

Overview of Device Development

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Idea

Exit

Topic Relevance by Timeline

Summary

- Device development can be summarized by the Three I's: Identification, Invention, and Implementation.
- The current era of “first to file” requires early patenting.
- There are a number of public and private sources for seed investment.
- Determining the appropriate pathway for regular approval requires accurate risk classification.

Introduction

Over the last decade, there has been an exponential escalation in the pace of medical device development. Part of this can be attributed to the acceleration of manufacturing and digital technologies through the advent of three-dimensional printing for physical devices and smartphones for mHealth applications. As has been the case in other industries, consumers expect rapid development and iteration of medical devices that are cheaper and better than in the past. Although this frenetic pace of innovation should be encouraged, it is nonetheless vital to ensure product safety. This chapter provides a broad overview of device development pathways, from the sparking of an initial idea, obtaining funding for initial seed development, and clearing the Food and Drug Administration (FDA) regulations to ensure a legal, safe commercialization strategy. It is meant to serve as a preface for more detailed subsequent chapters on these individual topics.

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The Three I's: Identification, Invention, Implementation

Established medical device companies generally iterate on existing products, both to mitigate risk and to capitalize on established expertise and partnerships. However, innovative new medical devices are often created on a smaller scale, when physicians or engineers observe an unmet clinical need in their immediate environment. Academic clinicians are uniquely positioned to identify such problems in healthcare, given their frequent exposure to complex and difficult-to-manage clinical cases. This is the first step in early medical device development, as summarized by the Stanford Biodesign Program's "Three I's" process (Schwartz et al.).

The identified clinical need, which can be viewed as the pre-development phase, can then inspire the invention of a solution, which often requires the assistance of an engineer for initial development and prototyping. Careful thought also has to be given to the implementation of the proposed device from a business mindset: discussions of intellectual property, strategies for early-stage research and development, and plans for future commercialization (also referred to as design transfer and post-marketing activities). These steps are discussed in more detail in the chapter "Surgical Device Development." Future commercialization in particular relies on reimbursement codes, which are described in the chapter "Reimbursement Strategies and CPT Codes for Device Development."

Early Patenting in the Era of "First to File"

After the invention of a device-based solution to a medical problem, developers must quickly take steps to protect their ability to commercialize their work. Prior to the passage of the America Invents Act in 2011, inventors were credited based on a "first-to-invent" system, in which patent disputes were settled by evidence proving the date of conception of the idea. This system often led to costly legal disputes, given the unreliable nature of these dates. The America Invents Act introduced a "first-to-file" system, in which the date of patent filing determined the crediting of an invention; this is known as the "date of constructive reduction" (DiMaio et al.). The new system created a radical shift in the timing of patent applications, which now have to be filed much earlier in the device design process, making consultations with patent lawyers a critical step immediately after invention and early prototyping. It should be noted that the patent policy at the academic institution should be considered at this stage; most universities have rights to the intellectual property that is created by employed staff. For more information on the intellectual property rights of a university compared to those of an academic entrepreneur, please see the chapters "Intellectual Property: Ownership and Protection in a University Setting," "Intellectual Property: Commercializing in a University Setting," and "Working with the University Tech Transfer Office."

After successful patent filing, an academic entrepreneur or a university holding intellectual property rights must then decide whether to license or assign their invention and intellectual property rights to a private entity for further development. However, if the academic entrepreneur decides to proceed with the development of the device on their own, they must take steps to secure the requisite funding for the commercialization progression, including the proper FDA approval pathway, in order to bring their idea to market.

Public and Private Funding Sources

Taking a device from the invention stage to market requires a significant investment, in the range of millions of dollars. Initially, accelerators and incubators are valuable sources of support (see the chapter on “Accelerators and Incubators”). Inventors may then look to both public and private sources for funding further device development.

The U.S. government, through the National Institutes of Health (NIH), provides the largest source of seed-stage funding for small businesses in the world, with a total annual budget of \$2.2 billion. With the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs, the NIH invested \$785 million in companies focused on health and the life sciences (Marek). These programs provide funding for a wide array of projects performed by small businesses, from preclinical to human clinical trials, and can be used by inventors who are in the early stages of commercializing a medical device. In particular, the National Heart, Lung, and Blood Institute (NHLBI) of the NIH has created a comprehensive ecosystem of programs to support nascent companies with commercializing their cardiovascular products (Marek). Additional details about the SBIR/STTR programs are available in the chapters “SBIR/STTR Grants: Introduction and Overview,” “SBIR/STTR Grants: Application Guidance” and “Department of Defense: SBIR/STTR Grants and Other Contracts.”

Although these robust public funding sources are available, the success rate of NIH grant applications is declining every year as the number of applications increases (DiMaio et al.). As a result, private funding will likely be necessary to commercialize a new product. Inventors can seek funding from venture capital investors, who, in exchange for equity, provide seed funds for the early development of new products (Kaplan et al.). For more information on angel investors and venture capital funding, refer to the chapters “Angel Investors” and “Seeking Venture Capital Investment.”

There are other new, innovative sources of funding on the horizon. Crowdfunding websites like Kickstarter and Indiegogo have revolutionized the development of products in other industries. However, the legality of crowdfunding for medical devices remains unclear under current FDA guidelines, as crowdfunding may be interpreted as advertising a product prior to its clearing approval by the FDA (Brenan; Smith). Other important pathways include foundations (see the

chapter on “Nonprofit and Foundation Sponsored Research: Developing New Models of Collaboration for Research and Development”).

Pathways to Regulatory Approval

A clearly defined regulatory strategy is vital to taking a product from idea to market launch. First, the new product should be thoroughly and accurately described: intended uses, indications for use, target population, anticipated risks, and whether there are existing predicate devices. This allows for subsequent classification of the device and the determination of the appropriate regulatory pathway (see the chapters “FDA Device Regulation: 510(k), PMA” and “Strategic Planning/Costs of FDA Device Regulation”). Understanding these various classifications and pathways and establishing a regulatory pathway before contact with the FDA allows for a smoother runway to market approval and commercialization.

Definition of a Biomedical Device

As defined by the Federal Food Drug and Cosmetics Act, a medical device is “an instrument, apparatus, implement, contrivance, implant, in vitro reagent ... which is 1) recognized in the National Formulary, or the U.S. Pharmacopoeia, 2) intended for use in diagnosis of disease or other conditions, or used in the cure, mitigation, treatment, or prevention of disease in man or other animals, or ... 3) intended to affect the structure or function of the body of man or other animals” (Van Norman). In addition to the above criteria, a medical device must also not act via a chemical action or depend on metabolism, which distinguishes medical devices from drugs (Office of the Commissioner, “Classification of Products as Drugs and Devices and Additional Issues”). If it is unclear whether or not a product should be classified as a device, the device determination officers of the Center for Devices and Radiological Health (CDRH) can be contacted by email at DeviceDetermination@fda.hhs.gov for an informal assessment.

Determination of Medical Device Classification

It is critical to understand the different FDA medical device classifications in order to choose the most appropriate approval pathway. Classification is generally determined by the indications for the intended use of the device and the risk that the device poses to users. Class I medical devices pose the least risk and thus require the least stringent regulations. Devices in this category include tongue depressors, oxygen masks, disposable gloves, and dental floss. Though low-risk, these devices are subject to general regulations to ensure continued safety after manufacturing, such as prohibition against misbranding, requirements for device listing and registration, and adverse event reporting standards (Kaplan et al.).

Class II devices pose a greater risk than class I devices, and therefore general controls would not be sufficient to ensure their safety and efficacy. In addition to general controls, class II devices involve special controls, including labeling requirements, device-specific performance standards and testing requirements, and post-market surveillance programs (Kaplan et al.). Examples of class II devices include X-ray machines, muscle stimulators, dialysis machines, and fetal monitors.

Class III devices have the greatest risk profile and require regulations beyond general and special controls to provide adequate assurance of safety and effectiveness. This class includes devices that are implanted in the body, sustain life, or have the potential for unreasonable risk of illness or injury. These devices require premarket approval from the FDA, which involves the submission of sufficient evidence proving their safety and efficacy. Examples of class III devices include implanted defibrillators, heart valves, invasive and non-invasive glucometers.

Selecting a Premarket Submission

Device classes differ with regards to the premarket submissions required for regulatory approval. Most class I devices are exempt from premarket submission and do not require formal FDA review (Office of the Commissioner, “Step 3: Pathway to Approval”).

Some class I and most class II devices, however, require FDA approval of a premarket notification application, also known as 510(k), before the device can be marketed. The 510(k) process requires evidence that the device is “substantially equivalent” to existing and legally marketed predicate devices that are not subject to the more stringent premarket approval (PMA) process (Center for Devices and Radiological Health, “Premarket Notification 510(k”).

Class III devices require PMA. This process requires extensive evidence that the benefits of the intended use of the device are greater than the theoretical or identified risks. A class III device must also benefit a large enough target population to merit approval. Data from all preclinical and clinical studies must be submitted; these devices generally require level I or II evidence, such as a randomized controlled trial, for approval (Van Norman). Importantly, data about other devices cannot be used to support new devices. Before these clinical studies can be performed, inventors must have the approval of an Investigational Device Exemption (IDE) by the FDA. During the PMA process, the FDA will ensure adherence to good manufacturing processes through direct inspection of the manufacturing facilities.

Class III devices that are intended for use in small markets can also be classified under the Humanitarian Device Exception (HDE) (Office of the Commissioner, “Step 4: FDA Device Review”). To do so, developers must submit the exemption application with proof that the intended use targets no more than 4,000 people, there are no similar and approved devices on the market, and there are no other pathways to market for the device. Additionally, devices under the HDE

must operate under local institutional review board (IRB) approval, which must include the collection of individual case report data, similar to an ongoing clinical trial (Kaplan et al.).

The FDA encourages early contact from inventors through a pre-submission process to facilitate PMA and 510(k) applications. Through these discussions, the FDA can determine if modified forms of PMA can be submitted. The modular PMA is one such application and is reserved for devices that are in the early stages of development; this PMA involves submission of each section of the application in modules as they are completed and may allow for more rapid closure (Center for Devices and Radiological Health, “PMA Application Methods”). Additionally, there is an ongoing pilot for streamlined PMA of high-risk medical devices (Van Norman).

It is also important to note that the submission of a 510(k) or PMA application requires payment of user fees to the FDA (Center for Devices and Radiological Health, “Medical Device User Fee Amendments (MDUFA)”). The fees for the current fiscal year can be found on the FDA website. This also highlights the need for early and appropriate classification and pathway choice with concurrent funding strategies. There are exemptions from user fees, including a waiver of the PMA fee for a first-time submission from a small business with gross receipts <\$30 million, a waiver of both 510(k) and PMA fees for devices intended solely for pediatric use, and others. Payments must be received and processed either on the same date as or before the application is sent. FDA applications without full payment will not be reviewed.

Conclusion

Medical device development involves an often complicated and costly series of steps to turn an initial idea to fix an unmet clinical need into a product that can legally and safely be marketed to the public. Early patenting, the establishment of financing and regulatory strategies, and timely and frequent contact with the FDA can flatten many of the hurdles between the idea for a novel device and its use in patients.

Resources

1. CDRH Learn
 - a. This site from the FDA’s Center for Devices and Radiological Health provides comprehensive information and educational video, audio, and software modules on all aspects of regulatory approval.
 - b. <https://www.fda.gov/Training/CDRHLearn/default.htm>.
2. Drugs, Devices and the FDA, Part 2: An Overview of Approval Processes: FDA Approval of Medical Devices (Van Norman)

- a. The article “Drugs, Devices and the FDA, Part 2: An Overview of Approval Processes: FDA Approval of Medical Devices” from *JACC* provides a comprehensive, text-based overview of medical device approval pathways.
3. How to Start a Biomedical Device Company: Physicians Can Lead the Team Effort (DiMaio et al.)
 - a. The article “How to Start a Biomedical Device Company: Physicians Can Lead the Team Effort” from *JACC* provides an overview of all aspects of commercializing a new medical device from the perspective of an academic clinician.

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