10. Status and Impact of Evolving Medical Device Venture Capital Landscape on Innovation

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Innovation in medical devices, and the subsequent health improvements they generate, predominantly comes from inventors, most often located in academia or small development firms. For these innovative devices to have their intended impact on human health, they must be fully developed, adequately tested, and made accessible to patients, while generating sufficient returns for their developers to grow and for their investors to generate attractive returns for this high-risk capital. These steps receive support mostly in the form of venture capital. Without such capital, important gains in the treatment of health problems decline. It is also important to note the value of the medtech industry to the economy. The US Department of Commerce reports that the US medical device market, currently the largest in the world, stands at $110 billion and is slated to grow to $133 billion by 2016. This is an estimated 38 % of the global marketplace. In the USA alone, there are an estimated 6,500 medical device companies, 80 % of which employ less than 50 people [1]. A healthy medtech industry carries substantial benefits to patients, the public health, and the overall economy. The enabling investments in these companies warrant attention. The status of such investments, their structure, and their impact on innovation in the medical device arena has changed in recent years, necessitating changes in the way innovators, investors, and their companies approach their efforts.

Venture capital is typically defined as high-risk capital made available to small businesses, usually startups, which do not have ready access to other sources of capital, yet offer substantial growth potential over time. For various reasons explained below and the complex nature

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of such innovation, these firms present high risk for investors as well as the possibility of high returns. While many medical device/technology firms are started with grants or individual investments (i.e., friends and family, angel investors, etc.), they soon need significant capital where traditional borrowing is not possible due to lack of revenues, short operating history, or insufficient collateral. However, early stage capital needs are most often below the minimums set for institutional investors and larger credit companies, and the companies themselves are viewed as too risky. In addition, venture capital investments often bring technical and management expertise. These resources are invaluable in many cases and outside the capabilities of the start-up company.

While venture capital is at times the only source of capital to new companies, founders must recognize that venture investors typically participate in company decisions and policies, and they own equity. This arrangement can be seen as invasive, or at least cumbersome, to some entrepreneurs.

Development of new, meaningful ideas is a challenging proposition, especially in light of the hurdles that exist between concept and commercial acceptance. Many of the areas involved are unpredictable and uncertain, and often beyond the control of the entrepreneurs. These hurdles, coupled with the time and resources needed to overcome them, underlie the risks faced by medical device companies and their venture capitalists partners. The detailed challenges faced and trends in each area are explored further in this chapter.

With respect to how the venture investment process usually works, five steps normally occur:

1. Venture Capital Fundraising. In a venture capital fund, the capital is raised from investors who become part of a limited partnership. Members are most often high net worth individuals, pension funds, insurance companies, endowments, foundations, and other pools of capital created by like-minded parties for investment purposes. Lately, corporations, philanthropic organizations, and patient advocacy groups have become more significant investors both through their own funds and participation in funds created by more traditional means. In each case, the partnership defines what types of investments will be made with accumulated capital, bounds on the size of individual investments, the phase of the companies supported, and the time frame or lifespan over which the fund will exist.
2. Investment. Once the fund is closed, its management team finds companies of interest, conducts diligence, and enters into deals.

These investments are often referred to as "portfolio companies." Funds are most often put into the identified firms at predetermined milestones and during various "rounds."

3. Growth and Management of Portfolio Company. The venture firm will often participate directly in a number of ways, mostly related to corporate policy and strategy, bring specific knowledge of use to the firm, and introduce potential partners, customers, and other contributors to the firm, and by membership on the Board of Directors.
4. Exit. With success, a typical investment will advance to the point of an IPO or acquisition in 5–10 years as a way of garnering substantial capital for continued operation and growth. This is the most substantial method for investors to achieve a return on their investment.
5. Return. Upon an exit, investors receive funds based on their relative ownership. These funds are then available for reinvestment in new opportunities as the cycle of development and growth continues [2].

The decision to invest in a given company involves multiple criteria including clinical needs, technical/scientific variables, market factors, business model, regulatory challenges, legal issues (especially around intellectual property), reimbursement, market acceptance, timing, and the management team involved. These items are discussed in detail later in the chapter. However, it is useful to discuss the recent history of venture capital support of medical device innovation and the implications of recent trends on this arena.

Historical Position of Venture Capital in Medical Device Development

Historically, medical device development is highly dependent on venture funding. Over the past 20 years, venture investment in the USA has gone through two apparent cycles: one peaking in 2000 and the other, much smaller, peak occurring in 2007 as seen in Fig. 10.1. Though 2014 showed an uptick in overall venture funding in the USA, all of the increase occurred in the Technology/Computers/Telecom sector and the Life Sciences sector saw a marked turndown.

Except for some late year activity in 2014, venture capital has remained relatively flat in total and has dropped as a percentage of total financing. Table 10.1 details the areas where capital was raised from all sources since 2007. As the largest growth in capital raise occurred via debt, innovation likely faced new hurdles as debt can hamper a young

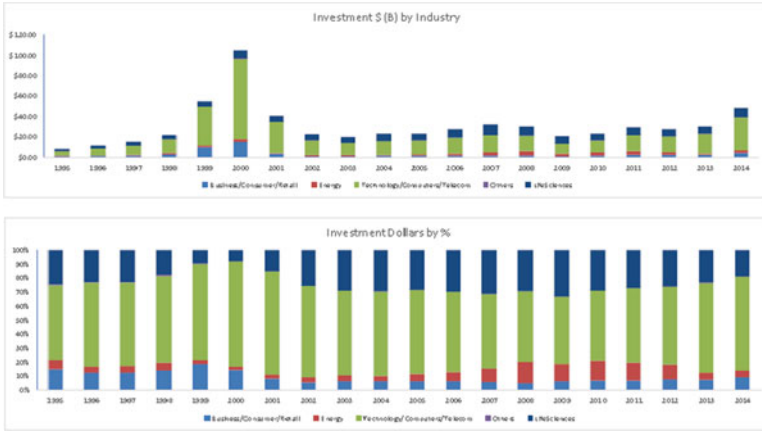

Fig. 10.1. Total investments by industry (US). (Data from the National Venture Capital Association).

Table 10.1. Capital raised in the USA and Europe (US $).

Type	2008	2009	2010	2011	2012	2013	2014
Venture	39 %	36 %	23 %	22 %	17 %	13 %	16 %
IPO	10 %	0 %	2 %	4 %	2 %	1 %	5 %
Follow-on and other	16 %	14 %	11 %	13 %	4 %	13 %	7 %
Debt	35 %	50 %	64 %	62 %	77 %	73 %	71 %
Total ($ million)	$1,311	$12,922	$20,820	$19,081	$26,023	$31,643	$27,306

Data from Ernst & Young, Pulse of the Industry, Medical Technology Report 2012

company's ability to raise additional capital, whether through venture capital or other vehicles.

Finally, when looking at the trend in the number of transactions executed as detailed in Fig. 10.2, the average number has been relatively flat over the last 10 years. With the total amount invested being slightly larger, there is the implication that certain, individual deals drive the average and that these deals are mostly later stage ones, that is, more mature companies.

More telling is the drop in venture capital support for medtech companies. As mentioned, these innovative companies are supported mostly by venture capital. The trends in the charts in Fig. 10.3 reflect

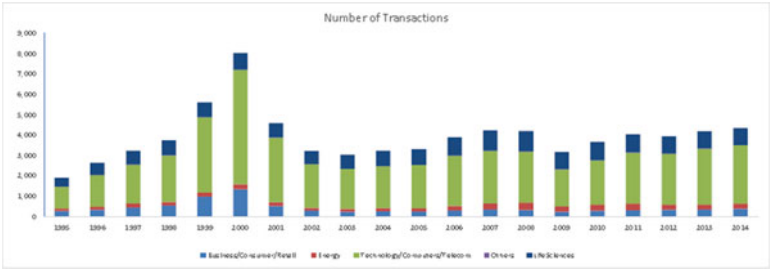

Fig. 10.2. Number of transactions. (Data from the National Venture Capital Association).

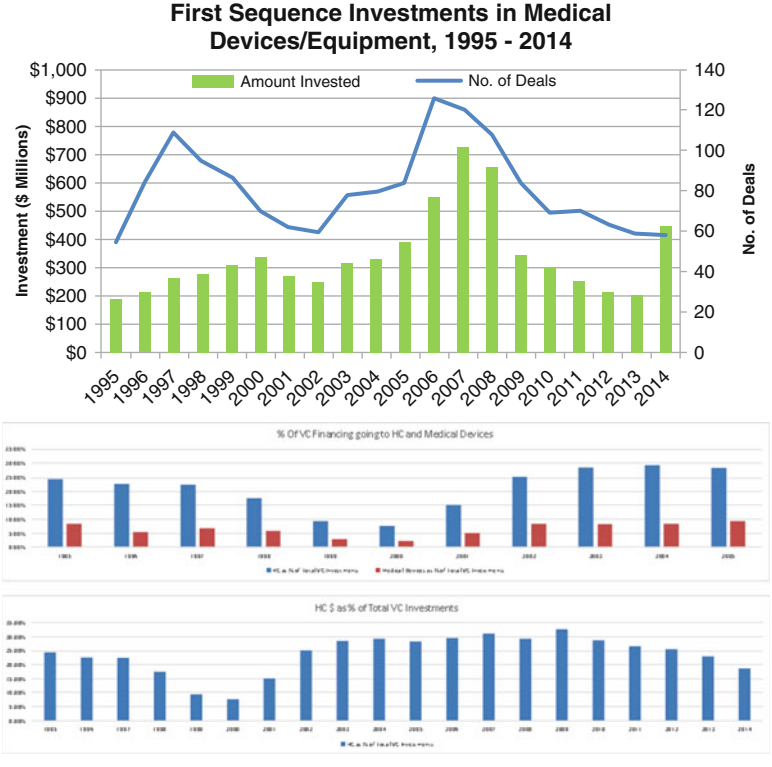

Fig. 10.3. Total investment in medical devices and equipment, 1995–2014. (Data from the National Venture Capital Association).

not only a decline in overall healthcare investment from the venture world, but a more rapid decline in the proportion of this funding taken in by medtech firms [3].

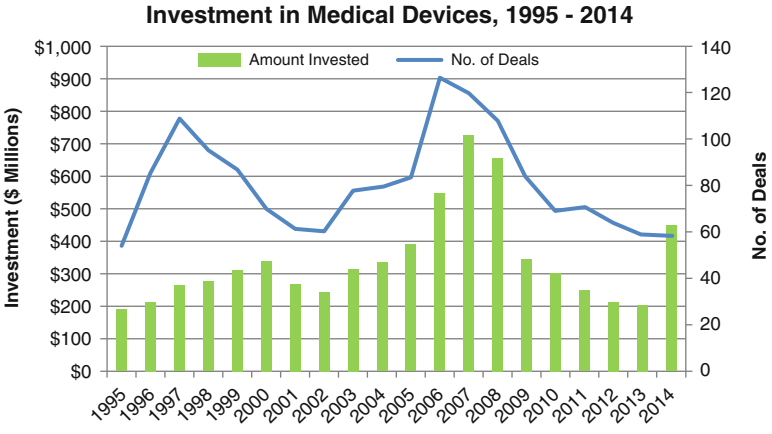

Fig. 10.4. First sequence investments in medical devices 1995–2014. (Data from The MoneyTree™ Report, PricewaterhouseCoopers and the National Venture Capital Association, 2015).

Finally, and potentially the most significant trend, Fig. 10.4 shows a precipitous drop in first sequence, venture investments in medical device development, both in terms of money and number of deals done. While there is an increase in 2014, this is likely due to a small number of large deals not typical for the last several years. As discussed, the lack of resources, especially from the source most likely to accept the risk-reward ratio involved, is a serious threat to the ability for this entire sector to bring new products to the market. In particular, fewer resources in the initial sequence stop new ideas from getting started.

According to PricewaterhouseCoopers, software, media and entertainment, and biotech garner the largest venture investments and this trend will continue [4]. Losing the battle with other sectors for capital amidst changing security regulations and tax codes is challenging enough for medtech enterprises. A number of other issues more specific to the medtech arena raise the level are of concern in the near future.

Medical Device Development

Life sciences as a whole may be the most complex investment area, facing downward trends as discussed. Overall, many factors are impacting the size, type, and source of venture funding such as movements to

emerging markets, competition from new markets outside the USA and Europe, changing and often more demanding and cumbersome regulations, changing/unpredictable reimbursement policies, changing decision processes, and changing models for the way care is provided.

Medtech carries many of these complexities along with some specific items that hamper the investment needed to drive innovation. Closer scrutiny of a few specific items raise particular concern for future investments in medical device innovation, especially in the USA, which remains the largest market and source of such innovation, including:

1. Overall trends in costs and time needed to get to market and/or exit
2. Increased regulatory burden
3. Increased tax burdens
4. Increased reimbursement/payment challenges
5. Increased industry consolidation and
6. Interactions across technologies

Each of these warrants consideration as development plans are made and investments are placed. All have an impact on the risks associated with getting to market, the time and expense of doing so, and the eventual return generated. The combination of so many factors creates management challenges for innovators running new companies and a more complex risk profile for investors with the option of putting capital into other less complex endeavors.

Overall Trends in Costs and Time

Creating and marketing medical devices is a risky pursuit. The process from idea to practical clinical application is long and expensive. Traditionally, early research is performed in academic institutions, while device development, testing, and production occur in the corporate environment. Processes are costly and frequently take years to accomplish. In spite of extensive testing of products, product failures do occur after they reach the market, potentially causing serious medical problems for individuals and financial disaster for the manufacturer.

A 2010 study, out of Stanford University surveying about 20 % of all US medtech companies, estimates that the average cost of taking a 510(k) product from concept through clearance is $31 million. For the more complex PMA process, gaining approval costs approximately $94 million [4].

Depending on the complexity of the device involved and the size of the target patient population, the average development time for a 510(k)

product to reach the market is 3–5 years, while one requiring the PMA process is 5–10 years.

These are large sums of money and long periods of time, especially considering the investments do not include the sales and marketing expenses necessary to launch the technologies, nor the cost to set up operations and manufacturing. These figures and timelines are to get the device through regulatory approval but not yet at the point where it starts earning revenue. Most investors and founders seek an exit, typically via acquisition or IPO, along the way to obtain their return earlier and not have to shoulder the burden of growing a market and supporting operations.

Increased Regulatory Burden

The Federal Drug Administration (FDA) oversees the approval process for new medical technologies sold in the USA, doing so under the two-fold responsibility of protecting public health and promoting innovation. Within the FDA, the Center for Devices and Radiological Health (CDRH) has the responsibility of reviewing applications for new medical devices. In recent years, after a number of notable safety issues and product recalls, FDA's emphasis has been more on patient safety than innovation.

With pressure from industry, investors and certain patient advocacy groups to improve regulatory review times and processes through added resources, Congress enacted legislation, first in 2003, then again in 2012 to create, and increase, user fees paid by industry applicants with their new product submissions. A review written jointly by the California Healthcare Institute and the Boston Consulting Group [5] pointed out that during the first phase of user fees, contrary to the intention, approval timelines actually increased, and that the more recent timeframe under higher fees shows some evidence of improvement, but there are insufficient data to confirm a lasting trend.

A number of studies have explored the issue of FDA approval timelines for medical devices, with specific comparison to medical device approvals made in Europe, the second largest market for such products. Two major differences in structure and approach between the USA and Europe exist that underlie the differences in how long it takes new devices to obtain approval. First, there is the difference in the type of evidence required. In the USA, FDA requires "safety and efficacy" proof for a PMA device and "substantial equivalence" for a 510(k) device,

which also includes an element of effectiveness. In Europe, the burden of proof to obtain a CE Mark, the marketing and distribution approval, relates only to safety. Second, the review and approval process itself is handled very differently. In Europe, this process relies extensively on entities called Notified Bodies, which may be private companies or foundations. There are about 50 such entities accredited by the member states of the European Union, which gives them the ability to determine whether a product, a medical device in this instance, meets the predefined standards of the EU Medical Devices Directive. If a positive determination results, then the company can obtain a CE Mark. These entities therefore offer numerous avenues for review versus the single, centralized agency in the USA, FDA's CDRH. While the differing structures do not guarantee differences in development timelines and costs, they certainly lay a foundation for different results.

In fact, significant differences have been found. The Stanford study pointed out that greater than 75 % of the development costs for a new medical device in the USA involve regulatory-related activities ($24 out of $31 million for a 510(k) device and $75 out of $94 million for a PMA device). The study also found significantly longer timelines for approval in the USA (510(k) and PMA applications) compared to those in Europe (CE Mark) (Table 10.2).

The additional 2–4 years that a device may take to obtain clearance in the USA is costly in multiple directions. By taking more time to get to market, more money is spent, time under patent coverage is spent, market

Table 10.2. 510(k) and PMA regulatory timelines.

	FDA reported review time	**US companies' experience in the USA**	**US companies' experience in Europe**
501(k)	Average time from receipt to final decision = 3 months	Average time from first filing to clearance = 10 months/ Average time from first communication to clearance = 31 months	Average time from first communication to certificate = 7 months
PMA	Average time from filing to approval on original PMA = 9 months	Average time from first communication to approval = 54 months	Average time from first communication to certificate = 11 months

Data from FDA Impact on US Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, J. Makower et. al. for Stanford University, MDMA, NVCA, and PricewaterhouseCoopers, LLP, pg 22

conditions change, and patients continue to go without a new therapy. As the FDA requires more evidence, this time is more costly still.

While the FDA may have a different structure than other agencies abroad, particularly those in Europe, it appears a considerable part of the gap in approval times and the consequential impact on investments, company values, and patient access is due to the manner in which the FDA interacts with applicant companies. More data from the Stanford Study reflect difficulties in dealing with the FDA. Across the areas of predictability, reasonableness, transparency, and overall experience consistently rated their experience dealing with the CE Mark process much more favorably than their experience with the FDA (Fig. 10.5).

Though these areas are difficult to quantify, the consistency of responses and the significant differences demonstrate a clear perception by companies that the FDA is less predictable, reasonable, and transparent than their European counterparts. Small start-up companies launching new technologies often have limited capabilities to negotiate regulatory issues. Coupled with limited financial resources, uncertainty as to the path they take and the expectations of those that determine their fate with respect to approval to market their product is a young company's worst nightmare. Consequently, it is predictable to see how an environ-

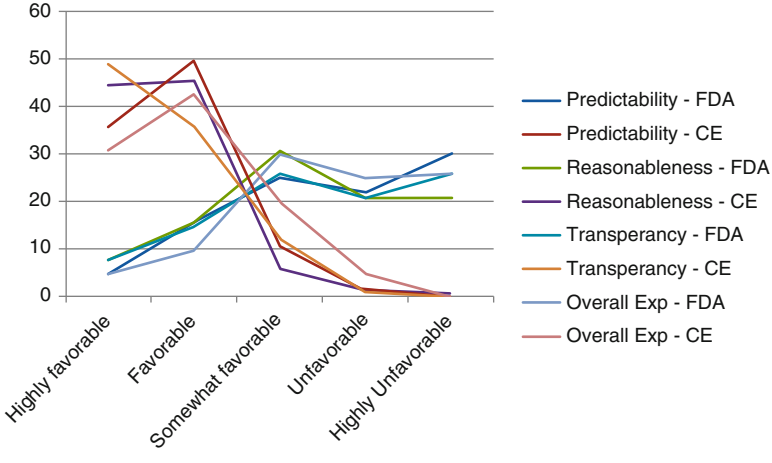

Fig. 10.5. Company ratings of FDA and EU regulatory interactions. (Data from FDA Impact on US Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, J. Makower et. al. for Stanford University, MDMA, NVCA, and PricewaterhouseCoopers, LLP).

ment with additional data requirements and unknown or changing expectations can lead to delays, additional costs, and lower investor interest. The outcome often becomes less innovation developed in the USA for US patients.

Increased Tax Burden

Two tax issues impact the economics of medical device innovation in the USA in important ways and with implications beyond the profitability of a given firm. One is general and one is very specific for this sector. The general item relates to the US statutory corporate tax rate, which stands at 39.1 % (a combination of a 35 % federal rate and the average state level rate), one of, if not the highest in the world. In comparison, the average rate in Europe is 18.6 %, and in a few countries around the world, it is 0 %. Also, the trend in most countries outside of the USA has been a decline in corporate tax rates, which encourages investment and growth in those locations [6, 7]. With deductions and other programs, the effective tax rate in the USA may be considerably lower. Such options exist in other countries as well, and the administrative burden of managing the accounting and filing complexities needed to achieve lower rates carries additional costs. As companies see high US tax rates as an increasingly negative issue for their bottom line, the logical step is to domicile their corporation in areas where tax rates are considerably lower, freeing up capital for growth and shareholder returns. The most notable move in this regard was the merger of Medtronic and Covidien, which resulted in the largest medical device company in the world forming its headquarters in Ireland. As more companies pursue this strategy, medical device innovation in the USA faces additional risk.

More specific to the medical device industry, in 2010 Congress enacted the Patient Protection and Affordable Care Act, which included a medical device excise tax of 2.3 % tax on medical device sales. For detailed language see:

- 26 USC 4191; Health Care and Education Reconciliation Act of 2010, Section 1405 (Public Law 111–152) [8].
- For purposes of the tax, a device is defined as intended for humans as defined in section 201(h) of the Federal Food, Drug and Cosmetic Act.
- Internal Revenue Service, Final Rule, Taxable Medical Devices, Dec. 7, 2012, 77 FR 72924 [9].

This tax is assessed without regard to profitability, placing a tremendous burden on young, early stage companies [10]. Ernst and Young estimate this to raise the effective tax rate for a medtech company by 29 %. The impact on after-tax profitability can be as high as 6.6 %, definitely a negative aspect for potential investors. The net effect of this tax on a "venture-financed, loss-making, young, start-up" is that expensive venture capital is paying the government taxes. This puts US venture-backed companies at a special disadvantage compared to other parts of the world where the governments are pouring money into venture funds to develop local industry.

The two leading trade organizations for this industry, the Medical Device Manufacturers Association [11, 12] and the Advanced Medical Technology Association [13], analyzed the impact of the excise tax, finding the following:

- 195,000 US jobs lost – 39,000 in the industry and 156,000 indirectly related jobs
- 53 % reduction in R&D investments by US medtech companies
- 75 % of companies postponed or canceled capital investments, new facilities, or new venture investments

Also, these companies said a repeal of the excise tax would lead them to:

- Hire new employees (85 % of respondents)
- Increase R&D spending (80 % of respondents) on average by 14 %

A prominent consumer advocacy group, the Consumer Protection Union, formulated a different view of the medical device excise tax [11]. The organization's brief outlines three justifications for keeping the tax:

1. Shared contribution to cover new insured people
2. Bigger pool of covered/insured people to sell to
3. Industry is profitable

While the increased funding to broaden coverage dictated by the Affordable Care Act is an obvious need, there is no obvious reason why the medical device industry should be singled out in this regard. There is the argument that more people will have coverage, and therefore, the number of potential customers in need of, and capable of, paying for new medical devices increases. In reality, the need does not change and the potential reimbursement is questionable as there is no assurance that the new device will be covered. There is also extensive discussion concerning the profitability of the medical device industry, and the relatively minor, financial impact such a tax has on the growth and returns seen by

these firms. However, the discussion itself points out that most of the high profit margins belong to the large, publically traded firms. In addition, the same discussion highlights the fact that the medical device industry is made up of many smaller firms, with their revenues and profits based on a single product, unlike other sectors within healthcare. As mentioned here, a sales tax is particularly hard on a smaller company, especially if it has not reached profitability. In many instances and in growing numbers, the very large medtech companies support development in smaller companies and later license the technology or acquire the smaller company. Here, they are essentially reinvesting their supposedly ultra-high profits back into innovation, which they can bring to market in a more expansive and effective manner.

Update: As discussed, the medical device excise tax enacted as part of the Affordable Care Act (IRS code section 4191) put a 2.3% tax on the revenues of medical device companies. However, The Consolidated Appropriation Act, 2016 (Pub. 6. 114-113) was signed into law December 18, 2015 providing for a two year moratorium on the excise tax. While this is a welcome development for the medtech industry, it still poses a bit of uncertainty as the 2 year period could end with no renewal, there could a permanent repeal of the tax, or there could be a string of extensions.

Increased Reimbursement Challenge

An important item to remember is that regulatory approval to market a medical device in the USA does not guaranteed coverage or payment for the device. Similar challenges apply in Europe and other jurisdictions. Once the regulatory hurdles mentioned earlier are cleared for a particular medical device, CMS, the agency that approves Medicare and Medicaid payments, must approve coverage of the device for the FDA-cleared indications under an independent process. There are also requirements for many new devices to demonstrate other, nonclinical, benefits such as resources utilization, cost savings, and reduced complications. Savvy companies collect much of these data during their clinical development, but uncertainties exist during that stage as to what data are pertinent for the later discussion. Some private payers have recently insisted that medical device companies show cost-benefit advantages to existing therapies in at least six peer-reviewed journals prior to making a coverage determination. Once coverage is granted, payment codes are generated. During the process, there are ongoing discussions with the company concerning value and pricing. Here again, there is considerable

uncertainty as to the timelines for coverage and setting codes, and the price. This process can take 12–15 months, and in some cases up to 3 years following FDA approval.

Private payers typically follow CMS in their coverage and coding decisions, building on the foundation built by CMS but delaying the opportunity further for a new technology to get to patients.

Adding to the uncertainty are changes in the manner in which healthcare technologies are paid for in terms of their perceived value (and subsequently agreed-upon price) and who has the most influence in evaluation and purchasing decisions for new devices. Traditionally, physicians drove the selection of what treatment, and specifically which medical device, a patient received. In Ernst and Young's report [14], survey results present a picture of considerable change in the near future on such decisions. The report depicts the move by hospitals away from mere cost-cutting on specific items to more emphasis on broader elements of cost and care. Specifically, items such as reduced hospital stays, surgical efficiency, drug utilization, and readmissions are becoming more important.

Even the focus on broader cost management does not fully capture the direction foreseen by the survey participants. The perceived shift away from cost-cutting to value generation at the level of the hospital is driven in part by new legislation and other initiatives. Health care reform initiatives are more central in the planning and decision-making for hospitals, particularly in terms of the services and technologies they offer. Once again, medical device companies face an imprecise future, forecasted to require proof of value that is not currently well defined or captured. The criteria used for such assessments will continue to evolve, another type of uncertainty making it difficult for companies to plan well as they bring new devices to the market.

While the study also showed that price remains central to the discussion and the uptake of a new device, a shift from user-centric areas for product differentiation to quantifiable impact on patient outcomes and service delivery is the new paradigm. Products will have to use data to demonstrate clinical outcomes, show value to the system, and share risks.

The combination of these trends leads to a reduction in the influence of physicians in the selection of the devices offered and used. Going forward, the expectation is that those with budgeting and spending authority, that is, CFO, procurement, purchasing and payers, will play a larger role in such decisions. If that is indeed the case, the development of new devices will involve new data and its presentation to new decision-makers.

Increased Industry Consolidation

The recent Medtronic and Covidien merger (over $46B and almost 2x larger than the next largest medtech deal) reflects a number of aspects of the corporate environment that pose new hurdles for the small, innovative medical device company. Such deals typically seek to bring cost savings through operational synergies, broader product offerings to create "1-stop shopping" model, and expanded distribution (typically to a global scale for large mergers). Recently, two additional trends have spurred consolidation of large firms. One is the corporate tax issue referenced above, where companies seek to protect profits that can be used to spur growth, development, and acquisitions. The other is the increase in divestitures (or spinouts) of certain divisions or product lines.

A small number of larger firms consolidate resources, intellectual capital, and access to the market. For those small, innovative companies looking to be acquired, or at least partner with a larger firm, there are fewer places to look and less of a competitive market for their offering as an acquisition. With increased divestitures, the acquirers themselves are putting competitive offerings into the field with mature operations. Once again, trends are difficult for a small firm with limited resources to address.

The contrasting opportunity may exist as mid-sized companies wishing to grow and compete acquire smaller firms rapidly.

Interactions Across Technologies

As discussed, the procurement environment is changing with different variables becoming more important and different people having more influence in purchasing decisions. Combining firms often means bringing multiple products together in the same sales effort. Even from a technological viewpoint, combining two or more devices, or devices with drugs, biologics, or services, may offer better, more coordinated care to patients and more efficiency to the system involved. While logic and opportunity may drive such combinations and product interactions, bundled technologies present increased complexity in terms of studying the collective effectiveness, gaining approval of the combination, managing relationships across multiple vendors, and marketing in a coordinated manner. Once again, the small, innovative medtech firm is faced with a more complex undertaking with a poorly defined path to success, and being highly dependent on products made and distributed by others.

The emergence of Accountable Care Organizations (ACOs) demonstrates one scenario where these issues all culminate. The decision-making is based on measures of quality of care and patient outcomes. Purchasing is done in a centralized manner. Selling to such organizations requires a sales and marketing enterprise beyond what is typical of small companies. It also points out the need for such caregivers to find, and optimally utilize, new technologies that combine improvement in patients' outcomes, process of care, and the economics of providing care.

Conclusions

In the USA, there are over 6,000 medical device companies in the USA where each faces multiple challenges:

- Decreasing capital from venture capital, the traditional source of enabling funds
- Increased international competition, both for technologies and for investment dollars
- Increased complexity in the marketplace
- Increased regulatory burdens in the USA
- Changing criteria in the methods by which new technologies are covered and reimbursed

Overcoming these challenges as a start-up, medical device company, no matter how innovative their technology may be, is impractical for many of these companies and their founders if traditional methods are used and trends of the last decade continue. Traditional venture capital support has leveled out, at best. For companies to thrive, they likely need new funding sources, niches where competition for resources is likely not as stiff, where partnerships readily present themselves, or where larger corporate players have a stronger and urgent need to add technologies to their portfolios. New opportunities exist in terms of looking at developing markets and new funding entities, but a lack of data about these areas makes forecasting risky and planning uncertain. The innovators of the future will need innovation beyond just their technology.

Recent Developments and Hope for the Future

While it appears many of the traditional, or "standard," methods of innovating and securing the necessary resources to create and develop new

medical devices face significant challenges and negative trends, there are a number of trends that point to a more positive future.

New Markets

World markets are changing and as population and economic realities change, so do the markets for medical devices. The BRIC countries (Brazil, Russia, India, and China) make up 40 % of the world's demand for better healthcare technologies and quality. Challenges continue in these countries with respect to intellectual property and contractual rights, as well as regulatory and reimbursement processes. However, many of these items continue to evolve with regulatory reform and cross-border collaborations creating opportunities for medical device innovators from the USA and Europe. These markets promise to be the largest in the world by 2050. Though they each spend considerably less per capital on health care than the USA, meaning per unit pricing may be a challenge to new companies, their collective middle class is forecasted to be twice as large as the G7 countries combined by 2020 [14, 15]. Populations this large with new wealth will need advanced healthcare options and present more space to compete.

Innovation Support

According to the Innovation Learning Network [16], there are over 100 innovation centers in the USA devoted to healthcare with their own membership made up of healthcare systems, health foundations, safety net providers, design/innovation firms, and tech companies. Couple this with the various translational medicine institutes at most academic medical centers as well as other leading providers, and the focus on innovation appears high and growing in new ways. These entities are bringing financial resources from the organizations directly as well as partnerships with investment firms. They also bring facilities, expertise, and access to patients. The new combination of expertise is meant to seek and develop technologies needed by providers and health systems utilizing their input from the outset. Since many medical devices emanate from academic medical centers and many future ones are likely to come from large, multihospital systems, these new models of collaborative financing show promise.

Regulatory Reforms

Earlier reviews of the FDA pointed to two major areas challenging medical device companies: poor interactions and slow processes. In an effort to improve collaborations with developers and field experts, the FDA has instituted a number of pilot projects such as the following, all showing promise in improving relationships between developers and regulators:

- Expedited Access Pathway Program [17]
- FDA-TRACK Program Areas and Dashboards [18]
- Third Party Review [19]
- Medical Device Single Audit Program (MDSAP) Pilot [20]

Possibly more promising are the reforms aimed at improving review and approval times. In "FDA Exempts 120 Medical Device Types from Most Regulation" posted June 30, 2015, Alexander Gaffney, RAC reports the FDA is showing its intent to exempt many devices from premarket notification requirements as provided in its new final guidance document, "Intent to Exempt Certain Unclassified, Class II, and Class I Reserved Medical Devices from Premarket Notification Requirements" [21]. Though many are low-risk devices, the direction of removing the heavier burden of a 510(k) process for some devices could be an indication of a more flexible agency [22].

In addition, the US House of Representatives approved in May 2015 H.R. 1455 "Speeding Access to Already Approved Pharmaceutics Act" [23]. Though not dealing with devices, the direction is a promising one for taking technologies approved in other areas and reducing US approval times by relying more on the process used elsewhere.

The most sweeping legislation may be H.R. 6 "The 21st Century Cures Act," which is a broad sweeping piece legislation that incorporates items from a number of other bills submitted in the last couple of years [24]. On the drug side, there are items related to reliance on surrogate endpoints and biomarkers that will no doubt raise concerns. In addition, there is a directive to consider other, nontraditional study designs. For medical devices, however, there are a number of sections that hold promise that the FDA is moving in the right direction. Examples include the ability to designate certain devices as "breakthrough" technologies providing them with faster reviews and earlier market entry based on early data and lack of suitable alternatives. There is the possibility of using patient-reported data, including in the postapproval phase, which can change the dynamic and expense of data collection in many cases. To promote innovation, there is a 3 % annual increase to the NIH's budget

as well as a newly created "Innovation Fund" allocated $2 Billion a year for 5 years. Though the final approval of H.R.6 has not occurred, it has bilateral support and points in many promising directions.

A final promising, and practical, note on the regulatory side comes with the approval of both the Edwards Lifesciences Sapien 3 Transcatheter Heart Valve on June 17, 2015, some 6 months ahead of expectations, and the Medtronic CoreValve Evolut R on June 23, 2015 [25–27].

Patent Reforms

Another piece of "The 21st Century Cures Act" addresses the addition of patent exclusivity time for certain technologies and devices. These can be of considerable value to a company. However, this is an active legislative area and where turmoil and confusion reign at the moment. No less than 14 bills have been introduced in the past 2 years addressing some aspect of patent reform.

The most practical item to actually pass was H.R. 160 "The Protect Medical Innovation Act" voted on June 19, 2015 and passing by a 2 to 1 margin [28]. This bill repeals the medical device excise tax and addresses one of the more painful issues facing US medical device companies, as discussed.

The best summary of such legislation and the status of each can be found at http://www.raps.org/Regulatory-Focus/News/Databases/2015/06/03/20955/FDA-Legislation-Tracker [29]. With much work and debate left, the results are yet to be seen, but there is at least attention to another area where clarity is needed for innovators to have a chance of plotting a successful course.

New Capital Sources

As future support from traditional venture capital sources remains uncertain, other, nontraditional sources look to participate in medical product innovation, offering services, facilities, knowledge, access to patients, and direct capital. As mentioned, the NIH budget may increase, which leads to increased funding to academic medical centers and the FDA is looking to establish an "innovation fund," both of which present opportunity to medical device developers. Since 1982, the US government has provided support via Small Business Innovation Research and Small Business Technology Transfer (SBIR/STTR) programs, encouraging

research focused on commercialization in numerous areas with life sciences included [30]. Jonathan J. Fleming of Oxford Biosciences offers in his article "The Decline of Venture Capital Investment in Early-Stage Life Sciences Poses a Challenge to Continued Innovation" [31], recommendations for policies creating targeted areas of interest for such funding (i.e., oncology, cardiovascular disease, neuroscience, etc.). Large health systems, often the leading consumers of medical devices and increasingly more accountable for the economic impact a device provides, look to participate directly in new product innovation, and they have substantial capital to deploy. There are numerous philanthropic funds that take on more direct roles, akin to that more often seen with a VC firm, such as the Coulter Foundation and Broadview Ventures. Finally, various patient advocacy groups have gone beyond awareness campaigns and put significant funds into facilities, research tools, and direct company investments. The Clinical Research Forum, a consortium of academic health systems, professional societies, and medical product manufacturers, commissioned a paper to summarize such efforts in a white paper, "Partnerships with Patient Advocacy Groups/Voluntary Health Organizations Can Bridge Gaps in Clinical Research." [32]

In summary, the funding of medical device innovation is at a crucial juncture. While there may be worrisome trends with respect to the way funding and development have worked in the past, there are signs pointing to a resurgence of certain elements as well as the emergence of new trends and organizations bringing capital and other resources. Innovators are driven to solve problems and challenges. With new funding sources and parameters in the mix, new innovators have new opportunities. A new product, despite its apparent novelty and promise, is not a successful innovation unless part of that innovation includes the means to successfully bring it into the marketplace. Unless a product is successfully commercialized, it will never make it to the patient's bedside in any meaningful way. This new environment presents the opportunity to innovate not just the devices under development but also the methods by which they are developed and brought into the marketplace.

References

1. www.commerce.gov/medical-device-industry-united-states/
2. www.nvca.org. Funding innovation.
3. The MoneyTree™ Report, PriceWaterhouseCoopers and the National Venture Capital Association, 2015.

4. FDA Impact on US Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, J. Makower et. al. for Stanford University, MDMA, NVCA, and PricewaterhouseCoopers, LLP.
5. Gillenwater T, Calcoen D, Elias L, et al. Taking the pulse of medical device regulation & innovation. California Healthcare Institute and The Boston Consulting Group; 2014.
6. "Table 11.1 Corporate Income tax rate" at www.stats.OECD.org
7. "The U.S. Has the Highest Corporate Income Tax Rate in the OECD" by K. Pomerleau and A. Lundeen at www.taxfoundation.org
8. 26 USC 4191; Health Care and Education Reconciliation Act of 2010, Section 1405 (Public Law 111–152). http://www.gpo.gov/fdsys/pkg/PLAW-111publ152/pdf/PLAW-111publ152.pdf
9. Internal Revenue Service, Final Rule, Taxable Medical Devices, Dec. 7, 2012, 77 FR 72924. See https://www.federalregister.gov/articles/2012/12/07/2012-29628/taxable-medical-devices
10. Ernst & Young, Pulse of the Industry, Medical Technology Report 2012.
11. "Medical Device Manufacture Profits" Medical Policy Brief, Consumer Protection Union, September 2013.
12. Medical Device Manufacturers Association (MDMA – see www.medicaldevices.org)
13. Advanced Medical Technology Association (AdvaMed – see www.advamed.org)
14. "Pulse of the Industry: Differentiating Differently," Medical Technology Report 2014, Ernst and Young.
15. www.globalsherp.org/bric-countries-brics
16. Innovation Learning Network (ILN – see www.innovationlearningnetwork.org)
17. Expedited Access Pathway Program. http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/ucm441467.htm
18. FDA-TRACK Program Areas and Dashboards. http://www.fda.gov/aboutfda/transparency/track/ucm195008.htm
19. Third Party Review. http://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/thirdparyreview/default.htm
20. Medical Device Single Audit Program (MDSAP) Pilot. http://www.fda.gov/medicaldevices/internationalprograms/mdsappilot/default.htm
21. "FDA Exempts 120 Medical Device Types from Most Regulation" Posted June 30, 2015, Alexander Gaffney, RAC.
22. Intent to Exempt Certain Unclassified, Class II, and Class I Reserved Medical Devices from Premarket Notification Requirements. http://www.raps.org/Regulatory-Focus/News/2015/06/30/22812/FDA-Exempts-120-Medical-Device-Types-from-Most-Regulation/#sthash.Usp5j3xH.dpuf
23. H.R. 1455 "Speeding Access to Already Approved Pharmaceutics Act."
24. H.R. 6 "The 21st Century Cures Act."
25. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm451678.htm
26. www.prnewswire.com/news-releases-edwards-recieves-fda-approval-for-sapien-3-transcatheter-heart-valve300101101.html
27. newsroom.medtronic.com/phoenix.zhtml?c=251324&p=irol-newsArticle&ID=2061818

28. H.R. 160 “The Protect Medical Innovation Act.”
29. http://www.raps.org/Regulatory-Focus/News/Databases/2015/06/03/20955/FDA-Legislation-Tracker
30. www.sbir.gov
31. Jonathan J. Fleming of Oxford Biosciences offers in his article “The decline of venture capital investment in early-stage life sciences poses a challenge to continued innovation”. Health Aff 2015;34(2):271–6.
32. Bond G, et.al. Partnerships with patient advocacy groups/Voluntary health organizations can bridge gaps in clinical research by (12/2011). www.clinicalresearchforum.org