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SCIENCE DIRECT®
Computers and Chemical Engineering 29 (2005) 1357–1368
Computers & Chemical Engineering
www.elsevier.com/locate/compchemeng

Modelling of the biopharmaceutical drug development pathway and portfolio management

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Available online 8 March 2005

Abstract

Given the time, cost and risk associated with drug development, biopharmaceutical companies typically need to have a portfolio of drugs in development to be successful. Current pressures of cost and speed to market are driving the need for more effective means of assessing the value and risks of such drug portfolios. This paper presents research to generate a prototype computer tool developed to predict the process and business outcomes for portfolios of biopharmaceutical drugs proceeding through the development pathway. The tool incorporates the interactions between drug development activities and the available resources. In addition to the business and process issues, the risks involved in the process of drug development have also been incorporated into the model. A case study is presented to illustrate how the tool can be used to assist business decisions regarding biopharmaceutical portfolio management. The example addresses scenario analysis and the question of outsourcing versus in-house manufacture of material for clinical trials and the market under uncertainty.

Keywords: Biopharmaceutical drug development; Computer-aided simulation; Portfolio management; Risk; Decision-support tool

1. Introduction

The rapid growth of the biotechnology industry as the backbone of high technology, highly specific and effective new medicinal therapies have had a profound effect on the pharmaceutical industry. The ability to genetically modify living organisms to produce a range of medicines has contributed to a plethora of biopharmaceuticals being developed. In 2000, 28 major protein-based products generated US$ 13.3 billion of sales and in 2002, there were 99 protein-based therapeutics in Phases III and II clinical testing (Ginsberg, Bhatia, & McMinn, 2002). However, the process of bringing these products to the market is a costly and risky business. On average it takes 7.7 years to bring a biopharmaceutical product to market (Foo, Karri, Davies, Titchener-Hooker, & Dunnill, 2001) and costs over US$ 800 million and this cost of research and development (R&D) for new drugs has been on the rise for the past two decades (DiMasi, Hansen, & Grabowski, 2003). Given the uncertainty associated with drug development, biopharmaceutical companies typically require a pipeline of drugs constantly to remain in business. Speed to market and pressure to reduce costs are critical factors driving the need for more effective means of assessing the value and risks of such drug portfolios. Various methods are used by the pharmaceutical industry for product portfolio management. Popular financial models used by companies include net present value (NPV), decision trees option models and computer simulations (Soegaard, 2003). Non-financial models, used to a lesser extent, comprise standard strategic models, risk-reward charts and scoring models (Soegaard, 2003).

Managing an R&D portfolio is complicated by constraints on budget, personnel and available capacity and how best to deploy these resources. Each drug is also subject to technical and commercial uncertainties. Technical uncertainties include the risk of failure during each phase of clinical testing; market uncertainties include the volatility in the forecasted demands and prices of drugs as well as the impact of competition. Given these factors the survival of a company can

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doi:10.1016/j.compchemeng.2005.02.010

depend on the key decisions made during the development of each drug within a portfolio.

Portfolio selection and capacity planning problems have been addressed in process engineering literature. Mathematical methods have been applied for the resource constrained scheduling of testing of new product development (Jain & Grossmann, 1999) and optimisation of new drug candidate portfolio under resource constraints (Subramanian, Pekny, & Reklaitis, 2000). Rogers, Gupta, and Maranas (2002), presented a real options based analysis of selecting R&D portfolios. Gatica, Papageorgiou, and Shah (2003) presented a mathematical programming method for capacity planning under uncertainty for the pharmaceutical industry and Levis and Papageorgiou (2004) outlined a mathematical approach programming approach for long-term, multi-site capacity planning under uncertainty in the pharmaceutical industry. Here, the approach used was to select the optimum portfolio from a given set of candidates and planning of the manufacturing schedules under constraints. Levis and Papageorgiou (2004) also provide a good review of the papers presented on mathematical approach to the problem of portfolio optimisation and task scheduling. However, these usually result in complex mathematical methods where a high level of knowledge is required for application. Such methods have been applied mostly to chemical entities and agro-chemicals. By contrast little attention has been paid to biopharmaceuticals.

The need for computer-aided simulation tools, capable of capturing the technical and business aspects of drug development as well as the risks, is critical for such decision-making (Karri, Davies, Titchener-Hooker, & Washbrook, 2001). The use of a prototype decision-support tool for controlling the cost of goods in biopharmaceutical manufacture under uncertainty has been demonstrated (Farid, Washbrook, & Titchener-Hooker, 2001; Mustafa et al., 2004). However, the impact of manufacturing decisions on development timelines and costs was not explored. Accurately computing the uncertainties inherent in product development poses the biggest challenge of all, creating difficulties in comparing and prioritising projects in development (Soegaard, 2003). This paper presents research to generate a prototype computer-aided tool to predict the outcomes of employing different development strategies for a portfolio of biopharmaceutical drugs proceeding through the development pathway. It seeks to quantify the outcomes in the form of simple economic metrics such as the NPV, which may be used as the basis for decision-making.

1.1. Benefits and challenges of portfolio management

High quality decisions about long-term business strategy often require the explicit analysis of uncertainty. Portfolio management is an established business process that is linked with other business processes including strategic planning and budgeting. Through portfolio management, decision-making and resource allocation are measurably improved. Keelin and Shew (2003) state that portfolio management is justified by a 100-fold return on investment.

Traditional portfolio evaluation models often rely on qualitative and semi-quantitative tools. New quantitative methods have been developed that compute directly how much value decisions add to a R&D portfolio (Keelin & Shew, 2003). Portfolio management applies to all areas of drug development. The decisions include which targets should be pursued at the point of drug discovery through to deciding on the appropriate level of manufacturing capacity needed, and finally to which areas of the market have to be captured. High quality valuation methods have to be applied to capture the risks and rewards implicit in applying different options in R&D projects. By being able to compute and then compare the array of possible outcomes and key sources of uncertainty, management is provided with a key tool to manage and balance the portfolio. Effective portfolio analysis can identify the optimal portfolio in terms of value creation for any given set of constraints.

1.2. Modelling biopharmaceutical drug development

Modelling the drug development process enables the interactions between the different tasks involved and the resource demands at different stages of development activities to be captured and quantified. Bioprocess modelling has been used to explore different process routes and assist decision-making with much success (Farid, Novais, Washbrook, & Titchener-Hooker, 2000; Lim, Washbrook, Titchener-Hooker, & Farid, 2004; Mustafa et al., 2004). Modelling of the drug development process is not presented much in the literature. However, Luehrman (1994) describes a model configured to assess the risks and returns of new projects. Karri et al. (2001) presented a hierarchical framework to assist decision-making in the biopharmaceutical industry while Stonebraker (2002) presents a model of a single project aimed at evaluating its commercial worthiness.

When modelling biopharmaceutical development the challenge is to model effectively the many different tasks involved in taking a drug through the phases of drug development, which increase in complexity and duration as the drug approaches the market. The company- and drug-specific business and process characteristics all have to be captured successfully and the resulting model be able to compute the time-to-market, cost, revenue and the risk, which all feature in the decision-making process. Simulating a portfolio of drugs and their development activities provides management with the capacity to explore, in silico, different strategies and to use the insight gained to make real-life decisions that would add value in both the short and long-term to the portfolio.

A typical example might be that the early planning of development tasks and the appropriate allocation of resources will help the company to identify resource bottlenecks and act upon them early. A tool that combines the biopharmaceutical drug development activities (e.g., process development, manufacturing and the clinical trials, etc.) and the resource flows