

Biomedical Innovation: Identifying Challenges and Prioritizing Needs for Medical Device Innovation September 2014

Introduction

Medical device innovation in the United States is entering an era of unprecedented change. Rapidly evolving technology, emerging markets, an increasingly globalized development process, and evolving health policy reforms are presenting device manufacturers with unprecedented opportunities for valuable innovation, but are also creating significant challenges to the current device development paradigm. In order to translate novel and emerging technologies into safe and effective devices that can benefit patients, it is paramount that the United States sustains entrepreneurship and maintains an environment conducive for innovation. Recent trends in medical device innovation in the United States have been worrisome; financial, regulatory, reimbursement and infrastructural factors have all been attributed as formidable challenges for device innovation.

The Engelberg Center for Health Care Reform and the National Institutes of Health (NIH) held an all-day forum to discuss challenges for developing novel medical devices that benefit patients, and for prioritizing medical device research that accommodates unmet medical need. Over the course of the day, manufacturers, regulators, payers, investors, patient representatives and other stakeholders discussed the challenges faced by medical device manufacturers and innovators. Challenges faced at all stages of the device development pipeline through the total product life cycle (from conception of the device through proof of concept, clinical trials, and establishment of the regulatory and reimbursement requirements to post-market surveillance) were explored to identify areas where policy improvements can have the greatest impact.

The meeting objectives included focusing on the following topics in order to recommend potential strategies:

- Incentives for investment in research and development for novel devices;
- Incentives for investment in small markets and rare diseases;
- Compelling business models for startups, small companies and academia for product development;
- Adequate and efficient infrastructure to support translational science, pre-clinical and clinical testing;
- Transparent, unambiguous regulatory pathways for new and emerging technologies;
- Efficient mechanisms and infrastructure to support evidence generation needed for approval and reimbursement decisions;
- Efficient mechanisms and infrastructure to support real-world effectiveness and post-market safety evidence generation;
- Clear formal and standardized ways for patients to engage in the decision-making process of device development.

Challenges in Medical Device Innovation

Devices are inherently different from drugs

In the early conceptual stage of designing treatment options for particular diseases, it is common to target the biology of the disease since most clinical researchers are trained in biomedical science. There is a scarcity of engineers and experts from the physical sciences in medical research and therefore the opportunity to develop devices, even in instances where it would be more effective in alleviating the disease, is limited. In general, novel therapeutic options based on medical devices suffer from a lack of interdisciplinary collaboration between biological and physical sciences. This fact is exacerbated in clinical practice because physicians (mainly due to their training) are more comfortable with prescribing drugs as a treatment for patients. Because devices may require physician training prior to use, the lag time for physicians adopting them is greater than for drugs. Therefore, devices are usually perceived by physicians only as an adjunct therapeutic tool and not as a first line therapy.

The nature of developing a novel medical device is in itself a daunting task. Unlike drugs, devices such as implantables may reside in patients for a long time. Therefore, the kinds of tests that must be conducted to demonstrate long lasting safety and effectiveness of the product are much more challenging. In addition, testing may need to be conducted on multiple versions of prototypes during the manufacturing process, and in some cases, software must be validated, including even cyber security. The iterative nature of device development prolongs the development process, which, when combined with rising healthcare costs, impedes innovators from realizing the promised benefit for cost and quality for novel, first-in-class medical devices because the cost of healthcare has been rising faster than the perceived value of these devices. For most startups and small companies, speed to market is an important feature for survival, and the risk of investing in novel and emerging technologies for medical device development is extremely high.

Venture capital, funding and other resources for device innovation

Funding nascent medical device technology often requires that the fundamental science behind the technology is well understood.¹ Recent initiatives for basic science research into medical device and imaging technology indicate that medical device technology remains a targeted long-term goal of American public policy. Such endeavors include the \$100 million dollar Brain Research through Advancing Innovative Neuro-technologies (BRAIN) Initiative and funding efforts from the NIH, including the National Institute of Biomedical Imaging and Bioengineering. Large medical device companies and venture capitalists contribute substantial amounts of resources and time towards developing promising medical technologies by commercializing the breakthroughs made at the level of basic research. Around \$2.1 billion in venture capital was spent in 2013 on medical device companies in the US.² This represents 7% of the \$29.4 billion in venture capital spent in 2013.

However, the “Pulse of the Industry – Medical Technology” report states that venture capital investment in medical devices in 2013 fell 17% from the previous year, a downward trend that has been observed for the past seven years.³ In addition, investment funding is also shifting towards less risky later-stage medical device companies instead of earlier stage ventures.⁴ The opportunity cost in pursuing early-stage medical device companies with unclear exit strategies and regulatory hurdles is high in comparison with software and information technology companies that often offer quick exits and low market entry barriers. These conditions are worrisome since early-stage investment companies can promote speculative and disruptive medical device technologies that introduce new therapeutic benefits or quantum improvements in patient care. Recent evidence indicates that larger medical device companies have also found it challenging to fund innovative technologies developed in-house or through acquisition because of lower revenues. Key factors that have reduced the availability of venture capital

for early-stage medical device companies pursuing pre-market approval include US regulatory unpredictability and delays in approval, and an uncertain reimbursement environment.

Additionally, there is global competition among countries to attract investors in the medical device industry. Countries such as Ireland and the Netherlands offer tax havens and other incentives for device developers in order to promote an environment conducive for entrepreneurship. Lower labor costs and less stringent regulatory requirements in other countries may add to the attractiveness for device companies to move out of the US (OUS). Moving to a country that has lower tax rates and less stringent corporate governance requirements may save large device companies billions of dollars.⁵ For example, the recent decision by Medtronic, one of the largest device company in the United States, to buy Covidien plc. of Ireland for \$42.9 billion may have been motivated by the promise of such benefits, since under current US law, this purchase provides an gateway for Medtronic to move OUS. **Although Medtronic has assured that no jobs will be lost due to this acquisition, it is speculated that the move was due to the large tax savings for the company.**

Lack of public-private partnerships and other collaborative efforts

Compared to the pharmaceutical industry, there have been far fewer public-private collaborations or industry-wide efforts in the pre-competitive space to share data and resources for developing medical devices. Transcelerate Biopharma, for example, is a non-profit organization established by ten pharmaceutical companies (Abbott, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Johnson & Johnson, Pfizer and Genentech), which collaborates in non-competitive space to develop mutually beneficial data platforms.⁶ Such collaborations include creating common clinical trial protocol templates, developing clinical trial networks for pediatric and minority populations, and establishing a global investigator registry. The National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health (NIH) is another such collaboration among government, academia, industry and nonprofit patient organizations that promotes innovative and collaborative approaches in translational science.⁷ These collaborative efforts target specifically drug development; device developers have not in general utilized similar mechanisms, and thus far have largely failed to leverage shared resources and standardized protocols for mutual benefit. The recently established Medical Device Innovation Consortium (MDIC) is the first of its kind to provide a common platform enabling all stakeholders in the medical device ecosystems to work in collaboration.⁸ Although it is too early to assess the impact of MDIC, it could provide a template for future joint ventures, e.g., multi-stakeholder collaborations between device manufacturers, patients and regulators, to harmonize the device development process in the pre-competitive stage, such as standardizing protocols for clinical trial design.

Uncertainty in regulatory and reimbursement processes for novel devices

The FDA's Center for Devices and Radiological Health (CDRH) has taken active measures to address some of the regulatory challenges faced by entrepreneurs in the United States for developing new and innovative devices and bringing them to market. In collaboration with the White House, CDRH initiated an "Entrepreneurs in Residence" program to recruit experts from the device industry to explore how the regulatory process can be streamlined, with the goal that patients in the US receive safe and effective novel devices first in the world. Through its Innovation Pathway program, CDRH identified several challenges for device innovation; two key regulatory barriers that greatly disincentivize entrepreneurs from investing in novel devices are the requirement for lengthy clinical trials and the lack of transparency and flexibility regarding the amount and sources of data that could be used as premarket evidentiary requirements. For entrepreneurs, these factors make the upfront cost was too high, such that risk outweighs the perceived benefit. Therefore, addressing these issues is vital, and to that end,

CDHR has highlighted streamlining clinical trials and balancing pre- and post-market requirements as 2014-2015 strategic priorities for the Center.⁹

Several current features of clinical trial design present barriers to the rapid development of safe and effective medical devices. Traditional frequentist-based randomized clinical trials are widely used as a prerequisite for approval of a novel device, but this statistical approach generally leads to lengthy trials. Conventional trial design, combined with the lack of infrastructure and standardized methods for patient recruitment involving multiple separate Internal Review Boards (IRB), tend to greatly delay the regulatory approval process.

Currently most of the regulatory evidentiary requirements for device approval occur in the pre-market space. Postmarket data can sometimes be used to supplement premarket information to satisfy evidentiary requirements for product approval of a similar device, or to expand the device label to a larger population, thereby reducing the time and cost of developing a medical device. Under certain circumstances (unmet needs), some of the premarket requirements for a novel device can even be shifted to the postmarket. Regulators apply stringent pre-market requirements prior to approval in part because of the presently inadequate measures for postmarket surveillance and the inability to gather reliable information while the device is being used in the real-world setting. This scenario is further exacerbated by the inability to uniquely identify specific devices and link them to patient information with relevant clinical outcomes. Therefore, in the current environment, it is difficult to prove the quality and effectiveness of a particular device while it is in use.

On the other hand, streamlining the regulatory process at the premarket stage, while potentially speeding device approval, may have negative downstream consequences for reimbursement. As a result of reducing evidentiary requirements upfront (at pre-market), payers may determine that the smaller available pool of clinical evidence is now inadequate to support coverage. Currently, there is no transparent, consistent mechanism for reimbursement of novel devices; rather, decisions are made more on a case-by-case basis at the FDA approval stage (once the device is already developed).

Due to the iterative nature of medical device development, the time a device predominates the market is short. The value for each iteration of a medical device is not achieved because incremental feature improvements (which in some cases may in fact greatly enhance the benefit of the previous device) do not receive incremental increases in reimbursement. Furthermore, there is currently no metric that accounts for more esoteric factors such as the improvement in quality of life when payers determine if a device should be reimbursed.

Most innovators are conscious of the regulatory requirements for FDA approval, but seem to be unaware or less heedful early in the device development stage regarding the criteria needed for reimbursement. Early engagement with both FDA and payers would be of great benefit to device developers to understand both processes and to plan their device development process accordingly.

Lack of patient engagement

Opportunities for patients to assert their views on their own needs and empowering them to influence the decision-making process in medical device R&D programs, have been very limited. Although patient and consumer data exists in market research and various surveys, basic researchers who prioritize the R&D agenda for smaller companies or startups do not necessarily have access to this information. Due to the silo'ed nature of data in the current healthcare ecosystems, this information cannot be shared among different stakeholders.

Much of the basic clinical research in the United States occurs in academic settings where only a limited number of patients can access state-of-the-art treatment or participate in clinical trials. In general, the majority of patients do not have an opportunity to be part of the medical device ecosystem and be actively engaged in the decision-making process. Regulatory decisions based on risk/benefit calculations, until very recently, focused mainly on the safety and effectiveness of the device and did not consider metrics such as improvement in the quality of life. Furthermore, patient preferences and their perception of benefits and risks were not widely considered.

Unmet needs

Developing novel medical devices targeted towards pediatric populations and rare diseases have even greater difficulties vis-à-vis the challenges mentioned above. Research cannot be prioritized to address these devices since there is currently no coherent mechanism to assess these needs through the patient perspective. There are few incentives for industry to develop novel devices for rare diseases and pediatric populations; the usual profit margins cannot be achieved by developing devices for rare diseases, while pediatric devices are too risky by nature, especially since clinical trials and other measures for testing the safety and effectiveness of devices are not appropriate for pediatric populations. Unlike drugs, device developers must go through the lengthy IRB process even for devices that are considered to be under the Humanitarian Device Exemption (HDE) rule.¹⁰ As such, these challenges severely constrain the incentive for entrepreneurs to develop devices for rare diseases and pediatric populations.

Strategies and recommendations

In view of the challenges that have been described above, we have synthesized strategies based on the meeting discussion and propose a set of recommendations to promote medical device innovation in the United States on these topics:

- Promoting cross-disciplinary research between the biological and physical sciences
- Fostering an entrepreneur-friendly business environment by creating analytic tools, introducing novel funding mechanisms and forming public-private partnerships
- Enhancing Federal support to provide financial incentives and infrastructure for innovators
- Reducing the regulatory challenges and amending the current structure for reimbursement process
- Increasing patient engagement and empowering patients to participate in the decision-making process of device development

Cross-disciplinary research and education

In order for devices to be considered as first line therapy rather than merely being perceived as a tool to aid in treatment, there must be a fundamental change in the mindset of how particular diseases can be treated. A vital component of changing the current mindset would be increased interdisciplinary collaboration between the biological and physical sciences at the pre-conceptual stage in the development of treatment options for those diseases. Integrated cross-disciplinary programs that enable input from both disciplines would be essential to conceptualize treatment options that target the physical properties as well as the biology of the disease. Large medical research facilities such as the NIH should initiate programs for cross-disciplinary research and provide platforms for collaboration among the various disciplines. This approach would be further aided by the inclusion of cross-disciplinary studies in university curriculums. For example, the National Medical Device Curriculum, already initiated by CDRH and Stanford University will provide students at academic institutions and science and technology innovators with the core information about the regulatory pathway to market. This includes an understanding of the expertise needed to design, test and clinically evaluate devices; identify the root causes of adverse events and device malfunctions; develop designs for devices with repetitive

functions; and, navigate the FDA's regulatory process.¹¹ In addition, once the safety and effectiveness of a medical device vis a vie other therapeutic options is established, mechanisms to disseminate that information should across the health care eco system, especially to practicing physicians should be put in place.

Creating analytic tools for the device development process

Early in the conceptual stage of the development a new device, a set of methods, tools and procedures should be available to provide device innovators with an understating of the factors impacting novel device development throughout its total life cycle. It is important for novel device developers, very early in the process, to be familiar with manufacturing processes, regulatory and reimbursement requirements, as well as the potential market value of the device. Large companies spend time and resources conducting market research and analyzing other relevant data in order to make informed decisions. A similar process, requiring development of data standards and analytics to evaluate various sources of data from the product development process, should be developed and made available to small entrepreneurs and novel device developers. Development of analytic tools by collaborative groups such as MDIC would help device innovators to evaluate factors like development cost, market need, market size, and value added to currently available treatment in terms of quality and cost. Ultimately, such tools should make the process more transparent and also somewhat mitigate the risk of investment.

Building public-private partnerships

MDIC is a non-profit, public-private partnership formed in 2012 by CDRH and Life Science Alley, a Minnesota-based trade association, to improve the state of medical device regulatory science.¹² MDIC accomplishes this mission by funding projects with the purpose of simplifying device design and promoting device innovation.¹³ MDIC is currently engaged in three different project areas: Computation Modeling and Simulation (CM&S), Patient Centered Benefit-Risk Assessments (PCBR), and Clinical Trial Innovation and Reform (CTIR). The aim of CM&S is to improve medical innovation by collaborating with industry, government, and academia to advance the use of computational modeling in medical device development and regulation.¹⁴ PCBR works to integrate patient preferences concerning the risks and benefits of certain medical devices into the FDA's consideration of future regulatory determinations and guidance documents, while CTIR seeks to make the clinical trial process more efficient by improving the methodologies of clinical research.¹⁵ All of these projects work to promote medical device innovation by streamlining and improving the regulatory process (including clinical trials) both from a technological perspective and from a patient perspective, across the total product life cycle.

Establishing MDIC is an important step to promote public-private partnership; the establishment of similar organizations to promote collaborations among diverse stakeholders in the medical device ecosystem is needed. These collaborations could be expanded to facilitate aid to innovators in the pre-competitive stage by taking steps ranging from obtaining initial seed capital to providing incubator or testing facilities for the early device development phase. For example, institutes such as the National Heart, Lung, and Blood Institute (NHLBI) and NCATS at the NIH as well as some academic institutions provide incubator facilities for innovative research to their employees. However, such facilities are currently limited and should be expanded to include eligible medical device innovators on a broader scale. Public- private partnerships fulfil an important role in the innovation space by providing initial capital for innovators for the public good that may otherwise be not funded by for profit ventures.

Novel financing and funding mechanisms

“Crowdfunding” raises monetary contributions from a broad set of people, typically via the internet, for a specific project or venture. Crowdfunding is gaining momentum as a viable funding mechanism.¹⁶ This

new mechanism, although thus far limited in the amount of capital raised, can be a potential future source of funding for device developers, particularly for devices that will fulfill a specific personal need. For example, the Rare Genomics Institute is a non-profit organization created through a crowdfunding model and dedicated to help patients with rare diseases through genome sequencing.¹⁷ The project connects patients with a research institution, and subsequently develops a budget that is crowdfunded. Since rare diseases are frequently caused by genetic mutations in the individual, genome sequencing promotes understanding of the disease. The Rare Genomics Institute also plans to utilize crowdfunding to develop cures for rare diseases using stem cells and aims to raise more money for rare diseases in ten years than the NIH.

Prizes and challenges (for example, developing a device for a specific disease condition), originating with the Federal government or through organizations such as the XPRIZE Foundation, attract interest among device innovators and have often been used as incentives to spur innovation in a given topic.¹⁸ These prizes and challenges have proven to be successful not only in driving innovation, but in many instances, also in promoting economic growth. The XPRIZE Foundation, for instance, is a non-profit organization that designs and manages public competitions intended to promote innovative novel technology for the benefit of mankind. Unlike other organizations, such as the Nobel Prize committee, which award prizes and financial rewards to individuals or organizations that produce novel advances in science, medicine and technology that are not pre-specified, the XPRIZE rewards the first to achieve a specific objective by fulfilling a set of predetermined requirements. This model may represent a viable mechanism to incentivize device innovation, particularly for unmet needs.

Federal support

The National Bioeconomy Blueprint, published by the White House in April 2012, lays the strategic objectives of the Federal government's efforts to enhance innovation in the biomedical field. The five main strategies identified in the report are: supporting R&D investments, increasing the focus on translational and regulatory science, improving regulations to increase predictability and speed to market while protecting public health, aligning training of students with national workforce needs, and developing public-private partnerships through collaborations at the pre-competitive stage. These strategies should be fully implemented, while also continuing and enhancing market-based innovation through the Research and Experimentation (R&E) tax credit. The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs are Federal sources of early-stage capital for innovative small companies in the United States. These programs allow US-owned and operated small businesses that have a strong potential for commercialization to engage in Federal research and development, and they have been successfully implemented through the NIH.¹⁹ In the current economic environment, the continued support of these programs is critical for maintaining opportunities for device innovation. In addition, Federal strategies for facilitating market-based innovation by creating an environment in the US that is conducive for high-growth entrepreneurship and by promoting regional innovative clusters are stated in the White House report "A Strategy for American Innovation" (February 2012). Strong implementation of these strategies by the Federal government can further aid device innovation in the U.S.

Reducing regulatory barriers

Data generated in the postmarket space provide a wealth of information regarding device use that can be leveraged for regulatory purposes. For example, data gathered through a repository that tracks the safety and effectiveness of a particular device can provide evidence to support an expanded indication of use for a larger patient population, but without the added burden of expensive and lengthy additional trials. Under certain circumstances, it may also be appropriate to reduce the level of evidentiary requirements for a particular device at the premarket stage by allowing the data to be collected

postmarket. To that end, the FDA recently submitted a draft guidance “Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval”.²⁰ More specifically, this guidance outlines how the FDA considers the role of postmarket information when determining the extent of premarket data necessary to support premarket approval, while still meeting the statutory standard of reasonable assurance of safety and effectiveness. There have been a series of previous guidances in which the FDA addresses how postmarket data can reduce the pre-market burden. The “Least Burdensome Guidance”, issued in 2002, was a precursor to the 2014 guidance described above.

The guidance “Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications”, issued in 2012, discusses the principal factors that the FDA considers when making benefit-risk determinations during the premarket review and clarifies how the FDA considers postmarket data in the context of the benefit-risk assessment. Finally, the “Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Needs for Life Threatening or Irreversibly Debilitating Diseases or Conditions” draft guidance, issued in 2014, states that the FDA may accept greater pre-approval uncertainty regarding specific benefits and risks of devices that demonstrate potential to address unmet medical needs, as long as the premarket data still support a reasonable assurance of safety and effectiveness. The FDA quarterly performance report through March 31, 2014 shows that these efforts are already generating positive signs for improvement; the review times for higher risk devices that must go through the premarket approval (PMA) process have declined since last year. Although this trend seems encouraging, the FDA could further advance these efforts and provide more clarity by establishing how and what data from the postmarket setting can be used as supporting evidence for label expansion. In addition, the FDA, along with manufacturers and other stakeholders such as patients and clinical societies, should explore when and how postmarket data from devices can be used for purposes other than postmarket surveillance, such as clinical evidence development or comparative effectiveness studies. They also should establish guidelines for leveraging medical device registries for clinical trials.

Since there is no uniform method for postmarket surveillance on medical devices, CDRH has launched several initiatives focusing on improving the ability to collect and monitor postmarket data. First, in collaboration with the Brookings Institution, the FDA has convened a multi-stakeholder Planning Board to develop the methodological infrastructure, business model and governance for a National Medical Device Postmarket Surveillance System. The national system, once in place, will mitigate some of the current challenges in monitoring devices by standardizing the collection of postmarket data across devices. Second, the surveillance process will be aided by the incorporation of Unique Device Identifiers (UDI); the FDA’s September 2013 “Final Rule for a Unique Device Identification System” mandates that, over the next 6 years, virtually all medical devices must have UDIs permanently marked on the device itself as well as in the labeling and packaging.²¹ UDIs will enable the identification and tracking of specific devices throughout their life span. Furthermore, linking UDIs with patient information and the relevant clinical attributes allows analysis of how a device was used, its quality, adverse effects and clinical utility for specific patient populations. Third, in collaboration with Duke Clinical Research Institute, the FDA has also convened a National Registries Task Force to operate under the Medical Device Epidemiological Network (MDEpiNet). The Task Force is charged to: identify registries that could contribute to the national system described above; leverage registries to meet multiple needs such as quality improvement, comparative effectiveness research, and reimbursement; identify registry best practices; and identify “priority medical device types for which the establishment of a longitudinal registry is of significant health importance.”²² Together these efforts should provide the capacity to monitor the safety and effectiveness of medical devices, build clinical evidence for novel devices, and compare the effectiveness between devices with similar intended use.

The effective postmarket surveillance of devices relies on strong collaboration and participation across all stakeholders in the healthcare ecosystem. For example, in order to build clinical evidence for a specific device or compare the effectiveness between devices, device-specific information needs to be linked to patient data, including relevant clinical outcomes that are usually captured via Electronic Health Records (EHR) at provider sites, and analyzed through a registry maintained by a professional society. The necessity for collaboration and interoperability makes it important that each stakeholder group fully understands the value they can derive from participating in the national systems. Small scale pilot studies could therefore be conducted to provide the necessary information to attract stakeholder participation.

Clinical trials constitute a costly and time-intensive step in the regulatory process necessary for bringing a medical device to market. For this reason, streamlining clinical trials to reduce their length and cost is a worthwhile goal for both industry and for public health. Adaptive trial design and the use of Bayesian statistics have been proffered as powerful tools to achieve such goals. These statistical designs allow for sponsors of novel devices to use prior information or trial adaptations to arrive at statistically significant conclusions faster or make beneficial changes to clinical trial protocol that do not compromise the validity or integrity of the study. CDHR has been moving towards the use of adaptive trials; reportedly, the FDA has reviewed approximately 120 adaptive medical device trial designs from 2007 to 2012.²³ The application of Bayesian statistics (in contrast to the frequentist approach) allows utilization of prior information in clinical trial design, which would be particularly advantageous for medical devices because of their often uniquely iterative nature. Advantages of adaptive trials include the ability to use smaller sample sizes and to more quickly assess failure of a certain test or device. Also, adaptive trial design enables a dynamic shift of proving non-inferiority to proving superiority of a product within the context of the same trial. These advantages clearly show that adaptive clinical trials and Bayesian designs should be encouraged for regulatory purposes when appropriate.

Addressing the regulatory aspects of designing clinical trials *per se* is insufficient to streamline the process; rather there must be amendments to methods of patient recruitment, obtaining informed consent from the trial participants, and the current mechanism by which IRBs operate. Standardizing patient recruitment and obtaining the informed consent from the trial participants through clinical trial networks could significantly shorten the time span of a clinical trial. The National Cancer Institute (NCI), for example, recently launched a new clinical trials research network intended to improve treatment for the Americans diagnosed with cancer each year. The new system, NCI's National Clinical Trials Network (NCTN), in response to recommendations made by the 2010 report from the IOM²⁴ will facilitate: rapid initiation and completion of cancer clinical trials based on improvements in data management infrastructure, the development of a standardized process for prioritization of new studies, consolidation of its component research groups to improve efficiency, and the implementation of a unified system of research subject protection. In addition, operating through a centralized IRB process for each trial, rather than through multiple separate IRBs within the same trial, could also substantially reduce the time and cost of getting a product to market.

It is important that there is a clear regulatory path for emerging technologies; usually novel and emerging technologies create new regulatory challenges, and both the sponsor and the regulators must work together to establish the appropriate regulatory requirements for each new technology. CDHR has developed a mechanism to identify specialists and experts in emerging topics through the "Network of Experts" program, with the goal of gathering subject matter expertise in these new fields for regulatory purposes. However, these networks can be expanded further by recruiting experts to help the FDA establish appropriate regulatory measures for emerging technologies.

A more transparent reimbursement model

The device developer should engage in early discussions with the FDA and payers to understand the various requirements for both regulatory approval and reimbursement. In addition to the requirements for FDA approval, device developers should take into account, early in their development process, the level of evidence needed for reimbursement. They must understand the process of how payers interpret data, and what criteria they use for evaluating devices for reimbursement. Unfortunately, streamlining clinical trials by shifting some of the evidentiary data collection into the postmarket setting misaligns these two processes. At the Medical Device Innovation Meeting (Brookings, March 2014), it was suggested that new models for reimbursement should be explored through reimbursement science, and resources need to be allocated for in-depth study of this field. Extant pilots that might serve as models for reimbursement focus on the parallel review of devices for regulatory approval and reimbursement (FDA and CMS), and on restricting the use of the device to a specific population that is more appropriate for the evidence generated through the clinical trial. These pilots, as well as new models, need be further explored to improve the current reimbursement process.

Patient engagement

Engaging patients is vital, not only for understanding of patient needs when prioritizing research and development, but it is also invaluable throughout the development of the device. Patient perspective is important in: designing clinical trials that take into account the risk patients would tolerate to improve a certain disease condition (benefit/risk profile), in aiding regulatory and reimbursement decisions, and finally as end users to provide feedback on the quality of the device at the postmarket level. The recently formed National Patient-Centered Outcome Research Institute (PCORI), authorized by Congress, funds and disseminates research regarding the best available evidence to help patients and their healthcare providers make better informed decisions.²⁵ Such organizations and other patient-interest groups should promote and provide avenues for patient engagement in the decision-making process regarding development of a device, and empower patients to have greater input regarding the devices they need or use to improve their quality of life. For example, PCORI could create partnerships between patient advocacy groups, manufacturers and the FDA to enable patient input in determining the benefit/risk profile of a clinical trial designed to test the safety and effectiveness of a novel device. Facilitating these kinds of collaborative partnerships should introduce the much needed patient voice to the device development process. The current efforts by PCORI to establish an Advisory Panel on Rare Diseases, which includes representatives from patients, patient advocates, industry representatives and other stakeholders, is an important first step towards engaging patients. These efforts should be given prominence by all stakeholders in the healthcare ecosystem and be further expanded to involve patients in the decision making-process of product development.

Conclusion

This paper summarizes the current challenges for medical device innovation by identifying broad environmental, financial, infrastructural, regulatory and reimbursement barriers. It also provides a snapshot of the challenges faced by different stakeholders of the healthcare ecosystem at each phase of the device development pipeline. The paper highlights the expert discussion on mechanisms to mitigate these challenges by collective collaborative action among stakeholders, and synthesizes some high-level strategies and recommendations. This event by the Engelberg Center for Health Care Reform was the kickoff of a series of meetings planned to explore in depth these challenges and their underlying causes, and to formulate a concrete set of actionable next steps to promote medical device innovation.

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