Estimating Social and Private Returns from Innovations Based on the Advanced Technology Program: Cases and Data Sources

Modeling Social and Private Rates of Return
Working Paper #4

Prepared for
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RTI Project Number 6715-1 WP

March 1997
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## Contents

1 Introduction 1-1  
  1.1 Objectives and Approach ............................................................. 1-1  
  1.2 Organization ................................................................................. 1-5  

2 Company Costs and Revenues 2-1  
  2.1. Measuring Producer Welfare ....................................................... 2-1  
  2.2 Calculating a Schedule of Benefits and Costs ......................... 2-2  
      2.2.1 Three Phases of Costs and Revenues .............................. 2-3  
      2.2.2 Data Requirements And Assumptions ............................ 2-5  
  2.3 Determining the Impact of ATP .................................................. 2-10  
      2.3.1 R&D Investment Incentives .......................................... 2-12  
  2.4 Summary .................................................................................... 2-16  

3 Calculating Social and Private Benefits 3-1  
  3.1 Alternative Measures of Economic Benefit .............................. 3-1  
  3.2 Social Costs and Benefits ............................................................. 3-3  
  3.3 Deriving Constant Dollar Costs and Discounting Benefits and Costs .................................................. 3-3  
      3.3.1 Adjusting for Inflation ..................................................... 3-4  
      3.3.2 Discounting ..................................................................... 3-4  

References R-1
Tables

Table 1-1  Summary of ATP-Funded Programs in Tissue Engineering ..........1-2
Table 1-2  Accounting for Stakeholders’ Benefits and Costs ..................1-4

Table 2-1  Private Sector Costs for New Technology Research,
            Commercialization, and Production........................................2-3
Table 2-2  Calculating Private Returns ..............................................2-11
Table 2-3  Impact of ATP on Total R&D ..............................................2-15
Figures

Figure 2-1  The Schedule of Costs and Revenues from Investments in ATP-Funded Projects in Tissue Engineering ...............................................................2-2
Figure 2-2  Impact of ATP Funding on R&D Spending by Companies ............2-13
1 Introduction

The National Institute of Standards and Technology’s (NIST’s) Advanced Technology Program (ATP) began in 1990 as a cost-sharing program to assist U.S. industry in pursuing high-risk, enabling technologies with significant commercial and economic potential. The ATP conducts economic analyses for the purpose of increasing and measuring the short- and long-run impacts of the technology development projects it funds and for the program overall.

Research Triangle Institute (RTI), under contract to NIST, is examining the economic impact of ATP-funded projects in tissue engineering. These seven projects, described in Table 1-1, constitute a “virtual program” in tissue engineering. Successful projects will serve as platforms for developing new therapies to treat a variety of diseases and injuries. These therapies contribute to social welfare by improving patient outcomes, reducing the cost of medical care, or both. In addition, these technologies may bring significant private returns to ATP recipients.

1.1 OBJECTIVES AND APPROACH

Our approach to modeling the social and private returns to ATP funding in tissue engineering is based on established principles of applied microeconomics and welfare economics, as demonstrated by Mansfield et al. (1977) in their paper “Social and Private Returns from Industrial Innovations.” This approach applies welfare economics principles as advocated by Harberger (1971) to value changes in resource allocation due to technological changes. Prices
Table 1-1. Summary of ATP-Funded Programs in Tissue Engineering
The first three companies listed below are candidates for in-depth case studies.

<table>
<thead>
<tr>
<th>Company Name: Aastrom Biosciences, Inc.</th>
<th>Contact: Dr. R. Douglas Armstrong</th>
<th>Phone: (313) 930-5555</th>
<th>Fax: (313) 665-0485</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address: 24 Frank Lloyd Wright Drive Lobby L Ann Arbor, MI 48104</td>
<td>Competition No./Funding Years: 91-01 2 years</td>
<td>Funding Level: $1,220,000</td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td>“Human Stem Cell and Hematopoietic Expansion Systems in Tissue Engineering”</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td>Develop prototype bioreactor to grow human stem cells, especially bone marrow cells</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Company Name: Integra LifeSciences Corp.</th>
<th>Contact: George L. Brode</th>
<th>Phone: (609) 936-2325</th>
<th>Fax: (609) 799-3297</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address: 150 Morgan Lane Plainsboro, NJ 08536</td>
<td>Competition No./Funding Years: 93-01 3 years</td>
<td>Funding Level: $1,999,000</td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td>“Structurally New Biopolymers Derived from Alpha-L-Amino Acids”</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td>Develop synthetic polymers for orthopedic applications (repairing cartilage and tendons)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Company Name: VivoRx, Inc.</th>
<th>Contact: Derek Brown</th>
<th>Phone: (310) 264-7768</th>
<th>Fax: (310) 264-7775</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address: 3212 Nebraska Ave. Santa Monica, CA 90404</td>
<td>Competition No./Funding Years: 94-01 3 years</td>
<td>Funding Level: $2,000,000</td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td>“Treatment of Diabetes by Proliferated Human Islets in Photocrosslinkable Alginate Capsules”</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td>Grow human islet cells and explore encapsulation techniques to help treat insulin-dependent diabetes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Company Name: Tissue Engineering, Inc.</th>
<th>Contact: Dr. Eugene Bell</th>
<th>Phone: (617) 946-0520</th>
<th>Fax: (617) 946-0684</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address: 305 Commonwealth Ave. Boston, MA 02115</td>
<td>Competition No./Funding Years: 92-01 3 years</td>
<td>Funding Level: $1,999,000</td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td>“Fabrication of Clinical Prosthesis from Biomaterials”</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td>Develop animal-derived extracellular matrix materials technology for future prostheses</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(continued)
Table 1-1. Summary of ATP-Funded Programs in Tissue Engineering (continued)

<table>
<thead>
<tr>
<th>Company Name:</th>
<th>Contact:</th>
<th>Phone:</th>
<th>Fax:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) BioHybrid Technologies, Inc. and (b) Synergy Research Corp.</td>
<td>John L. Hayes</td>
<td>(508) 842-4460</td>
<td>(508) 842-7535</td>
</tr>
<tr>
<td>Address: (a) Park Nine West 910 Turnpike Rd. Shrewsbury, MA 01545 (b) 325 Mount Support Rd. Hanover, NH 03755-5056</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Competition No./Funding Years: 93-01 3 years</td>
<td>Funding Level: $4,263,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Disease Treatment Using Living Implantable Microreactors”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Develop living implantable microreactors that contain transplant cells</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Company Name: Alexion Pharmaceuticals</td>
<td>Contact: David Keiser</td>
<td>Phone: (203) 776-1790</td>
<td>Fax: (203) 776-2089</td>
</tr>
<tr>
<td>Address: 25 Science Park, Suite 360 New Haven, CT 06511</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Competition No./Funding Years: 95-01 3 years</td>
<td>Funding Level: $1,999,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Universal Donor Organs for Transplantations”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Develop techniques to produce animal organs that will not be rejected by patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Company Name: Progenitor, Inc.</td>
<td>Contact: Douglass Given</td>
<td>Phone: (614) 488-6688</td>
<td>Fax: (614) 488-0404</td>
</tr>
<tr>
<td>Address: 1507 Chambers Road Columbus, OH 43212</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Competition No./Funding Years: 94-01 3 years</td>
<td>Funding Level: $1,996,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Title</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>“Application of Gene Therapy to Treatment of Cardiovascular Diseases”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Project Description</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Develop stem cells for cell-based therapies for vascular disorders and for antirejection (repair damaged tissue)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

and quantities of commodities traded in competitive markets can be used to compute Marshallian measures of welfare, that is, changes in consumers’ and producers’ surplus.

We have modified this approach for the case of innovations in tissue engineering. The absence of traditional markets for medical treatment (due to the intervention of health insurance and other institutional factors) implies that market prices and quantities will not adequately reflect social welfare; therefore, we must use nonmarket valuation techniques.
Table 1-2 shows our approach to accounting for the benefits and costs of the new technologies to each stakeholder group. Recall that we are trying to capture the flow of benefits to the users of the technology (changes in consumers’ surplus) and the benefits to the producers of the technology (changes in producers’ surplus). Patients are the main beneficiaries of the new technologies. However, because everyone who participates in the medical care system pays for medical care, these stakeholders also incur benefits (or costs) from new technologies if these technologies affect the cost of providing benefits to patients. Similarly, although the companies producing the technology may benefit from receiving prices in excess of their marginal cost, we must also consider the cost to taxpayers of the ATP program, as well as changes in the revenue of companies whose technologies may be displaced by the new technologies. After considering the benefits and costs to all stakeholders, we can determine the sum of benefits and costs to society and calculate summary measures, including the net present value (NPV) to the private sector and society, a private rate of return (PRR), and a social rate of return (SRR).

Table 1-2. Accounting for Stakeholders’ Benefits and Costs
Our analysis captures the benefits and costs to each stakeholder, except transfers within stakeholder groups.

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Benefits</th>
<th>Costs</th>
<th>Summary Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private sector</td>
<td>Revenue</td>
<td>R&amp;D, commercialization, and production</td>
<td>NPV, PRR</td>
</tr>
<tr>
<td>Patients</td>
<td>Value of changes in health outcomes</td>
<td>—</td>
<td>N/A</td>
</tr>
<tr>
<td>Stakeholders of the medical care system</td>
<td>Decrease in health care costs</td>
<td>Increase in health care costs</td>
<td>N/A</td>
</tr>
<tr>
<td>Taxpayers</td>
<td></td>
<td>ATP program costs</td>
<td>N/A</td>
</tr>
<tr>
<td>Society</td>
<td>Sum</td>
<td>Sum</td>
<td>NPV, SRR</td>
</tr>
</tbody>
</table>

This working paper builds on the work reported in previous working papers. Working Paper #1 laid the groundwork for the project by developing key assumptions about each tissue engineering project. Working Paper #2 showed how we measure the benefits to patients and to the stakeholders of the medical care system by measuring consumers’ surplus (net of the cost of the treatment). In Working Paper #3, we described how we will determine the quantity of these medical
technologies that would be produced and consumed, assuming they are technically successful.

In this working paper, we

- explain our method for measuring benefits and costs to the private sector,
- describe our approach to measuring the PRR, and
- describe our approach to measuring the SRR.

1.2 ORGANIZATION

Section 2 explains how we will measure the costs and benefits to the private sector. Section 3 describes how we will calculate the PRR given the schedule of costs and benefits we have constructed for the private sector. Then we describe how we will construct the stream of social benefits and costs and calculate the social rate of return.
2 Company Costs and Revenues

In this section we describe our approaches for modeling the costs and benefits to the private sector of investing in ATP-funded projects in tissue engineering and the ATP’s impact on these benefits and costs.

2.1. MEASURING PRODUCER WELFARE

One of the objectives of this project is to develop measures of benefits to the private sector of investing in the development of new technologies in tissue engineering. Net present value (NPV) and private rate of return (PRR) are appropriate choices for measuring these benefits because they have been widely used to evaluate public-sector research and therefore would provide comparable estimates (Link, 1996). They are also commonly used in the private sector to estimate the potential benefits of alternative investment projects.

However, as explained in Section 1, we would like our methodology to provide an economically meaningful measure of producer welfare. Thus, we would like to measure the producers’ surplus (also called quasi-rent) associated with companies’ investments in these technologies.

Accounting measures of companies’ benefits from investments in ATP-funded projects—NPV and PRR—differ from economic measures of producer welfare. NPV and PRR are accounting concepts that measure the profitability of investments such as conducting R&D, building a plant, or developing supplier networks. Because these investments are considered sunk at the time of production, they are not considered in economic measures of producer welfare. Thus, the NPV of these investments and the resulting estimates of the PRR differ from producers’ surplus by the amount of these sunk costs (Just, Hueth and Schmitz, 1982).
2.2 CALCULATING A SCHEDULE OF BENEFITS AND COSTS

Investments in R&D, particularly in the biomedical field, often lead to profits only after a long period of investment. To calculate the PRR, we must develop a schedule of costs and revenues to the private sector over time. Figure 2-1 demonstrates how we characterize the time path of benefits and costs. As explained in the next section, we have divided the schedule of costs and benefits into three phases.

Figure 2-1. The Schedule of Costs and Revenues from Investments in ATP-Funded Projects in Tissue Engineering
We have divided the schedule of costs and benefits into three phases.
2.2.1 Three Phases of Costs and Revenues

We divide the time path of costs and revenues into three phases:

- R&D phase,
- commercialization phase, and
- production phase.

In each phase, the firm incurs costs, while revenues are received only in the production phase. Table 2-1 details the type of costs incurred in each of the three phases.

Table 2-1. Private-Sector Costs for New Technology Research, Commercialization, and Production

We do not specify the distribution of revenues and costs among the potential private-sector stakeholders.

<table>
<thead>
<tr>
<th>Phase I: R&amp;D</th>
<th>Phase II: Commercialization</th>
<th>Phase III: Production</th>
</tr>
</thead>
<tbody>
<tr>
<td>R&amp;D</td>
<td>Regulatory review</td>
<td>Production costs</td>
</tr>
<tr>
<td>Administration</td>
<td>Development of marketing and supplier networks</td>
<td>Marketing</td>
</tr>
<tr>
<td>Finance</td>
<td>Building of production capacity</td>
<td></td>
</tr>
</tbody>
</table>

The R&D Phase

Throughout the R&D phase, companies incur costs but receive no revenues. Companies face significant uncertainty regarding whether the project will be technically successful. This will always be true of an ATP-funded project since, by definition, ATP funds high-risk technologies that are “technical challenges which display significant recognized uncertainty of success” (Ruegg, 1996).

At the end of Phase I, the company assesses whether the project has achieved its technical goals and can proceed to commercialization. If the project is successful technically, the company decides how to proceed with commercialization. The company may retain exclusive rights to marketing, manufacturing, and distribution; license the technology to another company that will retain these rights; or arrange some other type of agreement with a partner or licensee. Costs will not be incurred in this stage unless the project is technically successful.

We assume that revenue generated from licenses and royalties will be approximately the expected present value of the future stream of benefits. Thus, the distribution of

---

1We are speaking of the company narrowly as the business unit developing the new technology, under the assumption that it produces no other products.

2Many choices lie between selling all rights and retaining exclusive rights. As explained in the following paragraph, this choice is immaterial to calculating benefits and costs.
costs and benefits of commercialization and production among companies is irrelevant; no matter who actually engages in these activities, they will be part of the private returns to the investment.

The Commercialization Phase

We distinguish between the R&D phase and the commercialization phase by noting that during R&D, the technical success of the project is uncertain. The commercialization phase begins once this uncertainty has been resolved.

The commercialization phase begins after the technical success of the project has been evaluated. In the case of our seven ATP-funded projects in tissue engineering, we assume that the commercialization phase begins at the end of the ATP project.

In many cases, it is difficult to identify where R&D ends and commercialization begins. The commercialization phase will probably include substantial product development research—for example, the research required for regulatory review or to design a production process. However, the key distinction between the R&D phase and the commercialization phase is the uncertainty regarding the technical success of the project. The company’s uncertainty about the potential profitability of the project during the commercialization phase involves its potential market success.

This distinction has implications for how we construct the schedule of expected benefits and costs. We multiply all benefits and costs that occur during and after the commercialization phase by the probability of technical success. This formula is based on our assumption that companies will not commercialize or produce a product, and therefore will not incur the associated costs, unless they have achieved technical success.

The commercialization phase involves meeting regulatory requirements, designing a production process and building a plant, arranging marketing and supplier agreements, conducting market research, and making other investments necessary to produce and market the product. The private sector continues to receive no revenue during this phase.

The Production Phase

The production phase begins once the company has begun selling the product embodying the new technology. During this phase, the only costs incurred are tied to production and marketing. The company begins to earn revenue from the sale of products during this phase. Recall that we account for benefits and costs of a new technology for 10 years after its introduction to the market; thus, the production phase ends 10 years after market introduction.
2.2.2 Data Requirements And Assumptions

We need the following data to construct the schedule of benefits and costs:

- R&D investment in each year from the beginning of the project to the year prior to the first year of the commercialization phase,
- a schedule of investment in commercialization during the commercialization phase,
- variable costs of production,
- revenue, and
- probability of technical success.

As explained above, we calculate expected benefits and costs by multiplying revenue, production costs, and investment in commercialization by the probability of technical success.

We must construct a schedule of expected benefits and costs for both the with-ATP and the without-ATP scenarios. The without-ATP scenario can differ from the with-ATP scenario with respect to the level of R&D investment, the probability of technical success, and the timing of the stream of revenues and costs. In this section, we discuss our with-ATP assumptions. Section 2.3 describes our without-ATP assumptions.

R&D Investments

For the with-ATP scenario, we assume that the company’s R&D investment in the project is equal to its contribution to the ATP project’s total budget—that is, the total project budget minus the amount funded by ATP.
We acknowledge that this is a narrow view of the investment of these companies into these technologies. Although this narrow view is, in part, a consequence of the lack of data available for this analysis, we recognize its limitations for representing the company’s true investment in the process. R&D can be viewed as a production process whose inputs include the stock of the company’s knowledge resulting from previous R&D in related projects. These spillovers occur from projects that are successful as well as from those that are failures. Companies often take a portfolio approach to R&D investment. They understand that not all projects will lead to a commercial success but that even failures are valuable.

Our inability to account for these spillovers between projects within a company may underestimate the company’s investment in these technologies. This may be especially true for a company that has a history of R&D in areas related to the ATP project. As a consequence, our rates of return may be biased upward for some projects, especially those in which the ATP project builds on accomplishments of previous R&D by the same company. One example of this situation is the VivoRx project. The company’s investments in related R&D and consequences for the results of our analysis are described in the sidebar.

On the other hand, knowledge spillovers from these ATP projects to other projects are also likely. In fact, ATP projects are chosen because of their potential to lead to advances in science and technology that enable advances in other areas. Because of the need for pragmatism in analyzing the benefits of these technologies, we have defined the applications of these technologies fairly narrowly, and we do not account for these spillovers. For example, representatives of Integra LifeSciences told us that the application we are modeling (fracture fixation of specific types of fractures) is only the first application of their technology and probably will be less important than future applications.

**Fixed Costs of Commercialization and Variable Costs of Production**

As explained in Section 2.2.1, the costs incurred during the commercialization phase include the costs of undergoing regulatory review, developing marketing networks, building production capacity, and developing supplier networks. These expenses will not be incurred unless the project has been technically successful and has some chance for market success.

Very few of the companies we interviewed could provide an estimate of the cost of conducting these activities. A few offered estimates of the additional research, beyond the ATP project, that would be required to bring the project to market. But none of the
companies are close enough to commercialization to predict the fixed costs of commercialization or the variable costs of production. Thus, we must make some assumptions about the relationships between these costs and other information we have about the companies.

To develop assumptions about the magnitude of these costs, we consulted a profile of the pharmaceutical industry. The products embodying the ATP-funded technologies in tissue engineering can probably be classified in SIC 2835 (in vitro and in vivo diagnostic substances) and 2836 (biological products except diagnostic substances). However, in some ways, the markets for the products we are studying will be similar to the markets for pharmaceutical preparations (2834), where a significant investment in R&D is required to develop novel drug preparations. (Murray et al., 1996).

For industry 2834, the ratio of production costs (including capital depreciation) to the value of shipments is 0.41. This ratio is higher in SIC codes 2835 (0.60) and 2836 (0.56) (Murray et al., 1996); however, we believe that, for tissue engineering products, value added by R&D relative to value added by production will be similar to industry 2834.\(^3\) Thus, we will use 0.41 to represent the percentage of revenue that will be required for production. Because the costs included in the numerator of this ratio include capital depreciation, we do not need to account for the fixed costs of plant and equipment elsewhere.

The commercialization cost, as shown in Table 2-1, includes not only the costs of plant and equipment, but also the cost of developing the product and developing marketing and supplier networks. Neither of these costs is represented in the numerator of the production cost ratio. In the pharmaceutical industry, advertising, promotion, and sales costs represent about 33 percent of total revenue (PhRMA, 1996). We assume that one-quarter of these costs will be incurred prior to production and the remainder will be incurred annually. Thus, the fixed costs will be

\[
CC_M = 0.25 \times 0.33 \times \sum_{t=1}^{10} TR_t
\]

(2.1)

where \(CC_M\) represents the fixed portion of commercialization costs due to marketing expense and \(TR_t\) is total revenue in year \(t\). These costs are spread over the commercialization period, which begins at the completion of the ATP project and ends in the first year to market.

Of the seven companies we interviewed, four were able to provide an estimate of the additional research investment that would be required, post ATP, to bring the

\(^3\)We will try to verify this by talking with some analysts of the biotechnology industry. If necessary, we will change this ratio in the draft final report.
technology to market. These estimates include the costs of conducting research required for regulatory review. We include these estimates in our commercialization costs. For the companies that could not provide an estimate, we refer again to the pharmaceutical industry. We assume that total research spending, including the total ATP project budget, equals 19 percent of expected revenue, which is the average for the pharmaceutical industry (PhRMA, 1996). We subtract the ATP project costs from this 19 percent to calculate the second component of commercialization cost:

\[ C_{CR} = 0.19 \times \left[ \sum_{t=1}^{10} TR_t \right] - ATP_P - ATP_R \]  \hspace{1cm} (2.2)

where \( C_{CR} \) represents the portion of commercialization costs due to additional research. \( ATP_P \) is the public’s investment of ATP funds to the project, and \( ATP_R \) is the company’s contributions to the ATP budget. We spread this total over the number of years in the commercialization period.

This procedure probably overestimates commercialization costs due to additional research. The 19 percent of pharmaceutical revenue that typically is spent on R&D includes R&D for an entire portfolio of products, only a few of which will be marketed successfully. Unless we include the spillover benefits from these failed projects as well, we are overestimating costs relative to the benefits.

**Revenue**

Revenue is equal to the per-unit price, as predicted by the companies, multiplied by our estimate of the quantity that will be sold in the 10 years following the expected date of commercialization. The quantity estimates are derived from our procedures outlined in Working Paper #3.

**Probability of Technical Success**

To determine the probability of technical success, we use the companies’ own assessment of the progress they have made toward demonstrating the technical feasibility of the project and adjust it to account for the percentage of project funds that has been spent.

Assessing the probability of technical success for ATP projects in tissue engineering is very difficult, especially for projects that are relatively young. We considered using the company’s assessment of its progress toward demonstrating the technical feasibility of its ATP project, as reported in quarterly and anniversary business reports. However, because the projects are in different stages of their ATP award, we adjusted these numbers to normalize them for the stage in the ATP project. For example, Progenitor, Inc., reported in their report dated June 30, 1996, that they had made 0 to 25 percent progress in demonstrating the technical feasibility of their project. They began their research in 1995 (award was made from the 1994 competition), and the project period was 3 years. Thus, as of June 1996 they were at
the halfway point in their project. We applied the following formula to determine probability of technical success:

\[ P = \frac{TF}{PF} \]  \hspace{1cm} (2.3)

where \( TF \) is the midpoint of the range of technical feasibility and \( PF \) is the percentage of funding that has been spent at the time \( TF \) was assessed.

Thus, Progenitor’s formula (assuming they had spent half of their funds at the halfway point in the project)\(^4\) was

\[ \frac{0.125}{0.5} = 0.25 \]

These data are not available for Aastrom Biosciences and Tissue Engineering, Inc. For these two projects, we determined a probability of technical success based on our interviews with the company representatives. Although they did not provide a numerical assessment of this probability, they did identify the technical challenges yet to be met. Obviously, our assessment of this probability is quite subjective. We will use @Risk to provide a range of values and to conduct sensitivity analysis.

**Summary**

Table 2-2 provides an example of how costs, revenues, and returns will be calculated. The first section of the table provides some of the parameters of the analysis: the assumed first year to market, the company’s progress towards demonstrating feasibility, the percentage of funds spent on the project, and the resulting probability of technical success. The product price is also shown in this section.

The next section of the table provides an annual schedule of costs and revenues. During the R&D phase, only ATP project budget money is spent. During the commercialization phase, the up-front costs for advertising, marketing, and promotion are spent, as well as any additional R&D costs. During the production phase, production costs and commercialization costs are incurred, and revenue is generated from the sale of the company’s product.

The column labeled “net benefit” provides our estimate of the revenue minus all costs in each year, assuming a 100 percent probability of technical success. The column labeled “expected net benefit” multiplies all revenues and all costs incurred after the R&D phase by the probability of technical success.

---

\( ^4 \)If we cannot obtain an estimate of \( PF \) from project records, we will use the percentage of calendar time that has elapsed on the project.
2.3 DETERMINING THE IMPACT OF ATP

ATP can affect the level of private R&D investment, the probability of technical success, and the time path of revenues and costs.

To examine the impact of ATP on these variables, we must make some assumptions about how ATP funding affects the company’s incentives for investing in the project. We borrow a simple model of the R&D investment decision from Binswanger (1978) to discuss the impact of ATP on R&D investment and the implications for our modeling of the without-ATP investment decisions of firms. Then we describe how we will model the effect of R&D investment on the probability of technical success.
Table 2-2. The Schedule of Costs and Benefits to Companies Receiving ATP Funding

We multiply all costs and benefits by the probability of technical success to determine the expected net benefit.

**With ATP**

**Parameters:**
- Year to market: 2000
- Progress towards demonstrating feasibility: 0.63
- Percent of funds spent: 1.00
- Probability of technical success: 0.63
- Product price: $90

**Schedule of Costs and Revenues**

<table>
<thead>
<tr>
<th>Yr.</th>
<th>ATP Grant</th>
<th>Private R&amp;D</th>
<th>Commer Cost</th>
<th>Addition R&amp;D</th>
<th>Prod. Cost Quant. Sold</th>
<th>Revenue</th>
<th>Net Benefit</th>
<th>Expected Net Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td></td>
<td></td>
<td></td>
<td>$849,915</td>
<td>$433,333</td>
<td></td>
<td>–$1,283,248</td>
<td>–$802,030</td>
</tr>
<tr>
<td>1998</td>
<td></td>
<td></td>
<td></td>
<td>$849,915</td>
<td>$433,333</td>
<td></td>
<td>–$1,283,248</td>
<td>–$802,030</td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td></td>
<td></td>
<td>$849,915</td>
<td>$433,333</td>
<td></td>
<td>–$1,283,248</td>
<td>–$802,030</td>
</tr>
<tr>
<td>2000</td>
<td>$112,489</td>
<td>$184,500</td>
<td>5,000</td>
<td>$450,000</td>
<td>$153,011</td>
<td></td>
<td>$95,632</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>$179,982</td>
<td>$295,200</td>
<td>8,000</td>
<td>$720,000</td>
<td>$244,818</td>
<td></td>
<td>$153,011</td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>$337,466</td>
<td>$553,500</td>
<td>15,000</td>
<td>$1,350,000</td>
<td>$459,034</td>
<td></td>
<td>$286,896</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>$517,448</td>
<td>$848,700</td>
<td>23,000</td>
<td>$2,070,000</td>
<td>$703,852</td>
<td></td>
<td>$439,907</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>$742,426</td>
<td>$1,217,700</td>
<td>33,000</td>
<td>$2,970,000</td>
<td>$1,009,874</td>
<td></td>
<td>$631,171</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>$854,915</td>
<td>$1,402,200</td>
<td>38,000</td>
<td>$3,420,000</td>
<td>$1,162,886</td>
<td></td>
<td>$726,803</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>$922,408</td>
<td>$1,512,900</td>
<td>41,000</td>
<td>$3,690,000</td>
<td>$1,254,692</td>
<td></td>
<td>$784,183</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>$967,403</td>
<td>$1,586,700</td>
<td>43,000</td>
<td>$3,870,000</td>
<td>$1,315,897</td>
<td></td>
<td>$822,435</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>$989,901</td>
<td>$1,623,600</td>
<td>44,000</td>
<td>$3,960,000</td>
<td>$1,346,499</td>
<td></td>
<td>$841,562</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>$1,012,399</td>
<td>$1,660,500</td>
<td>45,000</td>
<td>$4,050,000</td>
<td>$1,377,101</td>
<td></td>
<td>$860,688</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>$1,012,399</td>
<td>$1,660,500</td>
<td>45,000</td>
<td>$4,050,000</td>
<td>$1,377,101</td>
<td></td>
<td>$860,688</td>
<td></td>
</tr>
</tbody>
</table>
2.3.1 R&D Investment Incentives

Companies invest in R&D because it provides a potential stream of future profits. A company determines its level of R&D investment by equating the expected payoff with the R&D cost. By reducing the cost of R&D, ATP funding increases the amount of R&D companies conduct and increases the likelihood that a project will be successful.

The R&D process can be characterized as a search or sampling process in which scientists sample from a distribution of potential solutions to the problem they are trying to solve. Each potential solution has characteristics that determine its payoff. For example, the expected payoff of a research study that searches for effective methods for proliferating human cells depends, in part, on the rate of proliferation that is achieved. The distribution of characteristics (e.g., proliferation rates) among the potential solutions is determined by nature and the state of basic science (Binswanger, 1978).

The total expected payoff to the research increases as the size of the sample (e.g., number of methods investigated) increases. As the size of the sample increases, the probability of discovering the best available solution also increases. However, the research is subject to diminishing returns; each successive draw from the distribution is less likely to yield a solution that is superior to the best of the previous draws (Binswanger, 1978). Thus, the marginal expected benefit of research spending (value of successive draws from the sample) declines with increases in R&D.

Because ATP provides matching funds, ATP funding reduces the cost to the private sector of each dollar of private R&D spending. For example, ATP’s grant to Aastrom Biosciences provided $1,220,000 to Aastrom’s $1,514,000. Thus, the cost of $1 of R&D to Aastrom was about 0.55. Figure 2-2 demonstrates the impact of this price change on the total quantity of R&D. If $C_1$ represents the cost of $1 of R&D with ATP and $C_2$ represents the cost of $1 of R&D without ATP, then if the marginal benefit function is $MB$, research will fall from $Q_1$ to $Q_2$.

---

5 This result holds under the assumption that each draw is randomly selected. The rate of decline of the returns to research is greater if researchers investigate potential solutions in order of their potential benefits.

6 Actually, the cost of an R&D dollar in the absence of the ATP may be greater than $1; it would be $1.10 if the company pays 10 percent interest.
Figure 2-2. Impact of ATP Funding on R&D Spending by Companies
When the cost of R&D rises from $C_1$ (with ATP) to $C_2$ (without ATP) companies will conduct less R&D. The amount by which R&D falls depends on the local elasticity of the marginal benefit function.

Determining the impact of this change in the cost of funds on the company’s total R&D spending is similar to determining the effect of a price change on the total expenditure of a consumer. When the price of a dollar of R&D increases from the with-ATP price to the without-ATP price, the total amount of private R&D spending on the project total R&D) will not change if the marginal benefit function has an elasticity equal to –1. It will rise if the marginal benefit function is inelastic (greater than –1); it will fall if the marginal benefit function is elastic (less than –1). In Figure 2-2, the impact of a cost change on total R&D is $Q_2 - Q_1$ for curve MB, but only $Q_2' - Q_1$ for the less elastic MB’.

The elasticity of a project’s marginal benefit function depends on a number of factors, including the productivity of research in the area that the company is researching relative to other research or investment opportunities. Our conversations with companies about the impact of ATP on their R&D investment indicate that this elasticity varies widely among companies. For example, Integra LifeSciences indicated that, in the absence of ATP funding, they would have significantly reduced their R&D effort in the specific area funded by ATP. This is at least in part because Integra is conducting research in a variety of other areas and could have applied their research effort in these other areas. Thus, we have reason to believe that their expected marginal benefit curve is elastic. Other companies with a less-diversified portfolio of research
opportunities probably have less elastic marginal benefit curves. Most of the other companies indicated that in the absence of ATP they still would have pursued their research and that the scope effects would have been small.

The degree to which ATP funding displaces private funding is an empirical question that is beyond the scope of this project. However, we do know that, unless the expected marginal benefit curve is completely inelastic (vertical), the elimination of ATP funding must reduce the total quantity of research. One situation in which elimination of ATP funding would not decrease the total quantity of research would be an instance in which the company could have obtained alternative funding for the project that provides a similar decrease in the price of R&D (e.g., provided a similar sized grant). We believe this situation is unlikely.

Impact of ATP on Private R&D Funding

Without empirical estimates of the marginal benefit function or its elasticity, we make the following assumptions:

- For companies that indicated a significant reduction in the scope of the project in the absence of ATP, we will assume that their marginal benefit function is equal to −2—elastic. The only company that will be assigned this elasticity is Integra LifeSciences.

- For companies that indicated that in the absence of ATP they would have proceeded with the project but under some possible funding constraints that may have affected the scope, we assume that they do not have a diverse research portfolio that would have provided a good substitute R&D investment project. Thus, we will assume that their marginal benefit function is −0.5—relatively inelastic. We assign this elasticity to Aastrom Biosciences, VivoRx, BioHybrid, Progenitor, and Alexion Pharmaceuticals.

- For companies that told us that the absence of ATP funding would have made no difference in the scope of the project, we will assume that the cost of R&D was immaterial to their decision to proceed with the project. We assume a price elasticity of −0.01. We apply this assumption to Tissue Engineering, Inc.

Table 2-3 provides a summary of the impact of these assumptions on our assumptions about the without-ATP level of research expenditures.

Table 2-3. Impact of ATP on Total R&D

The impacts of the ATP on total R&D depends on the with-ATP price of research funds and the elasticity of the marginal benefit curve.
<table>
<thead>
<tr>
<th>Company</th>
<th>ΔC</th>
<th>ΔT</th>
<th>TC</th>
<th>RC</th>
<th>ΔR</th>
<th>CR</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aastrom</td>
<td>-0.5</td>
<td>0.554</td>
<td>$1,514</td>
<td>$2,734</td>
<td>1.0</td>
<td>$2,034.5</td>
<td></td>
</tr>
<tr>
<td>Integra</td>
<td>-2.0</td>
<td>0.190</td>
<td>$469</td>
<td>$3,468</td>
<td>1.0</td>
<td>$89.1</td>
<td></td>
</tr>
<tr>
<td>VivoRx</td>
<td>-0.5</td>
<td>0.882</td>
<td>$1,4925</td>
<td>$16,925</td>
<td>1.0</td>
<td>$15,893.6</td>
<td></td>
</tr>
<tr>
<td>BioHybrid</td>
<td>-0.5</td>
<td>0.500</td>
<td>$4,262</td>
<td>$8,525</td>
<td>1.0</td>
<td>$6,027.7</td>
<td></td>
</tr>
<tr>
<td>Progenitor</td>
<td>-0.5</td>
<td>0.286</td>
<td>$799</td>
<td>$2,795</td>
<td>1.0</td>
<td>$1,494.4</td>
<td></td>
</tr>
<tr>
<td>Alexion Pharmaceuticals</td>
<td>-0.5</td>
<td>0.376</td>
<td>$1,204</td>
<td>$3,203</td>
<td>1.0</td>
<td>$1,963.8</td>
<td></td>
</tr>
<tr>
<td>Tissue Engineering, Inc.</td>
<td>-0.01</td>
<td>0.516</td>
<td>$2,128</td>
<td>$4,127</td>
<td>1.0</td>
<td>$4,099.8</td>
<td></td>
</tr>
</tbody>
</table>

**Impact of ATP on Timing of R&D Expenditures**

Almost all of the companies indicated that ATP had an impact on the timing of their introduction of the product to the market. For the without-ATP case, we will allocate total R&D spending over these additional years. This delay in R&D spending, we assume, also will delay the technical success of the project and subsequent introduction of the discovery to the market.

**Impact of ATP on Probability of Success**

We will assume a deterministic relationship between total R&D funding and the probability of success:

\[
Pr = f(R) \tag{2.4}
\]

This assumption is common among strategic R&D investment models such as those presented in Beath (1989), Loury (1979), and Lee and Wilde (1980). Their models assume that the probability of success in any year is a function of the R&D that is spent in that year.

Rather than assuming a specific functional form, we will specify an elasticity for this function:

\[
\frac{\partial \ln Pr}{\partial \ln R} = \phi \tag{2.5}
\]

where \(\phi > 0\).

This form ensures that as research funding increases, probability of success also increases; it increases at a decreasing rate. This preserves the downward-sloping marginal benefit function, since marginal benefit is the product of the marginal probability of success and the discounted stream of profits assuming success.
Because we have no empirical evidence for the value of $\phi$, we will assume it is 0.5 and conduct sensitivity analysis to determine the impact of varying this parameter on the results of the study.

2.4 SUMMARY

To determine the PRRs to investments in ATP-funded technologies, we must construct a schedule of costs and benefits for each year from the beginning of the ATP project to 10 years after the expected time to market.

Using this schedule of costs and benefits, we will calculate a total cash flow for each year, assuming that the probability of technical success is 1. Then we will calculate an expected cash flow, which is adjusted for the probability of technical success.

We will construct two tables: one with ATP and one without. The following parameters can vary from the with-ATP scenario:

- level of R&D investment,
- timing of R&D investment and product introduction, and
- probability of technical success.
3 Calculating Social and Private Benefits

For each of the seven ATP-funded projects in tissue engineering, we will calculate the NPV of the project to the company receiving ATP funding and the company’s PRR on its investment in this project. To assess the welfare benefits of each project to society, we will calculate the NPV of the ATP project given the net benefits to all stakeholders and the associated SRR.

3.1 ALTERNATIVE MEASURES OF ECONOMIC BENEFIT

$NPV$ provides the most straightforward method for evaluating the economic impact of a project. $NPV$ is

$$\sum_{i=0}^{n} \frac{NB_{t+i}}{(1+r)^i}. \quad (3.1)$$

Although $NPV$ is the most accurate measure of the economic value of a project, it does not allow for comparisons across projects of different sizes. The $NPV$ is also sensitive to the choice of discount rate, $r$.

Sometimes analysts use a benefit-cost ratio to adjust for these differences in sizes. However, this ratio is very sensitive to the allocation of cash flows to the benefit or cost side of the ratio. For example, the benefit-cost ratio might differ depending on whether the analyst calculates net revenue (revenue minus production cost) and counts this as a benefit, or explicitly counts revenues as benefits and production costs as cost. Furthermore, benefit-cost ratios may not be appropriate for ranking projects, since a project that yields a lower net benefit might have a higher benefit/cost ratio (Link, 1996).
A commonly used measure of the economic benefits from technology investment is the IRR. The IRR is the interest rate that forces the NPV of the project’s expected net benefits to be 0. Thus, to calculate the IRR, we solve the following equation for $r$:

$$\sum_{i=0}^{n} \frac{NB_{t+i}}{(1+r)^i} = 0,$$

(3.2)

where $t$ is the first year in which either benefits or costs occur, $NB_{t+i}$ is the net benefit (benefit minus cost) in the $i$th year after year $t$, and $n$ is the number of years over which benefits or costs accrue. When considering only costs and benefits to the company receiving ATP funding, we refer to the PRR; if we are considering the benefits and costs to all stakeholders, we refer to the SRR. The IRR can be interpreted as a percentage yield occurring over a defined period of time, and it is appropriate for comparison across projects. One important benefit of the IRR over NPV is that it does not require selection of a discount rate.

The IRR suffers from several potential shortcomings for evaluating investments in technologies. These shortcomings, which have been discussed by Tassey (1996), include its bias toward projects that provide benefits earlier in the study period and its failure to consider reinvestment of interim receipts. We will consider IRR’s bias toward earlier payoff projects by calculating both a rate of return and an NPV for each project.

A potential solution to the IRR’s failure to consider the reinvestment of interim receipts is to use the “adjusted” IRR, or AIRR. The AIRR was defined by Ruegg and Marshall (1990) as the annual compound percentage yield from a project over the study period, taking into account reinvestment in interim receipts. Calculating the AIRR requires choosing a reinvestment rate that represents the rate at which economic returns can be reinvested. However, we face a conceptual problem with assuming that the returns from medical innovations can be reinvested. A large portion of these benefits are benefits to patients who enjoy a better quality of life than they would in the absence of these new innovations. It seems inappropriate to assume that these benefits, which are embodied in patients’ well-being, can be reinvested. Thus, we have chosen not to calculate the AIRR.
Section 3 — Calculating Social and Private Benefits

3.2 SOCIAL COSTS AND BENEFITS

To calculate the net benefits to society and the corresponding SRR, we must set up a schedule of social costs and benefits similar to the schedule of private costs and benefits described in Section 2. The schedule of social costs and benefits must include all sources of costs and benefits to all stakeholders, including:

- R&D investment from both public and private sources;
- other private costs and benefits as described in Section 2; and
- benefits to patients and the medical care system, which are calculated in our health benefits model.

We have not yet considered one other source of benefits and costs: costs to companies producing the defender technology that will no longer earn rents on these products. Because we have no basis for making any other assumption, we simplify our analysis by assuming that profits on these defender technologies are equal to zero.

In a manner similar to calculating private net benefits, we calculate social net benefits assuming that the probability of technical success is equal to 1. Then we calculate expected net benefits by multiplying all costs and benefits, except those incurred in the R&D phase, by the probability of technical success.

Finally, we calculate the NPV of the investment and the SRR. We will calculate NPV and SRR for the with-ATP and the without-ATP scenarios.

3.3 DERIVING CONSTANT DOLLAR COSTS AND DISCOUNTING BENEFITS AND COSTS

To ensure that our measures are comparable to other studies of the social costs and benefits of federal programs, we will follow Office of Management and Budget (OMB) guidance for adjusting costs and benefits for inflation and choosing an appropriate discount rate. OMB’s guidelines are specified in Circular No. A-94.

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1 Alternatively, we could identify the companies that manufacture these defender technologies and try to determine the profit percentage from publicly available reports. However, these companies (e.g., Novo Nordisk, which manufactures insulin) manufacture a wide variety of products, so assessing the contributions of different products to their profits would be very difficult.
3.3.1 Adjusting for Inflation

Some of the costs that we collected from various data sources, including costs of medical care and costs to companies in R&D investments, are denominated in nominal values. We used the consumer price index (CPI) to adjust these values to constant (1996) dollars. When adjusting the cost of medical care (e.g., when we used the cost of a surgical procedure quoted in 1992 dollars), we used the medical care component of the CPI to adjust these prices to 1996 dollars.\(^2\)

OMB (1995) advises against making assumptions about future inflation. We assume that all data gathered about future costs and benefits are denominated in constant (1996) dollars. For example, when industry representatives provide an expected price for a medical procedure or device, we assume that their estimates are denominated in constant dollars, not taking into account the potential effects of future inflation on these prices.

3.3.2 Discounting

Once all costs and benefits are converted to a 1996 constant-dollar basis, we can apply a real discount rate. OMB recommends using a real discount rate of 7 percent. This rate approximates the marginal pretax rate of return on an average investment in the private sector in recent years.

Because we are discounting benefits and costs that have already been adjusted for the probability of technical success, we do not need to adjust the discount rate to account for risk.

\(^2\)Cutler et al. (1996) assert that the medical care CPI overstates inflation in medical care costs. However, we believe that some of the shortcomings of the medical care CPI (e.g., lack of adjustment for changes in quality) are mitigated by our explicit accounting for changes in the patient’s benefits from new treatment technologies.
In this section, we explain how we will use the @risk and other method for conducting model simulations and testing the sensitivity of the results to changes in certain parameters.

4.1 STRUCTURE
We will construct a spreadsheet program that allows us to vary certain parameter values to determine the sensitivity of results to changes in key model parameters such as:

- % Years acceleration
- % Probability of tech success, with and without NIST
- % Price of products per unit
- % Cost of production per unit
- % Cost of productive capacity plant

4.2 PUTTING IN DISTRIBUTIONS

4.3 RUNNING SIMULATIONS
References


