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Challenges and climate of business environment and resources to support pediatric device development

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ABSTRACT

The incidence of pediatric disease conditions pales in comparison to adult disease. Consequently, many pediatric disorders are considered orphan diseases. Resources for the development of devices targeting orphan diseases are scarce and this poses a unique challenge to the development of pediatric devices. This article outlines these challenges and offers solutions.

Introduction

Advancements in the treatment of orphan diseases are limited by multiple challenges that the innovator faces in the process of device development—from an idea all the way to a commercially available therapy. The United States Food and Drug Administration (FDA) defines an orphan disease as a condition that affects less than 200,000 people within the United States.[1] One of the primary challenges that hamper the development of devices for orphan diseases is the lack of industry support. In fact, the FDA's definition of an orphan disease is based on the fact that the costs for research and development of a therapy targeting a disease condition that affects less than 200,000 people exceeds the profitability and therefore does not draw industry interest.[2]

Today, there are at least 6800 diseases classified as orphan by the Office of Rare Diseases Research (ORDR).[1] Most of the disease states that the pediatric surgeon treats fall into this orphan category. As a result, development of pediatric surgical devices lags behind those targeting many adult conditions. In many cases, the pediatric surgeon applies adult instrumentation to the pediatric population.[3] For example, the surgical staplers we use, while approved for us in pediatrics, were not designed for pediatric patients. Moreover, when adult devices no longer maintain their profitability, production is stopped even if they have a beneficial pediatric application as occurred with the disposable Linvatec arthroscopy knife (CONMED, Utica, NY) that pediatric surgeons used for laparoscopic pyloromyotomy. In this section, we will outline the current challenges facing pediatric surgical innovation and highlight some of the actions that have been successful in promoting device development.

Challenges

Funding

Taking an idea through all phases of the device life cycle (Figure 1) including prototype development, preclinical trials, clinical trials, manufacturing, marketing, and commercialization is an expensive and time-consuming process.[3] A large amount of resources and expertise are necessary. This entails the need for engineers, quality systems, manufacturing systems, sterilization systems, insurance, animal studies, study coordinators, and research infrastructure for clinical trials, patent attorneys, as well as business and marketing experts to name a few.

For one of our devices, the magnetic mini-mover procedure (3MP), which was designed as an outpatient method to correct pectus excavatum, the total expenditures to carry the concept to a phase III, multi-center, FDA-sponsored trial has approached $4 million.[4] To date, the device, while shown to be safe in the first clinical trial, is still considered investigational and is only available through very limited clinical trials under an FDA investigational device exemption (IDE).[5] In other words, the device still does not have FDA approval. The total cost to see this project through to commercialization will exceed $6 million (Figure 2).

This magnitude of funding is not readily available. For the most part, industry and investors have little motivation to invest in products that will not yield a high return due to the target markets being limited in size which limits the potential for a profitable and therefore sustainable product line. In recognition of this dilemma,

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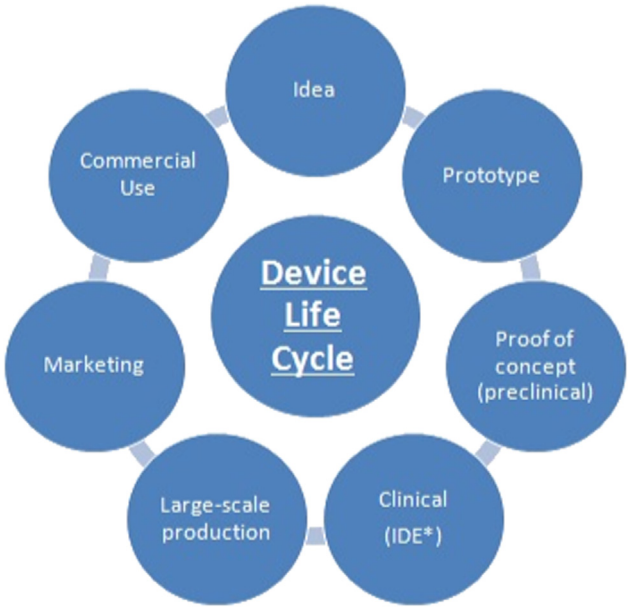

Fig. 1. Device life cycle [investigational device exemption (IDE)].

in 2007, the US Congress passed the Food and Drug Administration Amendments Act which included Title III, the Pediatric Medical Device Safety Improvement Act (PMDSIA). The PMDSIA established specific tracking of pediatric device development to identify needs specific to pediatrics. In addition, it provided limited business incentives for products approved under a Humanitarian Device Exemption (HDE) by eliminating restrictions on already small profits.[3]

The PMDSIA also allocated funds to help develop consortia to focus on the development of pediatric devices and see them through to commercialization. From this, the Pediatric Device Consortium (PDC) was established—initially at three centers. At present, there are five centers that are funded through the PDC, and to date, $11 million has been allocated to the PDC.[3] Within the consortia funded through the PDC, 219 pediatric devices have been proposed; however as of 2012, only three devices were commercially available.[3] In our experience, the limited amount of funding on a 2-year cycle received through the PDC is an excellent resource to initiate projects but is not enough to complete the device life cycle which can take upwards of 8 years to make it from idea to bedside. Therefore, it is not surprising that initial funding through the PDC has resulted in over $9 million of additional external funding.[3] However, while these efforts have increased the number of products approved for orphan disease, the growth is still overwhelmed by the existence of over 6800 orphan diseases.

The regulatory process

One of the primary contributors to the enormous cost of device innovation within the US is the regulatory process, specifically obtaining FDA approval for clinical use. The FDA functions to protect the public health "by assuring the safety, efficacy and security of…medical devices."[6] Therefore, not only must safety be demonstrated but also efficacy as well. Unfortunately, efficacy is an extremely high bar to set for the first use of a novel medical device. Proving efficacy requires costly pre-market clinical trials for conditions that may not be common in pediatrics. Therefore, enrollment can be sluggish and obtaining adequate power for a well-designed study adds an additional burden to the process. However, the distinction between efficacy and superiority can seem blurred at times, as well as exclusive of other potential benefits for an innovative device such as cost reduction, ease of use, and reduced pain.

Due to the complexity of the regulatory process, it can be overwhelming to the individual clinician with a novel idea. Multiple steps must be undertaken in seeing a device through the entire process. This starts with building a prototype and ultimately manufacturing the device in anticipation of clinical use. This process typically requires outsourcing to a capable manufacturer which is costly. Initial proof of concept as well as safety is first achieved through animal studies or in vitro experiments which add an additional, yet necessary, layer of complexity. In the US, human trials are conducted under an IDE with close FDA oversight. Our application for our most recent, multi-center 3MP IDE was 141 pages and took more than a decade to obtain. If the results from the trials conducted under the IDE are convincing, the investigators will seek FDA approval for the device. However, for devices targeting orphan devices, FDA approval is sought under an HDE,

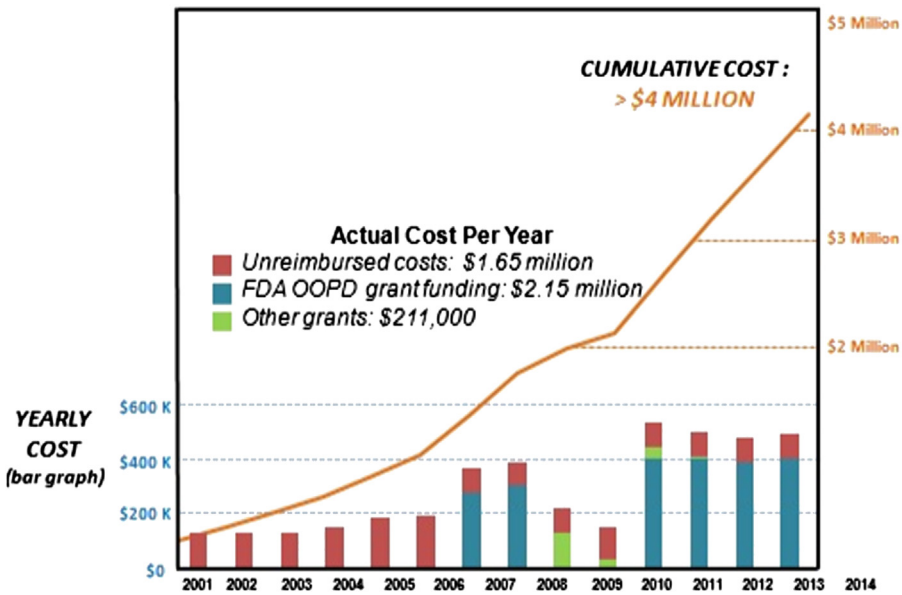

Fig. 2. Actual (bars) and estimated (line) costs for development of the magnetic mini-mover procedure (3MP) for the treatment of pectus excavatum.