary interventions and excess spend.

In formulating a risk mitigation strategy, it is important that device companies understand the substantial constraints that payors and providers face in their ability to act upon CER data. The most obvious restriction in the US is the specific legislative restrictions on CMS' ability to use cost-effectiveness data in its coverage decisions (only clinical effectiveness can be used). In addition, payors and providers cannot change policies toward widely adopted therapies absent extensive and irrefutable evidence of ineffectiveness. As an example, consider the case of vertebroplasty. Introduced in the early 1990s, over 80,000 vertebroplasties are performed each year in the US alone. Two randomized controlled trials published in the *New England Journal of Medicine* in 2009 failed to find any benefit of vertebroplasty when compared to placebo (i.e., sham surgery). However, these study results ran counter to the experiences of physicians and patients, and both groups have called the results into question. No US payors, either public or private, have yet made any moves to act on the study results through changes in coverage.

As another example, the US Preventive Services Task Force (USPSTF) recently reviewed routine breast cancer screening, and concluded that there was insufficient evidence of clinical effectiveness for annual mammograms in women aged 40-50, and recommended a decrease in frequency to biennial mammograms for women aged 50 to 75. (Notably, all recommendations were based on evidence of clinical effectiveness, with no consideration of cost.) The skeptical reaction from physicians, the media, and legislators was visceral, loud and immediate. Within 48 hours, there were calls for legislation to guarantee payor coverage for annual mammography. The American College of Radiology issued a press release that the new recommendations would "result in countless unnecessary breast cancer deaths each year." Within a week, the USPSTF chairman and vice chair were called before a House subcommittee to contritely acknowledge their missteps in framing

Exhibit 3

NIH Awarded $48 Million In Medical Products CER Grants In 2009



"Other" includes unknown, neuro/spine, renal, obesity, diabetes, miscellaneous

SOURCE: NIH Report; McKinsey analysis

and communicating their findings. Both examples illustrate how reluctant payors and providers will be to oppose strongly held physician and patient preferences.

Finally, our interviews of medical directors suggest that most regional payors and providers are not able to take full advantage of CER data. First, they are not resourced to conduct their own independent reviews of existing evidence, and instead effectively rely on technology assessments and coverage policies published by trusted bodies (e.g., BCBS TEC, United, Aetna and UK NICE). Second, they adopt a reactive posture toward medical products technology assessments. Most reviews are triggered by requests for additional spend (new procedure codes, higher reimbursement levels for existing codes, large procurement decisions), rapid growth in utilization, and new recommendations from the above bodies. Assessments of existing medical products utilization typically do not occur.

In light of these value chain dynamics, we recommend medical products companies adopt four targeted actions to defend against externally generated CER:

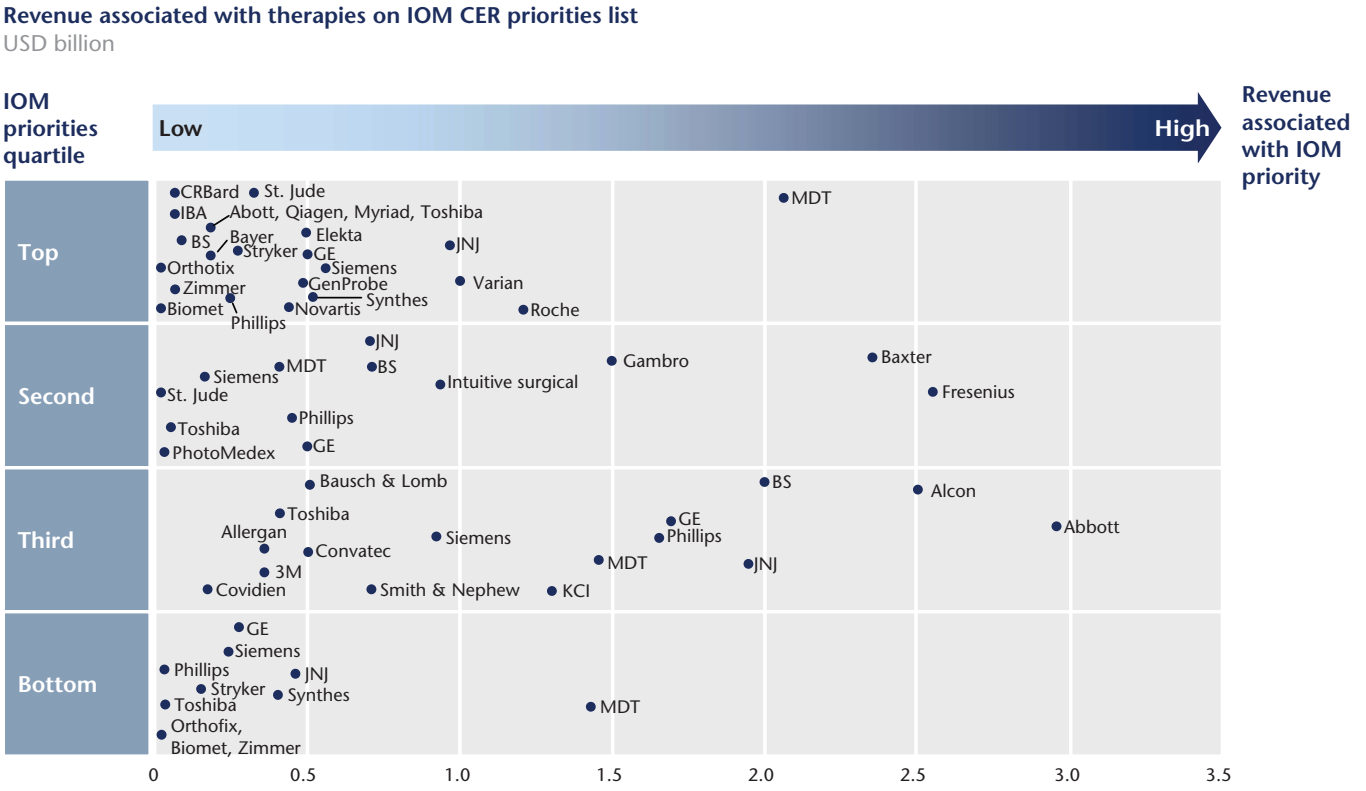
Perform an evidence audit. For your most important products, know the tally of clinical evidence assets vs. liabilities. Be able to clearly synthesize the value proposition (vs. cheaper alternatives) and supporting evidence for payor and provider technology review committees.

Monitor where CER investments are going, and get involved in shaping study designs. For example, much of the US CER funds will be distributed through traditional grant mechanisms that are readily tracked. Once it becomes clear that CER will be conducted, it is critical that manufacturers be a part of shaping the study design. Nuances in the choice of patient inclusion criteria, outcome measures, and statistical plan can create unfair bias against the medical product (e.g., CMS' non-coverage decision of CT colonography cited the lack of elderly patients in existing data sets).

Launch your own counter-research. Where externally generated CER is likely to cast your products in a negative light, invest in developing counter-arguments on a parallel timeline. For example, you could study your product in high risk patient populations, where comparative effectiveness signals will be stronger.

Exhibit 4

Medical Products Industry Has A Total Of $40 Billion In Revenue Associated With Therapies On IOM CER Priorities List



NOTE: Vertical position within quartiles does not indicate varying level of importance within quartiles (i.e. vertically within quartiles, the impact from CER is constant); IOM did not prioritize within quartiles.

SOURCE: IOM report (June 2009); Meryll Lynch report 2008; Credit Suisse report 2008; Apr 09 UBS analyst report on St. Jude Medical; Particle Therapy Co-operative Group; Orthopedic Network News 2008; IMV 2008 CT Benchmark Report; Global Medical Diagnostics Market 2008 Shares Cowen 2009; IMV 2008 MRI Benchmark Report, UK Government Department of Health (2005-06)

Activate grassroots support from physicians and patients. Enlist the support of those most directly affected by CER-based decisions, and mitigate the inappropriate application of evidence (e.g., extrapolation from highly controlled settings in randomized trials to community practice).

EVIDENCE OF VALUE CAN DRIVE GROWTH

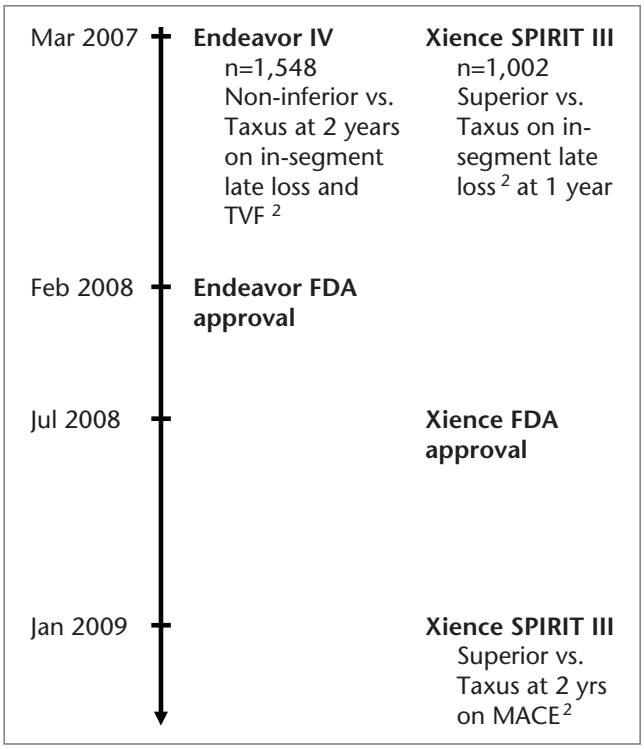
Compelling evidence of value drives growth for medical products along all three dimensions of price, market size and market share. In many categories, medical products pricing is governed by reimbursement levels for the therapy the device or equipment supports. Comparative effectiveness evidence can be a tremendous value lever here. As J&J experienced with its Charité spinal disc, the lack of evidence can lead to restrictive reimbursement policies that effectively kill a product. In contrast, in launching *Cypher* (the first drug eluting stent), J&J had a robust stable of evidence demonstrating superior clinical and health economic outcomes vs. existing bare metal stents. This evidence, combined with effective payor engagement, allowed J&J to launch Cypher at a unit price around 150-200% higher than bare metal stents.

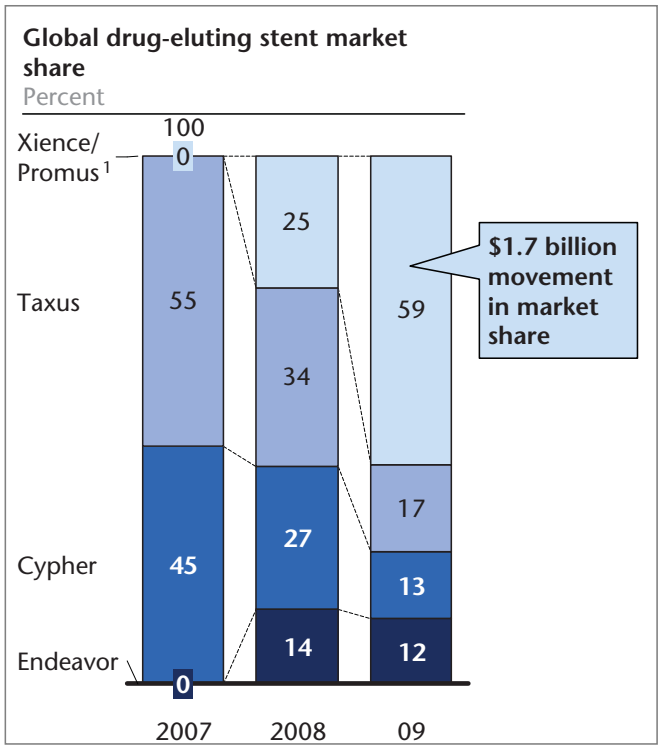
Comparative effectiveness can also be a powerful driver of therapy adoption, therefore impacting market size for a medical product. Consider the case of **Intuitive Surgical Inc.**'s *da Vinci* platform for robotically assisted surgery. At over $1 million per unit, the value proposition to hospitals of the device was unclear. The tipping point came as clinical studies began to suggest that robotically assisted prostatectomies had superior clinical outcomes when compared to standard open procedures. Blood loss was lower; hospital stays were shorter. Most importantly, while the incidence of impotence and incontinence side effects was never convincingly demonstrated in a randomized trial, a series of case studies suggesting this might be the outcome led many urologists – and their patients – to view a robotically assisted prostatectomy as the new standard of care. Community hospitals began to adopt the da Vinci equipment as a better economic alternative than losing their urology procedures to local competitors.

Evidence of value also moves market share. This has played out dramatically and recently among drug eluting stents (DES). In 2007, the global DES market was a two-player market shared between J&J's Cypher and **Boston Scientific Corp.**'s *Taxus* stent. **Abbott Laboratories Inc.**'s SPIRIT III trial compared its new *Xience/Promus* stent to the standard of care (Taxus) in 1,000 patients, and demonstrated clearly superior results in in-segment late loss. Within months of its launch in 2008, Xience/Promus had captured 25% share of the market, and by 2009 had reached nearly 60% share. While

Exhibit 5

Evidence Of Superior Clinical Effectiveness Transformed Drug-Eluting Stent Market Within 12 Months Of Data Release





1 Includes Abbott's Xience V sales, as well as sales co-promoted under the Promus brand by Boston Scientific
2 TVF, target vessel failure; MACE, major adverse cardiac events (composite endpoints including death, heart attack and need for revascularization)

SOURCE: SG Cowen (2009); company web sites

the SPIRIT III and SPIRIT IV studies were undoubtedly costly investments (likely more than $10-20 million each), the evidence of value they provided, along with the stent's perceived superior deliverability, contributed to a $1.7 billion movement in market share. (*See Exhibit 5*.)

Most of the high-tech implantable device companies are already acutely aware of the power of evidence of value, and have invested behind it. The landmark SCD-HeFT and MADIT-II trials of cardiac resynchronization therapy (CRT-D) devices created entire new multi-billion dollar markets for cardiac rhythm management. In contrast, we have observed a much lower willingness to invest in evidence of value among other implantable devices (e.g., spinal and orthopedic implants) and among medical equipment manufacturers (e.g., diagnostic imaging, surgical equipment), a resistance which has left money on the table in terms of unrealized price and volume.

Anecdotally, there are two primary drivers of this behavior. First, comparative effectiveness has not been historically demanded by regulators, physicians (especially surgeons) or hospitals, a fact that is now changing. Second, the cost and timeline of developing evidence is daunting. The total cost and duration of a large-scale clinical trial often exceeds that of developing and launching an entire new product. Faced with this choice, pragmatic general managers have chosen to invest their resources in more launches, not more evidence.

We believe medical device leaders can use this same pragmatism to capture the evidence of value opportunity. The basic and fundamental change required is that leaders ask and answer two basic questions during product development:

At the time of launch, what level of evidence will regulators, payors, providers and patients require for this product? Across the four health care value dimensions of safety, efficacy, quality-of-life and health economic impact, product development leaders should understand what evidence these stakeholders will require in order to approve, reimburse, and adopt a product or therapy. This sets the minimum bar for comparative effectiveness investments one must make for a successful product launch, and the costs of such evidence should be incorporated into a project's ROI in the same way prototyping, market research and validation expenses would be. In some cases stakeholders will require no evidence (e.g., surgical trocars, endoscope optics) or only non-inferiority (e.g., incremental innovations in joint replacements). In other cases, superiority along one or more of these dimensions will be required to secure the premium price point or convince physicians and patients to abandon the current standard of care (e.g., breast MRI).

Pharmaceutical companies are already adapting their product development processes to embed this question. Early on, scientists articulate a candidate drug's target product profile (TPP), representing a hypothesis on how the drug will compare to standard of care and other alternatives. They then test this TPP with physicians, patients and payors to understand the commercial viability of the product as well as what evidence points are most pertinent to these stakeholders. Finally, armed with this information they evaluate the cost and ROI of developing the required evidence.

Can evidence of value create differentiation and competitive advantage for this product? In addition to the "minimum bar" set above, additional investments in evidence are often wise for products that are superior to current standards of care. As with the Cypher, da Vinci and Xience examples, evidence of comparative effectiveness is a powerful tool in discussions with payors and customers.

To most effectively answer this question, we recommend keeping in mind two best practices. First, ensure that you are considering all four dimensions of health care value – superior safety or quality-of-life (e.g., post-prostatectomy impotence and incontinence) can be just as commercially powerful as traditional clinical or health economic outcomes. Second, explore a variety of indicated patient populations. Narrowing to a more specific population (e.g., high disease severity) can often dramatically enhance the apparent comparative effectiveness; conversely, broadening the patient inclusion criteria can dramatically expand the market for your product (e.g., manufacturers changed the definition of osteoporosis from proven fracture to simply low bone mineral density).

To improve the ROI of investing in evidence of value, medical device companies should employ and exploit the full range of potential study designs. Randomized, controlled clinical trials are the most recognizable, rigorous and expensive form of evidence, but are by no means the only way to show comparative effectiveness. Broadly, there are two dimensions to consider in optimizing study design and cost. First, a range of less statistically rigorous studies can provide evidence considered valid by CER decision makers within payors and providers (e.g., registry data; retrospective analyses of clinical data). Second, costs can be shared across multiple beneficiary parties, e.g. through partnering with academia, or co-funding studies alongside charitable organizations or governmental support. In decreasing order of cost, medical products companies should explore the use of:

Industry-wide landmark trials: typically dividing the cost among 3+ parties, these studies involve collaboration across multiple vendors that offer products for a given therapy. The goal of these trials is to drive adoption of the therapy (e.g., CT angiography vs. conventional), irrespective of the device brand used. To prevent conflicts of interest, these studies will typically be sponsored and managed by physician societies; as such, costs can often be further offset through public research grants (assuming the trials align with public funding priorities). This arrangement, however, introduces complexities in governance that can lead to inefficient clinical operations, delays and cost overruns.

Prospective registries: typically costing $1-5 million, these studies can capture large sample, longitudinal data that would be impractical in a clinical trial setting. Designed appropriately, registries are a powerful tool for demonstrating hard clinical end points (mortality, re-operation) and health economic value (costs of hospitalization, return-to-work).

Investigator initiated trials: typically costing $0.5-$2 million, these represent funding for studies conducted and led by academic physicians and

surgeons. The cost of the study is often subsidized in part by research grants, and the investigator frequently shoulders cost items that would normally be incurred in an industry-sponsored clinical trial (e.g., site monitoring, data management).

Retrospective studies and meta-analysis (systematic reviews): costing $100-500k, most externally generated CER will be of this form. These studies mine existing patient records and aggregate published analyses to build a case for or against comparative effectiveness.

One final note: a greater focus on evidence of value has interesting commercial implications for capital equipment manufacturers. Most comparative effectiveness evidence will be applied at a procedure or therapy level, and not at an equipment level. Therefore, business models that can better monetize incremental procedures will be better able to capture the value here than business models that rely on pure equipment sales. For example, consider the case of breast MR. Building evidence of value will increase the number of these procedures, both in terms of percent adoption among today's indicated patients and in terms of expanding the range of indicated patients. Despite this, most facilities have enough excess MR capacity (e.g., doing scans on Sunday) that these additional procedures will not translate into additional machine sales. In this case, a pay-per-click business model would better monetize this additional volume.

ORGANIZE TO WIN

To fully capture the evidence of value opportunity, most medical products companies will need to shift organizational mindsets toward evidence and allocate more resources against it. More broadly, this shift represents a step along a broader journey of medical products companies moving from being engineering companies (focused on product and feature innovation) to being health care companies (focused on outcomes and patient impact).

Investing behind comparative effectiveness and evidence of value represents a significant change from the historical business model for most medical products companies. At the risk of oversimplifying, medical products companies have historically focused on physicians as the fulcrum: their awareness and comfort drove therapy adoption, and their preferences drove market share. This focus has led to today's commercial model with extensive and highly trained sales forces, and extensive use of physician consultants in training and education. This focus has also driven product development decisions: akin to consumer electronics, frequent and incremental innovations in features are required to maintain physician excitement.

Many device companies reinforce this business philosophy through their budgeting and performance management systems. Resources are allocated at the business unit level, with a common pool of head count and funds for incremental and breakthrough innovations. Executive targets and executive compensation are similarly set at the business unit level, and frequently emphasize near-term (one year) market performance: revenue growth, market share, operating margins and rate of product launches. Together these approaches lead to underinvestment in long-term issues, including evidence of value, until they become near-term emergencies (e.g., CMS announcement of a national coverage decision review, or publication of externally generated CER).

In our observations of companies who have successfully captured the evidence of value opportunity, we note four important shifts in their business model:

Evidence of value mindset is embedded in R&D and commercial processes. The definition of customer extends beyond physicians, to include payors, regulators and patients. Customer requirements for this expanded group are addressed explicitly during the initial stages of product development.

Investments in evidence are ring fenced from short-term operating decisions. Evidence requirements for new products are included in project plans and ROI calculations. Once a project is approved, evidence investments are managed separately from commercial investments, and are out of scope for short-term earnings management decisions (e.g., dealing with an unexpected quarterly revenue shortfall). As an analogy, most companies already take this approach today with their manufacturing plant network, recognizing that decisions there have a large and long-lasting impact and should be managed separately from quarter-to-quarter earnings concerns.

Culture and incentives reinforce a "health care company" (vs. "engineering company") mindset. Product development leaders view their role as driving new therapies, and not simply launching new products. In this mindset, product development metrics focused on cycle times and on-budget performance fall short, as one can be highly successful on both fronts while producing products with little incremental value and therefore no acceptance by payors and evidence-savvy physicians. Instead companies can institute metrics that more accurately measure the market's belief in the comparative effectiveness of the product developed: therapy adoption metrics (e.g., percent addressable patients, percent of addressable physicians), or metrics tied to the reimbursement posture of major payors and HTA bodies.

Evidence of value capabilities are adequately staffed and resourced. Execution here requires a diverse set of functional capabilities, including health economics, biostatistics, clinical operations, medical affairs and a payor/HTA field force. Successful companies adequately resource these organizations, to ensure rapid response times and high levels of "customer service" to the product development and commercial organizations.

CER HAS ECONOMIC IMPLICATIONS

Greater requirements for evidence of value and comparative effectiveness will have a significant impact on the economics of product development in medical products companies. The costs of conducting evidence of value research will be significant. Industry-wide, medical device R&D spend is 6-7% of global revenues. Even at high-value therapeutic implantables companies (e.g., Medtronic and Boston Scientific), total R&D spend is 9% to 12% of revenues, of which approximately a quarter is clinical evidence. In contrast, most pharmaceutical companies invest

18-22% of their revenues in R&D, two-thirds of which is clinical evidence. The costs of developing even a modest portfolio of evidence (e.g., registry data plus two to three retrospective reviews, no clinical trials) for a 510(k) product will likely double the total project cost. (*See Exhibit 6.*) While the comparison between medical products and pharmaceuticals is imperfect for a host of reasons, the chasm is wide enough and the medical products baseline so small that medical products companies may conceivably need to double or triple their investments in clinical evidence to be able to answer the two fundamental questions: Does my product work? And if so, how much better is it than cheaper alternatives?

In addition to these direct research costs, there will be indirect costs associated with longer product development cycle times. This effect will be determined by regulators' and payors' stringency towards evidence of value for new products. Anecdotal evidence suggests that with the recent leadership changes, CDRH's review policies have increased in stringency (e.g., tighter statistical deltas and therefore larger sample sizes, more homogeneous patient inclusion criteria, and a focus on clinical/biological – vs. mechanical/physical – outcome measures). While data on approval rates is not publicly available, FDA approval times for 510(k) submissions have increased 37% from 2005 to 2009. (*See Exhibit 7.*)

This evidence bar may be set even higher by payors in deciding reimbursement (e.g., prior authorization policies written to only apply to patient populations where comparative effectiveness has been clearly demonstrated). Even best practice clinical trials require 3-4 months of work in addition to patient recruitment (three or more months) and patient follow-up (varies widely from under one week to after one year, depending upon study protocol). Broader incorporation of evidence into product development will dramatically lengthen today's typical cycle times of 18 to 24 months.

These economic tradeoffs suggest that, over the long-term, medical products R&D will bifurcate into two distinct categories. The first category comprises incremental innovations of in-market products (e.g., new coatings for hip replacements, higher slice-count CT scanners). The emphasis of product development is speed and efficiency, with little to no investment in evidence of value. Absent evidence, payors and providers will be unwilling to grant incremental pricing and reimbursement for these products. Instead, commercial priorities will focus on maximizing market development and market share. Overall, the dynamics of this segment will largely resemble today's business model – except for the decline in reimbursement and pricing power.

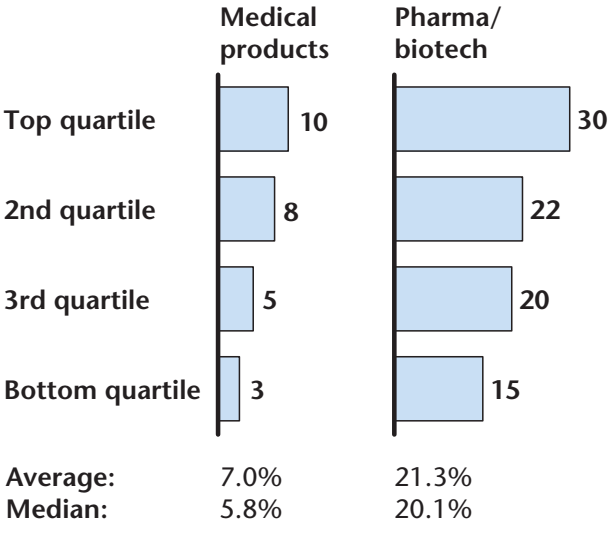
In contrast to these products are breakthrough innovations that go well beyond 510(k) predicate devices (e.g., artificial spi-

Exhibit 6

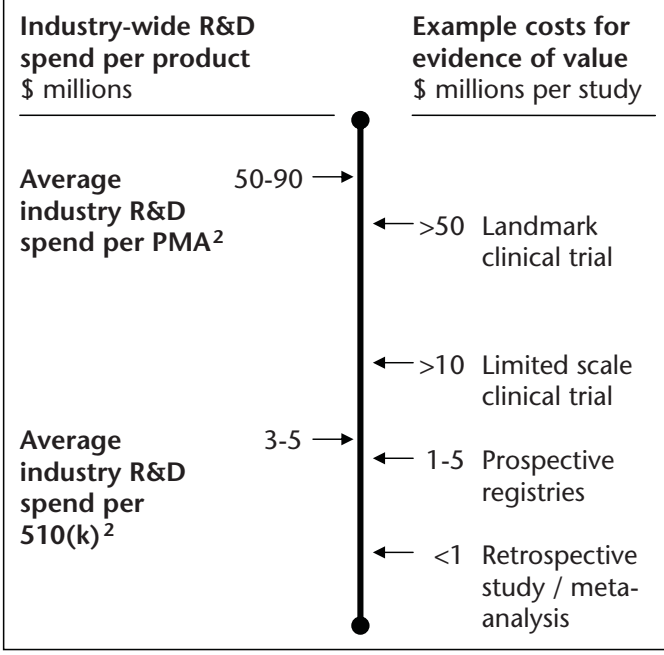
Cost Of Investments In Evidence Of Value Are Large Relative To Current R&D Spend Levels In Medical Products

R&D spend is <6-7% of sales for most medical products companies

R&D spend of leading companies [1]
Percent of companies



Investments in evidence of value will be costly relative to current R&D spend levels



1 Includes 24 medical products entities with global sales >$ 2billion and 26 pharma/biotech entities with global sales >$4 billion. For diversified corporations analysis only includes data for relevant division(s)
2 Assumes 20-30% of total medical products industry R&D spend is on PMA products, 70-80% on 510(k) products

SOURCE: HRI; company financial reports; FDA

nal discs, novel MR applications). Evidence of value investments will be important here. Overall product development will be costlier and slower than today's averages, leading most companies to de-prioritize niche therapies in favor of large addressable markets. Clinical effectiveness and health economic arguments will be used to secure premium reimbursements from payors and create a compelling value proposition for providers. Medical products companies will need to anticipate this change in their overall economic envelope and should begin the process of educating their Board and their investors on what to expect.

As with other sectors that have undergone fundamental shifts, the medical device companies who adapt will be positioned to lead, while those who do not may face slow decline as they risk having their products marginalized by the market.

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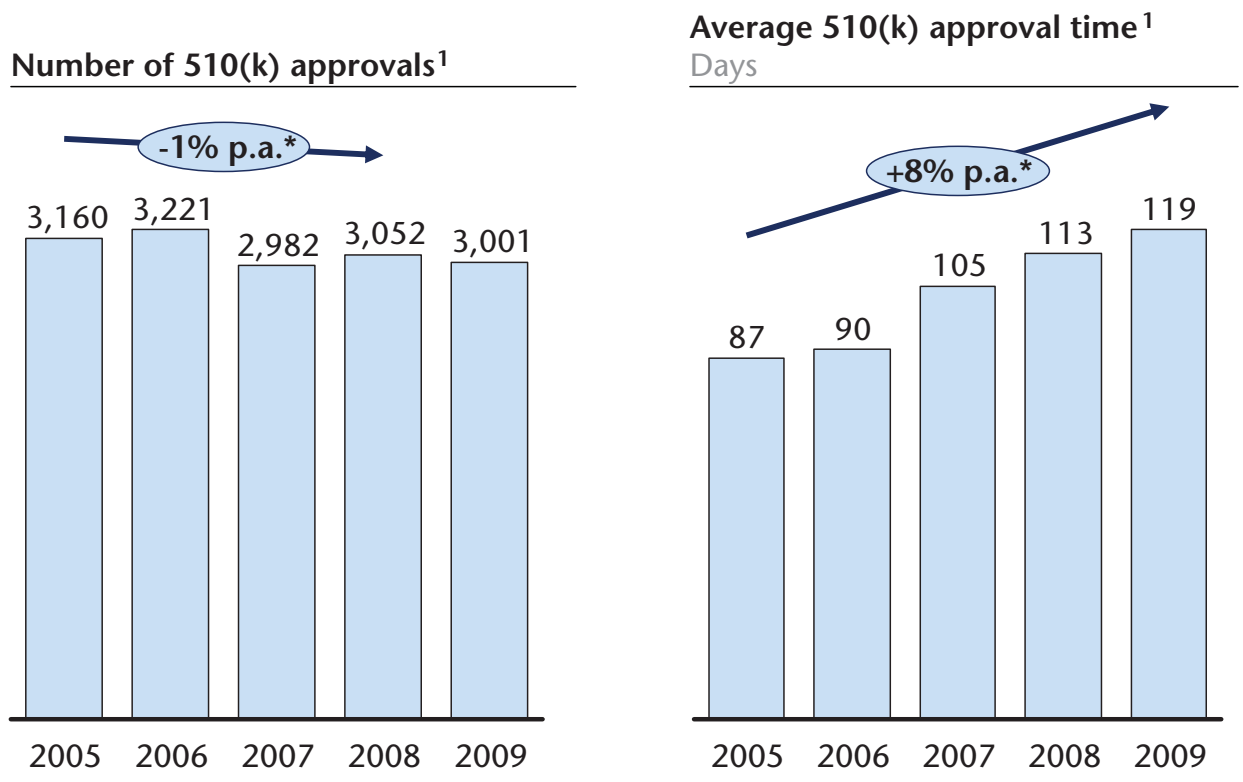
IV

COMMENTS: *Email the editor: S.Levin@Elsevier.com*

Exhibit 7

Although 510(K) Volume Is Flat, Approvals Are Taking 37% Longer



* Per Annum
1 Based on the year that the proposal was approved
SOURCE: FDA CDRH