

## Commentary

**Economics of Drug Delivery**Rob Chess<sup>1,2</sup>

Received September 25, 1997; accepted October 29, 1997

The role of drug delivery for biopharmaceutical companies in particular, noninvasive alternatives to injection as routes of drug administration, has changed over the last several years. Previously drug delivery was an after-thought—a way to extend patent life or broaden a product line. Now drug delivery is entering the forefront of product strategy for biotechnology and pharmaceutical companies as a vehicle to develop highly profitable products without the inherent risk of new chemical entities. This change in perspective is evidenced by the growth of U.S. sales of drug delivery products which have increased by \$1.5 billion in the past two years to \$11.5 billion in 1996.<sup>3</sup> More importantly, drug delivery is expected to grow even faster during the next decade.<sup>4</sup> Decision makers—whether they are scientists or business development managers or CEOs—are more and more evaluating alternative ways to administer drugs.

There are several reasons that large biopharmaceutical companies are viewing drug delivery differently. The growth of managed care has led pharmaceutical and biotechnology companies to seek ways of expanding their product lines in order to strike broader deals with these health supplier organizations. Drug delivery offers a low risk, rapid route to develop new therapeutics needed for filling in product lines.

Further, managed care organizations are placing a greater emphasis on cost effectiveness and total disease management costs. Many drug delivery products improve patient compliance through more patient friendly delivery and less frequent dosing regimens. With increased compliance, symptoms are reduced. For example, a study conducted by the Diabetes Control and Complications Trial Research Group (DCCT) concluded that if diabetics used intensive insulin therapy they could delay or slow the progression of severe diabetic symp-

toms.<sup>5</sup> Intensive therapy could be increased with a noninvasive system. This in turn leads to better disease control and reduced long-term management costs.

Added to the issues with patient compliance is the high cost of administering many injectable drugs. To ensure safety and compliance, physicians and nurses traditionally administer drugs usually in a hospital or office. This administration method drives up the cost and inconvenience of care for both the patient and the insurance payers. This is yet another reason why patients often do not obtain all necessary injections to immunize themselves or treat a disorder. To offset this cost, diabetics, for example, have attempted self-administration of drugs by injection, but even these dedicated patients generally do not take all their medicine as often as recommended.

As a result of these circumstances, pharmaceutical companies are beginning to realize that drug delivery is a strong strategic competitive weapon to gain market share in the managed care environment.

In addition to potential market share growth, drug delivery typically provides greater return-on-investment than drug discovery. The average cost of developing a new drug has increased from \$54 million in 1976 to \$359 million in 1990—some estimate it is now close to \$500 million.<sup>6</sup> Consequently, the hurdle for new chemical entity success has gotten far higher—anything other than a “blockbuster” is not a good investment for large pharmaceutical companies. On the other hand, alternative drug delivery products often can be developed in half the time at usually less than 10% of the development cost—meaning that return-on-investment is typically many times higher for drug delivery products than for new drugs.<sup>7</sup> Thus, drug delivery technology offers opportunities to pharmaceutical and biotechnology companies searching for new ways to contribute to the bottom line.

Pharmaceutical companies are not the only ones to benefit from drug delivery systems. Although outside the scope of this article, it should be pointed out that society as a whole receives a solid return-on-investment. The increased patient compliance resulting from the use of noninvasive systems could lead to decreased treatments of symptoms that would otherwise have occurred with injection as a delivery system. Further, costs would be reduced in the administration of drugs as non-invasive is more patient-friendly and would not require doctor administration.

Most relevant to this article is that drug delivery technology offers pharmaceutical and biotechnology companies new ways to contribute to the bottom line. This article focuses on the economic components and variables that are part of the alternative drug delivery decision and the tools to analyze the components and variables. It is intended to supply an economic framework for multiple types of organizations within the biotechnology or pharmaceutical world—whether they are scientific or business management—involved in the decision-making process.

<sup>1</sup> Inhale Therapeutic Systems, 150 Industrial Road, San Carlos, California 94070.

<sup>2</sup> Correspondence should be addressed to Joyce Strand. e-mail:joyce.strand@inhale.com

<sup>3</sup> Dillon Read Equity Research Industry Report, *Drug Delivery Industry*, New York, April 21, 1997, p. 20.

<sup>4</sup> “It is our belief, and one being shared by more and more senior executives in the drug industry, that drug delivery represents one of the highest returns of investment per R&D dollar and stands to be one of the major sources of revenue and earnings growth for the pharmaceutical industry over the next decade.” From Dillon Read, p. 12.

<sup>5</sup> The Diabetes Control and Complications Trial Research Group, *The New England Journal of Medicine*, volume 329, Number 14, September 30, 1993, pp. 977–986.

<sup>6</sup> Peter Ginsberg, Piper Jaffray, *The Biotechnology Industry*, August 1997, p. 29.

<sup>7</sup> Dillon Read, p. 17.

## PROCESS FOR EVALUATION OF A DRUG DELIVERY DECISION

Biopharmaceutical companies evaluate drug delivery opportunities much the same way that they assess an extension to a current product line or a molecule in-licensing opportunity. The key components typically include a determination of technological feasibility, the product's fit within the current product line, and the economics of the new drug delivery product. Scientists often focus on technological feasibility, and assume if the product can pass the hurdles needed to make it to market it will be a money maker for the company. However, a cold, hard look at the economics must be done before the decision to proceed can be made.

To determine when, if, and what drug delivery projects to pursue requires an evaluation of drug delivery opportunities against all other investment possibilities, such as new chemical entity development. To aid in this comprehensive economic evaluation process, a detailed analysis can be conducted using a spreadsheet model. A number of factors can be considered:

- the costs to develop products, including technology development, clinical trials, and toxicology;
- sales increases;
- margin changes compared with current products that would be replaced by the delivery product, i.e., developing a non-invasive version of an injectable product.

Sales increases can come from a price premium, higher market share, and higher market penetration due to patient preference and increased compliance. Profit margin changes can be due to royalties payable to the delivery company, increases or decreases in the amount of bulk drug needed, and costs of manufacturing the delivery system.

## ECONOMIC MODEL FOR EVALUATION OF A DRUG DELIVERY DECISION

An illustrative example of how a non-invasive drug delivery system might be evaluated is as follows:

### Scenario

A biotechnology product has been on the market five years as an injectable and has reached peak sales of \$400 million per year without much competition. The product is not covered by a composition-of-matter patent but rather maintains market exclusivity due to a key-process patent which is due to expire in five years. Once this happens, the company expects two or more competitors to enter the market shortly thereafter resulting in their losing market share of 50% within two years. Based on their market research, they believe that if they could introduce a non-injectable delivery system at approximately the time of patent expiration, they could maintain 90% of their patient market share and receive a 10% pricing premium due to better patient compliance and patient preference (lower disease management costs).

To determine if it makes sense to develop such a product, the company completes a technical and economic analysis of this opportunity. The key technical analysis focuses on whether or not one or more technologies from drug delivery companies are commercially viable and might meet the product objective of

having an easy-to-use, non-injectable dosage form. Once the technology analysis is satisfied, they turn their attention to the commercial analysis. The commercial analysis takes into account the expected income differences for both scenarios.

**Scenario One** is that they do nothing and lose 50% of their market share. **Scenario Two** is that they develop this dosage form and maintain 90% of their market and receive a 10% pricing premium.

The next step is to determine the cost of the development program. This includes the cost to develop the pharmaceutical product including development milestones to the drug delivery company, the cost of the toxicology program and the cost of the clinical trial program including the activities required to achieve regulatory approval. They then estimate the factors that will affect the margin of the product once it reaches the market including likely price of product, cost of goods, royalty to the drug delivery company and incremental marketing and sales costs to introduce a new product. Two financial models were run.

With this analysis, the model can take into account the cash flow from the two scenarios which can be discounted back to today's dollars to determine the net effect of going forward with the project and the internal rate of return. The rate of return can then be compared to other projects to determine if it makes economic sense to go forward given the other alternatives available to the company. Table I lists the types of economic assumptions that a company can use in a model to determine the viability of a project.

In **Scenario 1**, the biopharmaceutical company assumes the current plan of action and does not develop the new delivery product.

In **Scenario 2**, sales for the alternative (non-invasive) form of drug delivery would begin in Year 6. In order to create a more realistic market situation, sales from the non-invasive system would begin at an initial 25% market share and grow by approximately the same amount each year, reaching a peak at Year 4 of 90%. Sales revenue during the three-year mix (transition) period would come from both injectable and the non-invasive sales. The non-invasive scenario shows an increase in Net Present Value (NPV) of just under \$188 million over the ten year period following patent expiration on the injectable form compared to Scenario I. This increase in Net Present Value takes into account the likely costs associated with the development of the non-invasive system, i.e., direct and indirect costs of Research and Development, milestones, and toxicology.

This \$188 million figure is the present value, or value in today's dollars that assumes a 10% discounting over the 15-year period. The difference in net cash flow (actual dollars) between the two scenarios over this ten-year period would be over \$530 million. These are fairly conservative figures in that they do not take into account any natural market growth that may have occurred over the years (the market remains flat from Year 1) as well as any newly converted patients that may have opted for the non-invasive system rather than abstaining from the injectable form.

## VARIABLES OF ECONOMICS

For different situations, the economic analysis will have very different results. The primary variables are: competitive vs. non-competitive market, e.g., G-CSF vs. growth hormone;

**Table I.** Example of Assumptions for Economic Model

In this example, the following assumptions were made by the company to determine the viability of the project:

|   |   |
|---|---|
| • commercial life of the project going forward                    | 15 years                                  |
| • peak year sales without drug delivery                           | \$400 million                             |
| • loss of market share without drug delivery                      | 25% Year 6, 50% thereafter                |
| • market share with drug delivery, patients                       | 90%, plus 10% pricing premium             |
| • development time for drug delivery product                      | 5 years to approval, sales begin Year 6   |
| • cost to develop the product                                     | \$8 million                               |
| • fully burdened clinical costs                                   | \$20 million                              |
| • toxicology costs  | \$1 million                               |
| • milestones to the drug delivery company                         | \$9 million spread out during development |
| • cost of goods sold with injectable                              | 15% of selling price                      |
| • cost of goods sold with non-invasive system                     | 20%                                       |
| • royalty rate to the drug delivery company                       | 10%                                       |
| • marketing and sales for the injectable                          | 10% of revenue                            |
| • marketing and sales for the non-invasive system                 | 15% of revenue first 3 years, then 10%    |
| • general and administrative                                      | 5% of revenue for both scenarios          |
| • company tax rate  | 35%                                       |
| • company's discount rate for calculating Net Present Value (NPV) | 10%                                       |

motivation of user, e.g., cancer vs. osteoporosis patient; and pricing spread and margin. Companies also look at the time the underlying drug will be viable with and without an improved delivery system. They take into account the possibility of a short life of an alternative drug delivery system assuming the possibility that it could be overtaken by new products.

On pricing, companies examine the reimbursement situation for the drug and whether a premium can be supported. This depends on the value to a user and overall cost. For example, beta interferon therapy costs \$8–10,000 per year. Considering the high price of this drug, a premium may be hard to justify. Insulin, with an annual cost of \$420 (\$260 for drug, \$160 for injection system) may be easier to justify. A higher-priced drug delivery system is unlikely to receive reimbursement unless the pharmaceutical company can demonstrate either great patient compliance, significant quality or pharmacoeconomic benefits. Reimbursement is a major issue in today's environment. Companies can't just assume that because a product is more convenient and easier to use that people will pay a premium price. Although patients might understand the benefit of an alternative to the needle, healthcare insurance may not, as so often happens with new drugs. To help with this issue, companies should be prepared to demonstrate to patients and to insurance companies the long-term cost benefits of using a drug delivery system that encourages compliance, i.e., the reduction of symptoms and the lowered cost of self (rather than doctor) administration.

There are also some non-traditional costs that could be factored into a model. Patients are much more sophisticated consumers than 5–10 years ago, particularly for chronic diseases. They are knowledgeable about alternative drug delivery systems and may demand alternatives to injections. The best marketing strategy may be to market directly to consumers, so these costs (such as consumer advertising) need to be factored into the business model. Consumer advocacy is also a mechanism for product reimbursement despite higher costs, provided the products deliver value to the patient.

### THE STRATEGIC ROLE OF DRUG DELIVERY

The decision to develop an alternative drug delivery system is basically an economic one. Although technology feasibility is a factor in the decision, it is only one component. Important to the analysis is that drug delivery products take less time to develop at less cost than a discovery drug, and hence provide a quicker return. An alternative drug delivery system is therefore a good fit for the current environment where fast time to market is important. There is also less risk involved with new drug delivery systems. Further, it has been shown that alternative drug delivery systems can increase patient compliance resulting in long-term return on investment for the healthcare system as a whole. Bottom line: when reviewing all these factors, drug delivery technology is increasing its strategic role in the growth of pharmaceutical companies due to the economics.