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In search of innovative techniques to evaluate pharmaceutical R&D projects

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Abstract

This paper is a conceptual paper that examines a new integrative evaluation approach for pharmaceutical R&D projects. It describes recent changes in the health care economy and the underlying scientific and technological revolution that has markedly altered the business environment in which the pharmaceutical industry operates. Changes in cost and technology resulting from managed care organizations, marketing, generic drugs, new drug development risk, and scientific and technological evolution forced us to think of a new way to evaluate R&D projects in the early phase of the project. These changes have placed increased emphasis on the need for improvements in technology management methodologies. A real options approach, especially when combined with other project risk management processes, offers a significant improvement in project selection and review, and resource allocation decisions.

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1. Introduction

> While governments and large institutional buyers continued to exert strong downward pressure on drug prices and company earnings, a scientific and technological revolution promised to change the way in which drugs were discovered, developed, and tested, and in the process to expose the industry to a wave of new competitors (Fagan and Hayes, 1998).

The decade of the 1990s has been a period of turmoil for the pharmaceutical industry as it has faced the dual challenges of radical changes in health care economics and in science and technology (Agnew, 2000). Meeting these challenges has brought a major consolidation of the industry through a series of mergers and acquisitions that a few large firms now dominate the industry. However, the cost savings resulting from the elimination of redundant cost centers and the economies of scale achieved by these structural changes are no guarantee of long-term success (Carr, 1998; Kearney, 1997).

These insights have placed new emphasis on the development of management tools and practices to compete more effectively. Adapting and implementing project management tools, techniques and principles will play an important role in this process. The pharmaceutical industry has been using project management techniques and methodologies for some time, but overall its development and impact are behind that of other industries (Byers, 1989; Krusko and Cangemi, 1987; Murphy, 1989; Foulkes, 2000). In large part this has been due to the inherent difficulties in managing R&D projects. The development of new technology has an inherent unpredictability that has kept it outside the domain of conventional approaches to project management (Sheasley, 2000).

This situation is changing as the result of recent efforts to develop improved techniques for technology management. The application of real options analysis to R&D projects has gained support in the last few years and promises to yield a significant improvement in technology management. This paper reviews the recent environments and trends on R&D project management and its impact on the pharmaceutical industry.

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2. Cost, technology, risk and environmental changes in the pharmaceutical industry

The pharmaceutical industry has faced intensifying cost pressures through the 1990s. These pressures are expected to continue. The source has been several fold.

2.1. Managed care organizations

Managed care organizations, seeking to control health care costs, have had a major effect on the economics of health care. The number of patients under managed care has increased steadily from 1980, when approximately 5% of patients were covered under managed care organizations, to the early 1990s, when 80% were covered (McGahan, 1994). They have expanded the use of lower cost generic drugs, developed closed formularies, and limited prescription reimbursements. Cost consciousness has been increasing as well in Europe and Japan, which with the US make up the three largest markets in the world (McGahan et al., 1995).

2.2. Marketing

Marketing expenditures have grown as a result of changes in regulations allowing direct advertising to consumers. Now, in addition to marketing to doctors, companies must mount major advertising campaigns on TV and in magazines (Carr, 1998).

2.3. Generic drugs

Prior to 1984, companies introducing generic forms of patented drugs had to wait until the patent expired and then had to do clinical and safety studies before the drug could be marketed. Barriers to the entry of generic drugs have fallen significantly following passage of the Waxman-Hatch Act (1984) which permitted introduction of the generic if it could be shown that it was equivalent to the original without having to go through separate clinical and safety trials. This has significantly reduced the period of time during which a drug is protected by patent and could command premium pricing.

2.4. Drug development: increased cost and complexity

The increasing complexity of drug development has also added cost to the process. A major shift in usage has occurred during the last 20 years. A large and growing proportion of drugs are now prescribed for chronic conditions rather than for short-term conditions (Agnew, 2000). This means that regulators look more closely at a drug's long-term effects. Drugs that will be taken for years for conditions such as hypertension or diabetes have to have very good safety profiles. As drugs are increasingly taken in combinations, it is imperative that drug interactions be eliminated. The standard of performance has been raised so that many new drugs that were marketable 20 years ago are no longer acceptable today.

In addition, new drugs need not only be safe and efficacious they must also be cost effective. They must be significantly better than other therapeutic options. Studies demonstrating cost effectiveness and long-term safety are expensive. Overall, costs of clinical trials account for roughly 40% of R&D budgets, with another 10% going to production and scale-up costs. These costs are expected to increase.

2.5. Risk

Drug development is a research-intensive, high-risk endeavor. Typically, more than 5000 compounds must be screened to produce one marketable drug. Considerable resources must be expended in the early stages of development. Total costs to bring a drug to market are currently between US$350 and 500 million. This figure includes the cost of failed projects. It is not uncommon for drugs to fail in phase III trials. There is a high and unpredictable level of attrition at each stage of the development path such that 40–50 projects are needed at the research stage in order to assure one new chemical entity introduced into the market. In addition, there are uncertainties at the other end. One cannot be sure that a drug will live up to its commercial potential. Other companies may launch similar products at the same time, or unexpected toxicities can lead to curtailment of use or withdrawal (Kaufman, 2000).

2.6. Scientific and technological revolution

At the same time that the industry was trying to cope with the effects of changes in health care economics, the nature of the drug discovery and development process was changing as the result of a revolution in science and technology. Advances in biochemistry and molecular biology have led to "rational drug design", targeting fundamental disease processes. Combinatorial chemistry has dramatically increased the number of compounds that chemists can make, and high throughput screening technology has improved the efficiency of screening those compounds.

Molecular genetics is having an enormous impact on drug development. Not only is it providing a large number of potential new targets for therapeutic intervention, it promises to make therapies that are tailored to the genetic makeup of the recipient. Exploitation of this new knowledge will require much larger R&D programs. One of the major driving forces behind the recent mergers is the need to expand R&D efforts.

The accepted thinking is that size is a key success factor. The largest companies will be the ones able to

develop new drugs more quickly and effectively than smaller companies. It remains to be seen whether the largest companies will be the most effective in exploiting the new technologies and in delivering new drugs with the potential to be blockbusters. Many are skeptical, suggesting that the large companies are too large, too slow to recognize opportunities, and too slow to act. The newly combined firms need to launch four to five new drugs per year in order to sustain acceptable growth. Many have fallen far short of that target thus far.

Overall, the companies face significant challenges in the coming years. Big pharma has the advantage of having large resources available to take advantage of the new science, but it is not clear that they will be the ones to capitalize on this advantage (Mirasol, 2000a, 2000b). Big pharma is ill prepared for the new competitive game, being rigid and slow to adapt to the new realities (Gershon, 2000). Questions have been raised about the effects of the mergers beyond the short-term cost savings resulting from elimination of redundant assets. Are they now too big to maintain the flexibility to move quickly? There is a clear need to manage technology better, to develop effective technology strategies and to implement them.

3. Trends and recent developments in technology project management

> Technology is rapidly changing the nature of the competition and strategy in the late 20th century, moving toward a new competitive landscape in the 21st century. The new competitive landscape represents new issues, new concepts, new problems, and new challenges…. One thing is clear: much more research is required to understand the new competitive landscape, and how firms can successfully navigate within it. (Bettis and Hitt, 1995)

The "Risk, complexity, and uncertainty [that] define the business environment of the 1990s" (Nichols, 1994) places increased pressure on management to develop effective strategies for achieving competitive advantage within this environment. Project management — "The systematic integration of technical, human, and financial resources to achieve goals and objectives" (Badiru and Pulat, 1995) provides a framework for dealing with the complexities and uncertainties facing business leaders today (Frame, 1994). Project management has matured considerably since its inception as a management discipline in the early post-war period, continuing to develop standards and resources to deal with today's highly competitive business environment (Duncan, 1996). However, the emphasis is traditional project management has been on "Doing projects right", (Cooper et al., 2000) while the new environment places equal emphasis on "Doing the right project". Project selection, resource allocation, and management of the company's portfolio of projects are as important as management of individual projects. There is growing recognition that effective technology management is a key element of the business process and that it must be integrated into the strategic plan of the company (Bone and Saxon, 2000).

3.1. Value of project management and risk management

> "Risk Management's project management maturity was the lowest among all eight knowledge areas" (Ibbs and Kwak 2000).

> "The idea that risk management should be an important and integral part of the project management process is not well established" (Ward, 1999).

> "Some of the techniques assume that risks are identified and can be uniformly addressed by increasing project time frame or resources. Unfortunately, these assumptions don't always hold true" (Royer, 2000).

One of the major challenges today is to develop more robust and sophisticated methods for dealing with the uncertainties associated with R&D projects, especially those at the earliest stage of development. The key issue is how to deal with the fact that early in development at the discovery level — the point at which important decisions about projects must be made — the information that is typically used in project valuation, decision analysis, and risk management is at its most incomplete and uncertain. The modeling processes that have yielded important benefits for later stage projects have proved to be of little value when assessing early stage R&D projects (Jarrett, 2000).

In reviewing the literature on project selection tools, Henriksen and Traynor (2000) and Tritleet al. (2000) noted the following methods:

- Unstructured peer review.
- Scoring.
- Mathematical programming, including linear, integer, non-integer, goal, and dynamic.
- Economic models: NPV and IRR.
- Decision analysis: multiattribute utility theory, decision trees, risk analysis, and the analytic hierarchy process.
- Interactive methods: Delphi, Q-sort, behavioral decision aids.
- Artificial intelligence, including expert systems and fuzzy sets.
- Portfolio optimization in which a proposed project is considered concomitantly with other projects in a portfolio.

While all of these methods have been used to make selection decisions on individual projects and to develop "optimal" portfolios of projects, they all suffer from a variety of defects. Many have little theoretical backing and others have strong theoretical grounding but are difficult to implement. Some rely upon unreasonably strong assumptions about the decision makers and their attitudes toward risk and others require implausibly detailed inputs describing the parameters of the decision maker's utility function (Graves et al., 2000). Several surveys of R&D managers have found that because of these defects, or simply the complexity of the models, they have found little practical application in real world decision making (Henriksen and Traynor, 2000) (Graves et al., 2000).

3.2. Real options analysis

A major advance in development of project selection tools came with the application of options reasoning to R&D. While the "options" character of R&D projects was recognized more than 20 years ago, it has only been the recent availability of software programs and sufficiently powerful desktop computers that it has gained more widespread use. The options approach to project valuation seeks to correct the deficiencies of traditional methods of valuation, net present value (NPV) and discounted cash flow (DCF) through the recognition that active management and managerial flexibility can bring significant value to a project.

What are options? In a typical financial option scenario, one purchases a contract, or option, that gives one the right to purchase an asset, usually a stock, at a predetermined, or exercised price. The key point is that the purchaser has choice. He or she can exercise the right to purchase the asset or not. If the value of the asset at the time the option is exercised is greater than the purchase price of the option, then the purchaser will have made a profit. The purchaser also has the right to *not* exercise the option. Thus, the option holder has the potential to make a significant profit, but at the same time, the potential loss is limited to the option purchase price. Paradoxically, a highly volatile asset, such as an Internet stock, has a greater option value than does a stable, predictable asset, such as a utility stock. It is the element of choice along with the potential to make a large profit while at the same time limiting the potential for loss that makes options attractive. The concept also recognizes and values active rather than passive management (Luehrman, 1998).

Real options deal with real assets that are managed by a business. These options may belong to one of several categories (Edleson, 1994).

- Growth options.
- The option to expand scale.
- The option to wait (timing).
- The option to switch inputs, outputs, or processes.
- The option to contract scale.
- The option to abandon.

Each option might be exercised under a given set of conditions. For example, if a company were planning an expansion that required capital, a rise in interest rates might lead the company to postpone the decision to begin.

An early application of real options analysis to technology management was Merck's analysis of potential partnerships with small biotechnology companies (Nichols, 1994). Pharmaceutical companies typically enter into an agreement for a specified period of time: an initial payment followed by other payments depending upon partnership performance and business conditions. Partnerships of this type are very common in the pharmaceutical/biotechnology industry. The option character is derived from the fact that it has great, but unknown, upside potential, with downside potential limited to the amount invested in the project. The option price is the amount invested in the project. Successful completion of the project creates an asset — the right to initiate commercial development. Otherwise, the project can be abandoned either if unsuccessful or sold to another company in the form of licensing a technology (McGrath, 1997).

Clearly, real option models are superior to simple NPV valuation models in that they recognize the importance of managerial flexibility. However, in practice, it has proved very difficult to obtain a specific dollar value. Real options differ from financial options in several respects (McGrath and MacMillan, 2000). Financial options models rely on several key assumptions. The asset must have a price, the price must be known, and the asset must be liquid or tradable (Black and Scholes, 1988). Technology options, on the other hand, do not have an easily determined value. The value could be markedly different from one company to another depending on business objectives and the other assets in the portfolio. Technology assets can be sold or traded, but they are much less liquid than financial options. In practice, real options are difficult to identify; multiple types are mixed up together, and "The valuation of even the simplest real-life options can be fraught with a magnitude of complexities, making the approach even more difficult to apply than more traditional approaches" (Edleson, 1994).

A number of attempts have been made to deal with these limitations and apply the model more or less rigorously (Herath and Park, 2000; Reiss, 1998; Jagle, 1999; Lint and Pennings, 1998; Perlitz et al., 1999; Angelis, 2000). Changing probability distributions and various assumptions can produce better results in specific situations, but have thus far been difficult to apply generally to technology management.

4. An integrative approach

A more insightful approach has been to view project valuation as a combination of merit such as scientific excellence, innovation, synergies (Henriksen and Traynor, 2000) and cost, and to address the qualitative uncertainties of the project (Tritle et al., 2000) in an integrative fashion. This approach to technology management utilizes options reasoning in conjunction with other evaluation methodologies in an effort to arrive at a balanced view of the project in the context of the business as a whole (McGrath and MacMillan, 2000; Perdue et al., 1999; Sheasley, 2000; Cooper et al., 2000; Day and Schoemaker, 2000).

Although various studies emphasize risk management, decision analysis, or options reasoning to different extents, and arrive at judgements in somewhat different ways, they have a common theme: a focus on the quality of information about a given project. The soundness of a decision on resource allocation or project continuation is ultimately based on the quality of information available (Sharpe and Keelin 1998; Cooper et al., 2000). Several important points can be taken from these studies.

- Make the evaluation fit the situation. The information available for a project — its type and reliability — varies greatly with the developmental phase of the project. Trying to assess the commercial value of a project in the conceptual or discovery phase is pointless.
- Technology is knowledge and cannot be quantified, and developing new technology is acquiring new knowledge. However, there must be some measure of utility to the company. At early stages, focus on learning — what the team hopes to learn. Project reviews should evaluate what has been learned.
- Where there is a high degree of uncertainty, judgment scales can be developed that will provide a sound basis for decisions.
- Where judgements are involved in project evaluation, it is essential to get the appropriate people — both the right number of people and people with the right expertise. This could involve outside experts, representatives from several levels of management, as well as peers from other project teams. The two key factors here are the need to get sufficient breadth of experience, both scientific and business, as well as to develop a process that has broad-based support and buy-in. This sets a firm foundation for project practice and develops the discipline necessary to make tough go/no go and resource allocation decisions.

5. Conclusion

The competitive landscape in which the pharmaceutical/biotechnology industry operates has changed radically due to increasing cost pressures as a result of the rise of managed care organizations and to a scientific/technological revolution that has changed the process by which drugs are developed. It is generally recognized that R&D will play a major role in the response to these developments. Long-term success in this environment will require superior management skills. Managers will not only have to be attentive to costs, they will also have to manage technology much more effectively than they have in the past. Project management and risk management are playing an increasingly important role in technology management.

An important development in the past few years has been the recognition by managers that "Much of the value of R&D is embedded in options" (Boer, 1999). Integration of this concept with other decision analysis and risk management techniques is bringing major improvements in technology management.

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