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A robust R&D project portfolio optimization model for pharmaceutical contract research organizations

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ABSTRACT

Pharmaceutical drug Research and Development (R&D) outsourcing to contract research organizations (CROs) has experienced a significant growth in recent decades and the trend is expected to continue. A key question for CROs and firms in similar environments is which projects should be included in the firm's portfolio of projects. As a distinctive contribution to the literature this paper develops and evaluates a business support tool to help a CRO decide on clinical R&D project opportunities and revise its portfolio of R&D projects given the existing constraints, and financial and resource capabilities. A new mathematical programming model in the form of a capital budgeting problem is developed to help revising and rescheduling of the project portfolio. The uncertainty of pharmaceutical R&D cost estimates in drug development stages is captured to mimic a more realistic representation of pharmaceutical R&D projects, and a robust optimization approach is used to tackle the uncertain formulation. An illustrative example is presented to demonstrate the proposed approach.

1. Introduction

Americans spent over $2.6 trillion on healthcare last year. This represents about 17.9% of the total US GDP. The World Health Organization estimates that the healthcare share of US GDP could climb to 34% by 2040 and warns of adverse consequences for the world economy if the current cost trajectory is not corrected. A closer look at the healthcare expenditure shows that pharmaceuticals accounts for over 12.9% of total expenditure and it is projected to be the fastest growing portion of healthcare spending. This is due to high prices of prescription drugs, particularly brand name and specialty drugs, and rising costs associated with the Research and Development (R&D) of new drugs (CMS Report, 2011). The pharmaceutical industry has long argued that the process of drug discovery through R&D is very expensive and requires substantial capital expenditure. For example, an average cancer drug costs around $1.75 billion to research and develop and may take up to 10 years to test and market. In 2008, American pharmaceutical companies spent over $45 billion on developing new drugs or modifying existing drugs. According to the Science and Engineering Indicators 2012 report published by the National Science Foundation, pharmaceuticals and medicines are the highest R&D intensive industries in the world after semiconductor and communication industries. The average R&D intensity in the pharmaceutical industry—the ratio of total R&D spending to total sales revenue—is 12.2%, which is more than three times that of the average manufacturing firm in the US.

R&D expenditures in the pharmaceutical industry might be as high as 40% of the cost of a newly developed drug (Gassmann et al., 2008). A significant contributor to the high R&D costs in pharmaceutical drug development projects is the high prevalence of technological and market uncertainties (Rogers et al., 2002). Technological uncertainties are related to the efficacy and safety of the drugs being developed while market uncertainties are related to the supply and demand factors in the marketplace. Despite these uncertainties, pharmaceutical companies have increasingly grown their expenditures on R&D in an effort to boost profitability through the introduction of novel drugs for treatment of various ailments (Lowman et al., 2012). This rising expenditure in pharmaceutical R&D projects is due to increases in cost of discovering

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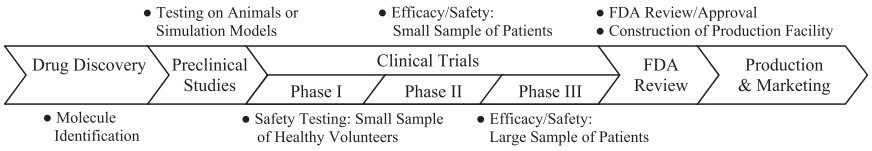

Fig. 1. Pharmaceutical drug development pipeline.

new drugs, as well as higher costs associated with conducting clinical trials for developing these drugs. It is also important to note that recently discovered drugs with demonstrated higher levels of sophistication may require an even more costly and time-consuming clinical trial phases to ensure their safety and efficacy before they could be introduced to the market (Craig and Malek, 1995; DiMasi and Grabowski, 2007).

As shown in Fig. 1, pharmaceutical drug development pipeline includes drug discovery, pre-clinical and clinical trials, FDA review, and production and marketing phases. Among these development phases, clinical trials are the most time-consuming and investment-intensive ones. Clinical trials take about 6 years to complete and represent more than 50% of total pharmaceutical R&D spending (Zeller, 2002; Mirowski and Van Horn, 2005; Parexel, 2004).

Given the cost and complexities associated with developing new drugs, pharmaceutical companies typically outsource some of their drug development activities to specialized organizations in order to better focus on their own core competencies. These specialized organizations are referred to as contract research organizations (CROs). CROs were "born" in the late 1970s and quickly assumed a significant role in the pharmaceutical industry in order to help the industry balance the need to consolidate its operations while simultaneously address getting drugs quickly through the development pipeline (Piachaud, 2002). The Association of Clinical Research Organizations (ACRO) estimates that over 46% of pharmaceuticals have outsourced their R&D projects to CROs. ACRO also estimates that CROs employ over 2 million people and are present in 115 countries (ACRO, 2013). The CRO industry represents over 33% of the total spending on pharmaceutical R&D (Lowman et al., 2012). It is estimated that in the near future, CRO's share of total pharmaceutical R&D will exceed 60% (ACRO, 2013). The leading CROs manage more than 45,000 clinical trials annually with revenues in excess of $20 billion (Milne and Paquette, 2004; Tufts Center, 2006a; Getz, 2007). The CRO industry is also very concentrated; the top 10 out of existing 1000 CROs in the global market control more than 80% of the total market share (Shuchman, 2007; Getz, 2007). This indicates that the CRO market consists of a few big multinational companies with R&D departments even larger than some of their pharmaceutical clients along with numerous small or medium sized companies with a niche in national or regional markets (Piachaud, 2002).

The CRO market has expanded from drug discovery and preclinical work to clinical trials, drug manufacturing, and even marketing (Tufts Center, 2006b; Mehta and Peters, 2007). While it seems that it is the increase in the quantity of R&D projects that has promoted the need to outsource clinical trials, there are basically other motivations for pharmaceutical companies to use more outsourcing (Piachaud, 2002). These include higher cost efficiency (Huang et al., 2009), less time to market (Mahnke et al., 2006), increased opportunity to gain needed knowledge, availability of advanced skills and technologies (Coombs et al., 2003), and the increased globalization of drug development (Gassmann et al., 2010). The CRO of today is a key driver of drug development success (Lowman et al., 2012).

Although the practice of drug development outsourcing to CRO has been the motivation of numerous researchers (Alexander and Young, 1996; Rettig, 2000; Dickert et al., 2002; Piachaud, 2002; Quelin and Duhamel, 2003; Mirowski and Van Horn, 2005; Angell, 2008; Hsuan and Mahnke, 2011; Zirpoli and Becker, 2011), the majority of conducted studies are descriptive in nature and have been studied from the perspective of the goal attainment for the pharmaceutical companies and not for the CROs. Within the pharmaceutical business, for example, short time to market increases the novelty of a potential blockbuster drug to achieve a prolonged competitive advantage (Arlington, 1997; Piachaud, 2002). A prolonged clinical testing may significantly reduce the commercial value of a drug or may even render the whole project infeasible (Bauer and Fischer, 2000). In fact, studies show that financial and commercial reasons account for more than one third of research abandonment which often occurs during late clinical testing phases (DiMasi, 2001). Thus, the role of the CRO is very critical in achieving the drug development goals of client organizations. A 2010 survey of about 400 drug manufacturers and biotech companies showed a potential growth of about 4–8% in CRO R&D budgets, indicating that the number of outsourcing activities is on the upward trend. Given this trend, the question that needs to be asked is whether CROs have the ability to absorb all the demand from client organizations. And if they do not, how should they balance their capabilities with the contract project loads in order to sustain long term profitability and growth? In other words, CROs must decide on which R&D projects to include in their optimum mix of project portfolio given their capacity constraints and profitability goals. Selecting a wrong mix of projects not only adversely impacts the contractual and financial obligations, but may also reduce the ability to successfully execute other projects already in the portfolio.

Realizing this necessity, the goal of this paper is to develop a business support tool to help CROs make their contract decisions effectively by integrating project opportunities with existing technical, financial, and resource restrictions within a mathematical model. There is very limited research on CROs in this context. The closest body of literature that underpins such models is referred to as the project selection and scheduling (PSS). Since the PSS literature is developed for generic projects, we need to modify the problem definition to account for pharmaceutical R&D projects as a special category of R&D projects. From a modeling perspective, the distinguishing characteristics of R&D projects from those of generic projects occur on the highly uncertain nature of R&D projects in that R&D cost and revenue estimates are very unreliable and the market outcome is very risky (DiMasi, 2001). To account for this uncertainty we employ a recently developed approach, called robust optimization, to solve our formulated model for pharmaceutical R&D project portfolio decision making.

The remainder of this paper is organized as follows. In the next section, we review the PSS literature, introduce the robust optimization concept, review its recent applications in project selection and project scheduling, and discuss its relevance to R&D PSS. In Section 3, we formally define the problem and propose our nominal model. Section 4 is dedicated to the introduction of a robust optimization framework and formulation of the robust counterpart model. In Section 5, we present the results of our robust CRO portfolio optimization approach using an illustrative example. Finally, Section 6 provides some managerial implications along with the conclusions.