# Executive Summary:
## Examining the Relationship Between Market-Based Pricing and Bio-Pharmaceutical Innovation

### Introduction

As escalating pharmaceutical expenditures draw increased scrutiny from policy makers, the media, and consumer advocacy groups, the debate over pharmaceutical price controls is emerging as a key political issue. Notably absent is the consideration and investigation of the impact of market-based pricing patterns in the United States on bio-pharmaceutical innovation and related economic contributions. The Technology and Innovation division of Arthur D. Little, Inc in Cambridge, Mass. has taken a next step in contributing to that process with a new study into the relationship between market-based pricing and bio-pharmaceutical innovation creation.

Bio-pharmaceutical innovation is created and driven by a variety of factors, such as the size of the R&D budget, the level of venture capital activity attracted to the industry, and the extent to which local economies can provide skilled employees to pursue new drug therapies. So, while the study examines the underlying question--Will bio-pharmaceutical innovation be affected by price regulation?—it does so by addressing these key issues. It also seeks to provide a framework for constructive public dialogue—to help policy-makers and consumers begin to consider the many inter-related elements at stake in this debate.

### Background

The “price of bio-pharmaceutical innovation” affects everyone in the United States from patients and physicians/providers, to payers/employers and policymakers/legislators. As the largest market in the world and as the only remaining major country with a market-based system, the United States occupies a unique position. Nearly all pharmaceutical and biotechnology firms worldwide seek to launch their products in the U.S., making this country the epicenter of global innovation. The United States is likewise the world’s meeting ground for pharmaceutical intellectual capital.

This country devotes just 1.4 percent of its GDP to pharmaceutical expenditures, which is about average among the major industrialized nations. While pharmaceuticals currently represent about 10 percent of total health care costs in the United States, this is not a new phenomenon as the rate has fluctuated between 4 and 10 percent during the past four decades. Certainly, increased drug utilization plays a major role in the growth of pharmaceutical expenditures. An aging, and often less healthy, population has sent the demand for arthritis, cardiovascular, and diabetes medications soaring. Drugs are now available that often preclude the need for hospitalization and expensive treatments. However, controversy still exists over the industry’s role in maintaining its price points for innovative drugs and over the issue of access.

## Objective and Approach

The objective of this initiative is to assess the relationship between U.S. market-based pharmaceutical pricing and bio-pharmaceutical innovation by focusing on the expected impact that price controls would have on elements that drive bio-pharmaceutical innovation. To address the study objectives, we reviewed the secondary research and conducted primary research. We developed key questions to enable policymakers to explicitly address the issues and then established a framework to explore the impact of market-based pricing on:

- Industry returns
- R&D investments
- Degree of innovation in the U.S. market
- Economic contributions

## Findings and Conclusions

This study enables us to better gauge the degree to which a market-based pricing system is doing its primary job of encouraging the creation new bio-pharmaceuticals to address current and potential medical needs. As a result of both our secondary and primary research, we established that, under the current market-based pricing system:

- The pharmaceutical sector has maintained the alignment of industry returns with the associated risk.
- The bio-pharmaceutical sectors experienced significant decreases in venture capital investment and market valuations, particularly in the biotech sector, due to proposed price intervention.
- The U.S. market is positioned as a world leader in bio-pharmaceutical innovation.
- The bio-pharmaceutical sectors contributed to the U.S. economy in terms of:
  - Direct, indirect and induced revenues, income labor, employment;
  - Formation of biotechnology enterprises; and
  - Deployment of risk capital.

Contrary to the widespread belief that the pharmaceutical sector enjoys a high rate of return even when the substantial risks inherent to the industry are considered, our analysis found that returns are aligned with risk. Moreover, industry returns have remained steady since 1981. The industry's risk-adjusted return is lower than that of other R&D-based industries, such as computer network and software services sectors.

Using past experience to predict the impact that price intervention could have on the level of investment in pharmaceuticals and biotechnology, we believe there would be a decline in stock prices, R&D spending, and venture capital funding. Though both sectors would be affected, biotechnology would be particularly vulnerable to changes in pricing policy. Furthermore, the value of public R&D funding might be diminished if private R&D funding is weakened, which means that new, gene-based knowledge might not be translated into useful therapeutics.

As the world's largest and only remaining market-based pricing environment, the United States has emerged as the global leader in innovative drugs with more new product launches than all other countries combined. The U.S. biotech industry likewise surpasses the rest of the world in terms of drugs under development.

Significant economic benefits accrue in environments with strong pharmaceutical and biotechnology businesses. In our post-industrial economy, pharmaceutical and biotechnology sectors form a foundation for building and maintaining a strong economy.

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## Examining the Relationship Between Market-Based Pricing and Bio-Pharmaceutical Innovation

### Introduction

As escalating pharmaceutical expenditures draw increased scrutiny from policy makers, the media, and consumer advocacy groups, the debate over pharmaceutical price controls is emerging as a key political issue. Currently, 37 state legislatures are considering bills (totaling more than 180) that address the costs of prescription drugs, while at a national level, politicians are calling for an examination of the industry's pricing practices through hearings and Congressional investigations.

However, existing research into the reasons behind these price points is limited. Notably absent is the consideration and investigation of the impact of market-based pricing patterns in the United States on bio-pharmaceutical innovation and related economic contributions. The Technology and Innovation division of Arthur D. Little, Inc in Cambridge, Mass. has taken a next step in contributing to that process with a new study into the relationship between market-based pricing and bio-pharmaceutical innovation creation.

Innovation is truly in the "eye of the beholder." It can be defined as running the gamut from modest incremental novelty, such as a new drug delivery mechanism, to the creation of ground-breaking treatments that cure the underlying causes of disease. For the purposes of this report, the term "bio-pharmaceutical innovation" is used to better reflect the converging discovery and development efforts of both the pharmaceutical and biotechnology industries.

Bio-pharmaceutical innovation is created and driven by a variety of factors, such as the size of the R&D budget, the level of venture capital activity attracted to the industry, and the extent to which local economies can provide skilled employees to pursue new drug therapies. So, while the study examines the underlying question--Will bio-pharmaceutical innovation be affected by price regulation?—it does so by addressing these key issues. It also seeks to provide a framework for constructive public dialogue—to help policy-makers and consumers begin to consider the many inter-related elements at stake in this debate.

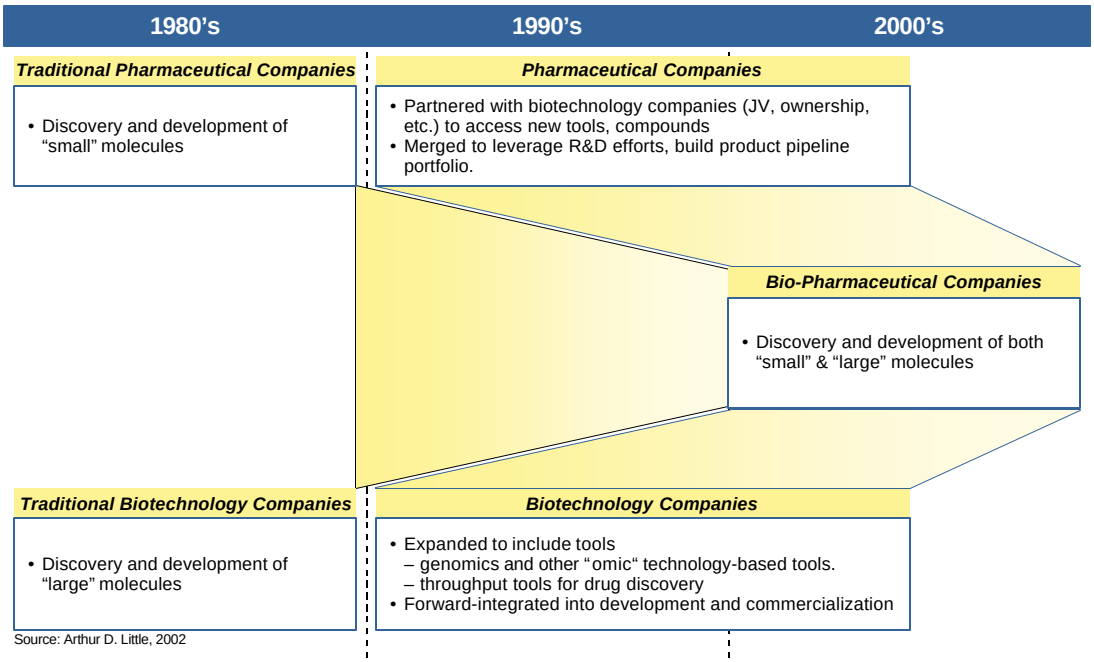
This report summarizes the key aspects of this "market-based pricing and bio-pharmaceutical innovation" initiative. It is organized as follows:

- Background: *An overview of the reasons behind this study*
- Objective and Approach: *The objectives and our framework for the initiative*
- Study Findings: *The findings from our secondary and primary research (e.g., data analysis, interview program)*
- Overall Conclusions: *The lessons from this initiative and areas requiring further exploration*

## Background

As pharmaceutical companies have incorporated more and more of the capabilities of biotechnology into their organizations and as some biotechnology companies have forward integrated into clinical development and marketing, the distinction between pharmaceutical companies and biotechnology companies is becoming blurred. The Biotechnology Industry Association[1] defines biotechnology as "the use of the cellular and molecular processes to solve problems or make products". As illustrated in Figure 1, bio-pharmaceuticals firms have emerged which discover and develop both "small" and "large" molecules.

**Figure 1: Bio-Pharmaceuticals Reflect the Recent Coverage of Traditional Pharmaceutical and Traditional Biotechnology**



Source: Arthur D. Little, 2002

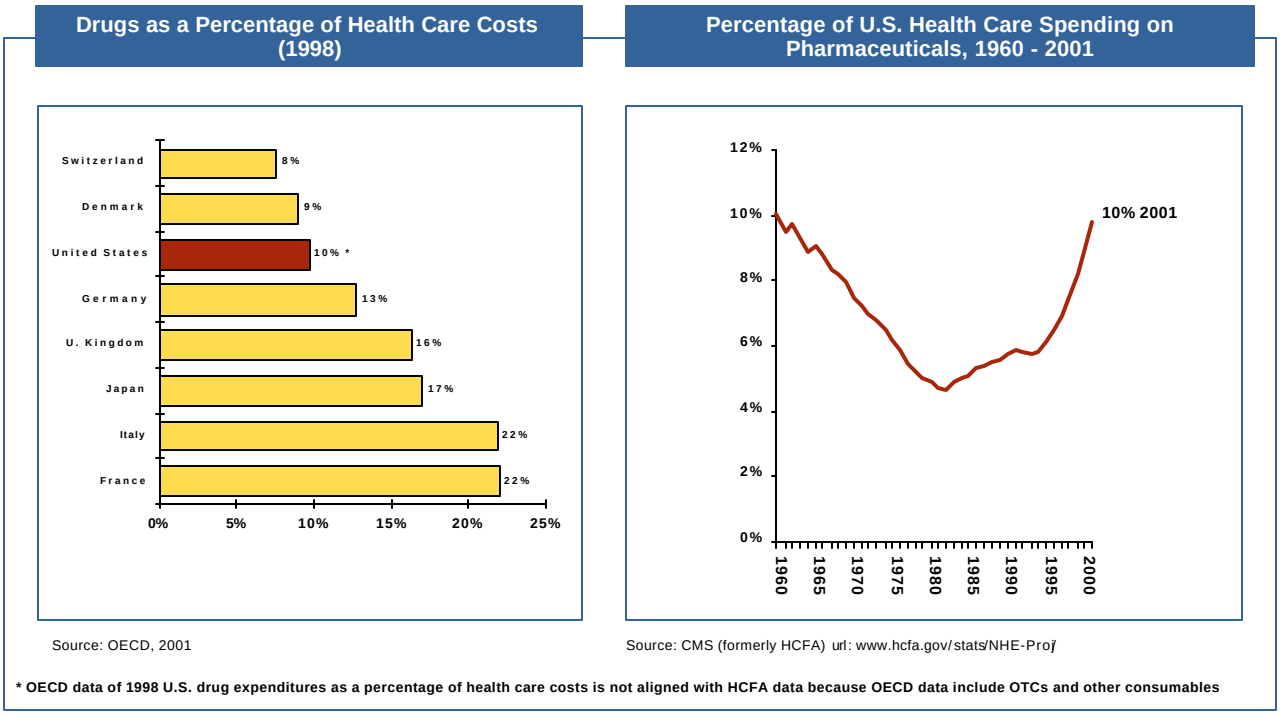
The "price of bio-pharmaceutical innovation" affects everyone in the United States from patients and physicians/providers, to payers/employers and policymakers/legislators. As the largest market in the world and as the only remaining major country with a market-based system, the United States occupies a unique position. Nearly all pharmaceutical and biotechnology firms worldwide seek to launch their products in the U.S., making this country the epicenter of global innovation. The United States is likewise the world's meeting ground for pharmaceutical intellectual capital. But while the United States is the leader in the development of new breakthrough drugs for the rest of the world, this level of innovation does not come cheaply. It places a huge financial burden not only on U.S. employees and retirees, but also on payers and employers. That's because the price covers more than just the direct production of medication itself. It also includes the level of innovation behind that particular therapy—not to mention the hugely expensive efforts that went into the development of other drugs that ultimately failed to make it to the market. According to the Tufts Center for the Study of Drug Development, the cost of developing a new drug now averages $802 million and it takes 10 to 15 years to bring

[1] http://www.bio.org

that drug to market[2]. Of every 5000 medicines tested, only one is eventually approved for patient use (PhRMA 2001). "The price of innovation, in terms of R&D costs, is borne worldwide almost exclusively by the U.S. private insurance and out-of-pocket markets," said a leading health care ethicist. "And the drug companies correctly point out that innovation is expensive, but the burden of paying for it is completely misplaced."

Just how much *do* we spend on prescription drugs in the United States? This country devotes just 1.4 percent of its GDP to pharmaceutical expenditures, which is about average among the major industrialized nations. While pharmaceuticals currently represent about 10 percent of total health care costs in the United States, this is not a new phenomenon as the rate has fluctuated between 4 and 10 percent during the past four decades[3] (see Figure 2). While this 10 percent of total health care expenditures is not unprecedented, drug expenditures have increased at a compounded annual growth rate of nine percent since 1996.

**Figure 2: Pharmaceutical Expenditures Worldwide and Percentage of U.S. Health Spending on Pharmaceuticals, 1960-2001**




However, drug expenditures have been driven by volume, not price. A study that analyzed trends in drug spending[4] found substantial drug spending increases in seven diseases/drug categories ranging from 43 percent to 219 percent during the three-year

[2] "The full capitalized resource cost of new drug development was estimated to be $802 million (2000 dollars). This estimate accounts for the cost of failures, including research compounds abandoned during development, as well as opportunity costs of incurring R&D expenditures before earning any returns". Tufts Center for the Study of Drug Development, November 30, 2001.

[3] CMS url: www.hcfa.gov/stats/NHE-Proj/

[4] Dubois, R. etc., "Explaining Drug Spending Trends: Does Perception Match Reality?" *Health Affairs*, March/April 2000, 231-239.

observation period. Although the average transaction price rose in every case but one, the impact on the rise in drug spending was greatly exceeded by that growth in medication volume. According to the National Institute for Health Care Management Foundation, spending on prescription drugs rose for a "complex array of reasons" including increased incidence and prevalence of chronic conditions, higher rates of physician treatment of these conditions, greater managed care coverage, expanded marketing, and franchise extension. The report attributes a 17% increase in retail prescription drug spending from 2000 to 2001 to the following: shift to higher cost drugs (4%), increase in number of prescriptions (7%), and price increases (6%); however, the analyses "are not adjusted for rebates or discounts for individual drugs [and] are not adjusted for dosage level…or prescription size" [5]. Consequently, the 6% increase attributed to pricing is likely overestimated.

Certainly, increased drug utilization plays a major role in the growth of pharmaceutical expenditures. An aging, and often less healthy, population has sent the demand for arthritis, cardiovascular, and diabetes medications soaring. Drugs are now available that often preclude the need for hospitalization and expensive treatments. "If a drug will keep the patient out of the nursing home, the institution, the hospital, then it is worth it," said a Medicaid Director. "Pharmaceuticals have and will continue to reduce health care expenditures," said a health care policymaker. "Should we pay for the $50,000 coronary bypass graft or a $50 drug?"

However, controversy still exists over the industry's role in maintaining its price points for innovative drugs and over the issue of access. Bio-pharmaceutical innovations work best if people can make use of them. "We should provide seniors a real affordable prescription drug benefit now," Senator Edward Kennedy said in a statement. A senior representative from a consumer advocacy group added: "With an aging population, pharmaceuticals are critical and a major part of modern medicine. The thought of not having access to drugs is petrifying." . "The pharmaceutical industry has tremendous value," said the president of a think-tank focusing on health policy. "But Policymakers must be very careful about how they implement a drug benefit because if it were to include price controls, it would erode the industry's ability to develop future innovative drugs."

The rapid rise in the percentage of health care costs attributed to drugs has motivated payers and consumers to question the appropriateness of the existing market-based pharmaceutical "pricing system" in the United States. Public attitudes toward pharmaceutical companies have recently deteriorated. A 2000 *NewsHour with Jim Lehrer/*Kaiser Family Foundation/Harvard School of Public Health survey of a nationally representative sample of 1,700 adults found:

- The public's faith in the ability of pharmaceutical companies to serve consumers has been waning. In 1997, 62 percent said that pharmaceutical companies were doing a "good job." That support dropped to 45 percent in 2000.

[5] NIHCM, "Prescription Drug Expenditures in 2001: Another Year of Escalating Costs", April 2002 (www.nihcm.org)

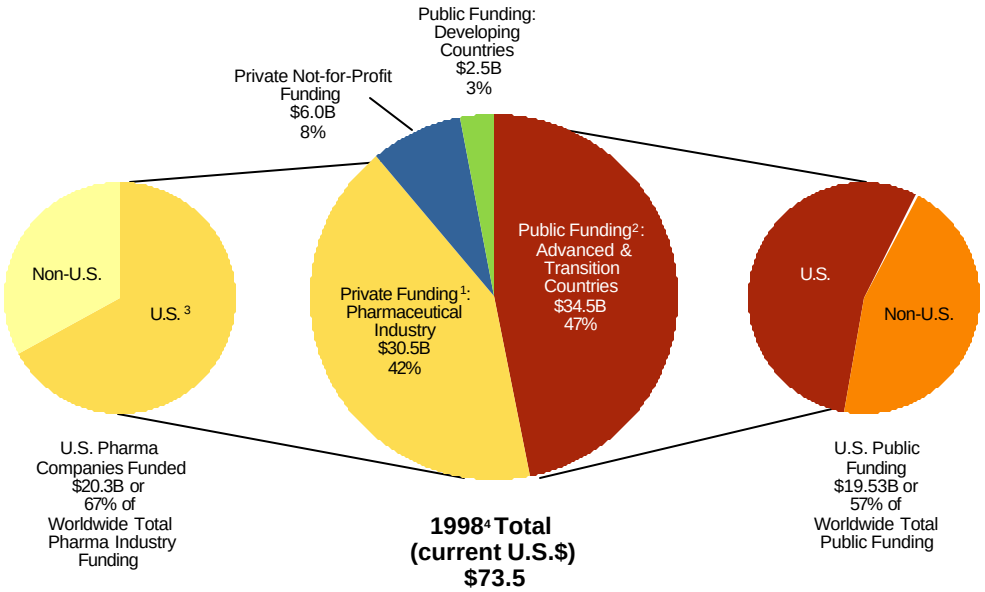
- Pharmaceutical companies were identified by 73 percent of the public as making excessive profit. Only tobacco companies (76 percent) and oil companies (75 percent) ranked higher. The elderly were more likely than the non-elderly (85% to 70%) to say that drug companies make too much profit.

- About 62 percent of Americans believe that the price of prescription drugs has risen "faster than most other things" over the last five years. Furthermore, 63 percent also believe that people in Canada, Mexico, and Western Europe pay lower prices for the same drugs.

- A majority of the population (60 percent) thinks there should be more regulation for prescription drugs. However, when the point is introduced that price controls could lead to less R&D of new drugs, support for regulation drops to 42 percent.

A less widely recognized fact is the major role that U.S. pharmaceutical companies play in funding worldwide R&D. As demonstrated in Figure 3, U.S. pharmaceutical companies provided $20.3 billion or 67 percent of worldwide private pharmaceutical funding in 1998. In addition, U.S. companies funded $19.5B, which accounted for 57 percent of worldwide public funding for health R&D that same year.

**Figure 3: Worldwide Health Private and Public R&D Funding**




[1] Pharmaceutical firms, private non-profit organizations, academic/research institutes, hospitals/laboratories, NGOs
[2] Government departments (national aid agencies), academic/research institutes, hospitals
[3] U.S. pharmaceutical companies private funding worldwide
[4] 1998 is the latest year in which public and private data are available worldwide
Source: Global Forum for Health Research/WHO, "Monitoring Financial Flows for Health Research," 2001

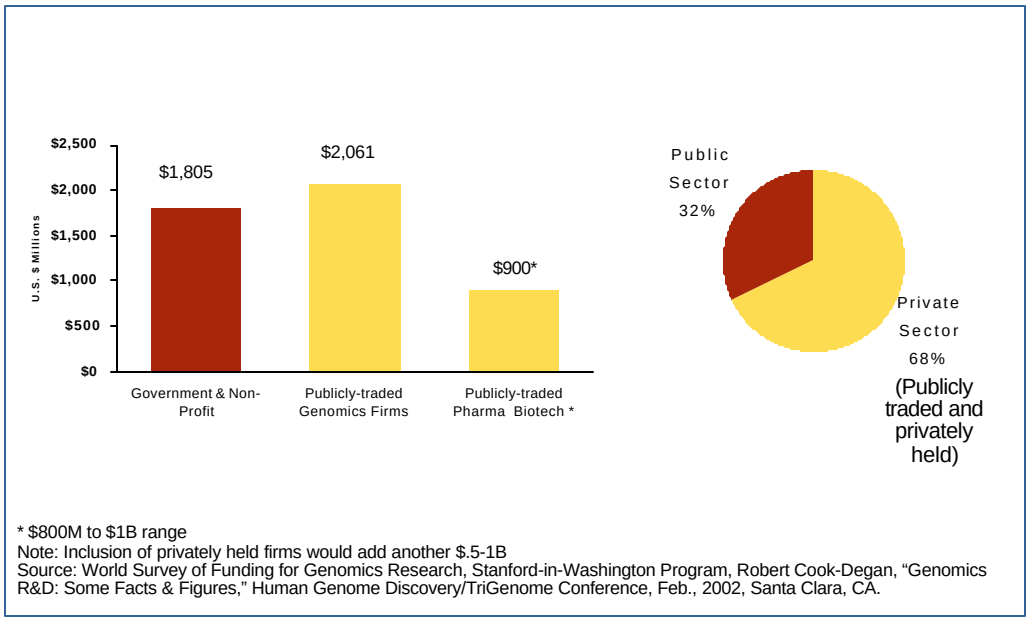
Public R&D efforts which are largely basic research would not lead to marketable products without the private R&D capabilities and support (e.g., clinical trials, distribution). The private sector plays a vital role in translating the knowledge about diseases into final therapeutic products for the patients. This public-private partnership has been well recognized for over two decades beginning with the Stevenson-Wydler Act (1980) and Bayh-Dole Act (1980) and continuing with the Federal Technology Transfer

Act (1986), National Technology Transfer and Advancement Act (1995), and the Technology Transfer Commercialization Act (2000). For example, NIH's Office of Technology Transfer states as its goals[6] to: "benefit the public health, attack disease in multiple fronts, attract new R&D resources, obtain return on public investment, and stimulate economic development.". In addition, the existence of basic research in the private sector provides further stimulus to public research through scientific exchange at professional conferences, peer-reviewed periodicals, and public debate.

There is also a significant lag between the scientific discovery and the creation of a useful therapeutic. "The estimates also suggest that the lag between funding and commercialization is seventeen to nineteen years and support the hypothesis that the contribution of public science to new technological opportunities comes in the earliest stages of pharmaceutical discovery."[7]

Genomics, transcriptomics, and proteomics are especially dependent upon this partnership because of the critical role that the private sector plays in applying the knowledge from these types of research into useful therapies (see Figure 4).

**Figure 4: Worldwide Genomics Research Investments, 2000**



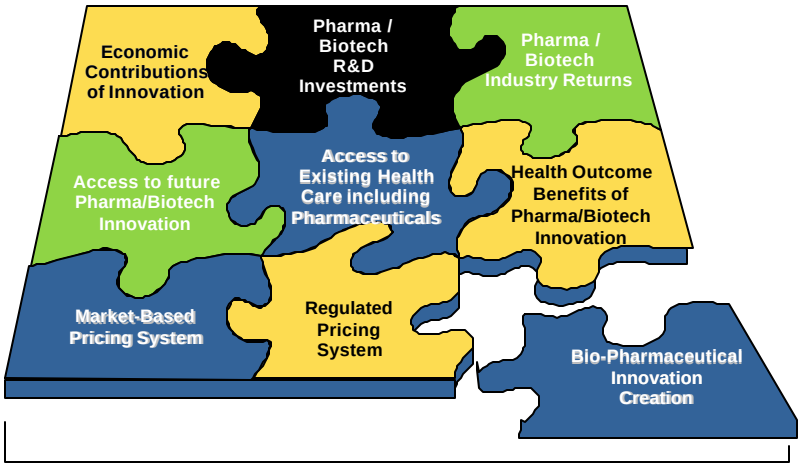

* $800M to $1B range
Note: Inclusion of privately held firms would add another $.5-1B
Source: World Survey of Funding for Genomics Research, Stanford-in-Washington Program, Robert Cook-Degan, "Genomics R&D: Some Facts & Figures," Human Genome Discovery/TriGenome Conference, Feb., 2002, Santa Clara, CA.

A healthy, venture capital-based, entrepreneurial biotechnology industry in the United States has evolved as part of this public-private R&D partnership. According to the National Venture Capital Association, of the $36.5 billion in venture capital funding available in the United States in 2001, about $3 billion—or 8.2 percent—went into biotech. In Europe, about half that amount, or 1.7 billion euros, went into similar research. The nature of the large, U.S. market-based pricing environment has supported not only domestic biotechnology entrepreneurship, but also worldwide biotechnology entrepeneurship, though to a lesser extent.

[6] Presentation by Rohrbaugh, M., Acting Director, Office of Technology Transfer, NIH, 2002
[7] Toole, A.A. "The Contribution of Public Science to Industrial Innovation: An Application to the Pharmaceutical Industry" Stanford Institute for Economic Policy Research Policy Paper 98-6, June 1999

Bio-pharmaceutical innovation is shaped and affected by complex global dimensions and issues, represented by the interlocking puzzle pieces in Figure 5. The presence of both market-based and regulated pricing systems, access to existing and future innovation, health benefits of innovation, broader economic benefits to nations and regions, industry returns, and R&D investments are all critical components in innovation creation.

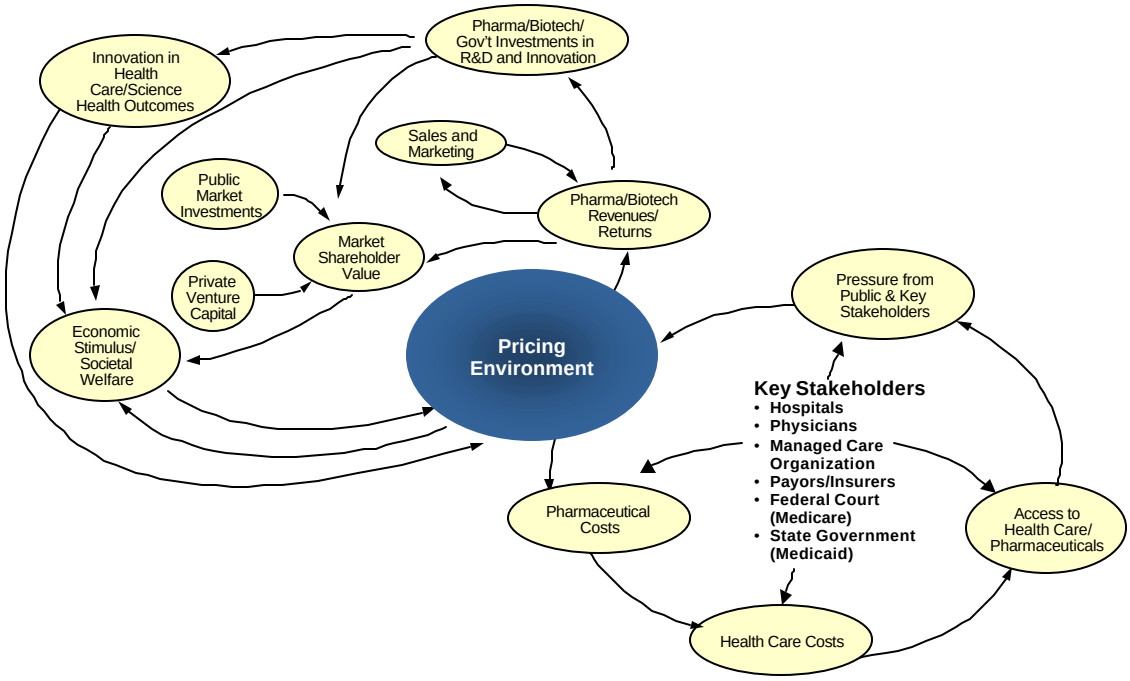
**Figure 5: Worldwide Components of the Pricing and Innovation Puzzle**




Worldwide Components of the Pricing and Innovation Puzzle

Figure 6 delves deeper into these complexities by mapping the relationship between pricing and innovation. As the figure illustrates, the "pricing and innovation equation" is intricately influenced and linked by a range of factors.

**Figure 6: The Pricing and Innovation Relationship**

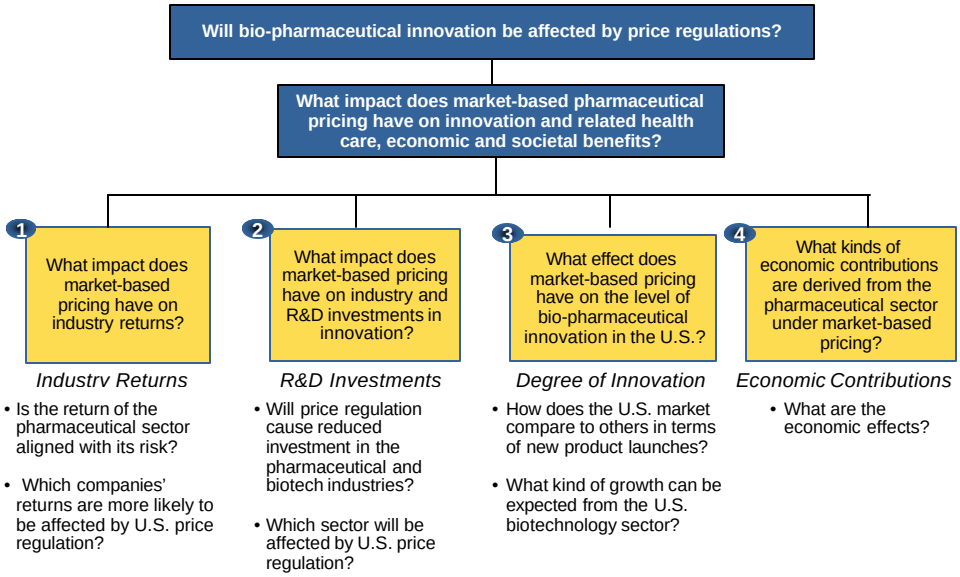


## Objective and Approach

The objective of this initiative is to assess the relationship between U.S. market-based pharmaceutical pricing and bio-pharmaceutical innovation by focusing on the expected impact that price controls would have on elements that drive bio-pharmaceutical innovation (see Figure 7). We developed key questions to enable policymakers to explicitly address the issues and then established a framework to explore the impact of market-based pricing on:

- Industry returns
- R&D investments
- Degree of innovation in the U.S. market
- Economic contributions

**Figure 7: Relationships Between Market-Based Pricing and Bio-Pharmaceutical Innovation**




To address the study objectives, we reviewed the secondary research and conducted primary research.

1) **Secondary Research: Literature Review, Data Collection and Synthesis.** We conducted a comprehensive review of secondary sources to understand what has been addressed and identify any information gaps. During this process, we also identified key contacts (e.g., academic researchers, opinion leaders) for our interview program. We leveraged the high quality secondary studies and data in some of our analyses. Furthermore, we collected data to conduct our primary research analysis.

2) **Primary Research: Data Analysis and Interview Program.** We conducted new primary research to address the "pricing/innovation" component relationships. We also conducted a comprehensive interview program with approximately 60 individuals representing a wide variety of perspectives including: consumer groups, payers, regulators/legislators, economists, policy makers, opinion and thought

leaders, venture capitalists, biotechnology and pharmaceutical industry executives. Acting as an objective third party, we engaged this broad spectrum of stakeholders and concerned parties in in-depth discussions to explore the diverse issues and perspectives.

## Findings

This study enables us to better gauge the degree to which a market-based pricing system is doing its primary job of encouraging the creation new bio-pharmaceuticals to address current and potential medical needs. As a result of both our secondary and primary research, we established that, under the current market-based pricing system:

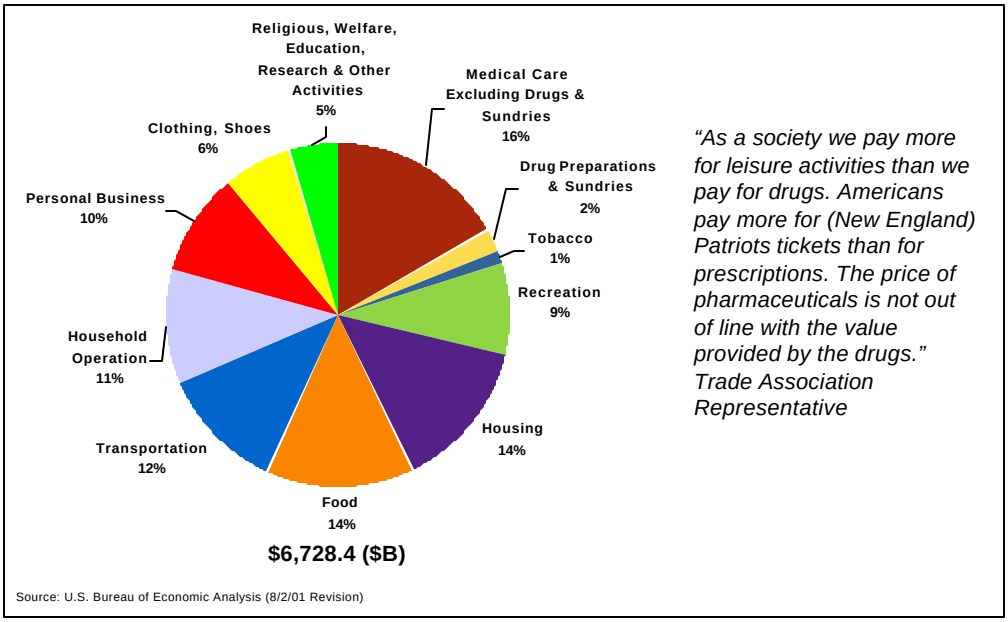
- The pharmaceutical sector has maintained the alignment of industry returns with the associated risk.
- The bio-pharmaceutical sectors experienced significant decreases in venture capital investment and market valuations, particularly in the biotech sector, due to proposed price intervention.
- The U.S. market is positioned as a world leader in bio-pharmaceutical innovation.
- The bio-pharmaceutical sectors contributed to the U.S. economy in terms of:
  - Direct, indirect and induced revenues, income labor, employment;
  - Formation of biotechnology enterprises; and
  - Deployment of risk capital.

Through our interview program, in which we identified both converging and diverging perspectives, we learned that values form the cornerstone of this debate and that any discussion must address values explicitly, rather than implicitly. Values drive the perceived benefits and costs of bio-pharmaceutical innovation. Our fragmented payer system and silo budgets contribute to distorted perceptions of the value (or lack thereof) of innovative bio-pharmaceuticals. A key "value-related" issue raised was the specter of a difficult tradeoff among price regulation, innovation and access. Is the broader access suggested—but not guaranteed--by more affordable drugs worth the risk of reducing the potential for new therapies that enhance the quality of life? In our interview program, access was considered one of the most important issues confronting the U.S. health care system. A pharmaceutical executive said: "The question becomes who is going to finance access…is it going to be government alone? Private and government? What about consumers contributing too?" Interview participants across various stakeholder groups indicated that the access issue needs to be embraced and proactively addressed by the pharmaceutical industry, but not alone. "Access to pharmaceuticals is a systemic, multi-stakeholder problem, not just a drug issue," said a senior representative of a consumer/patient advocacy group.

As one pharmaceutical buyer commented: "It's all about values. Would we be happy as a society spending 50 percent of our health care dollar on drugs and having very profitable companies? Or moving money away from the defense budget to cover the Medicare drug benefit or the 40 million people who are uninsured? Where does the margin-benefit value chain stop?" As illustrated in Figure 8, values dictate our spending habits; personal expenditures on drugs represented one quarter of personal expenditures on recreation in 2000. "As a society we pay more for leisure activities than we pay for drugs," said a trade

association representative. “Americans pay more for [New England] Patriot tickets than for prescriptions. The price of pharmaceuticals is not out of line with the value provided by the drugs.”

**Figure 8: U.S. Personal Expenditures in 2000**




Many interview participants recognized linkages/component relationships (e.g., returns, investments, health care, economic outcomes) that affect bio-pharmaceutical innovation. They believe that the market-based approach to pricing supports a level of pharmaceutical prices that generate the kind of revenues/returns that, in turn, support expensive R&D. They also note the important role that the pharmaceutical and biotechnology sectors play in job creation and economic growth. “The partnerships that the pharmaceutical and biotechnology industries form with academia, hospitals, and the marketplace result in lots of jobs, as well as knowledge and intellectual capital,” stated one financial investor.

They further argue that pharmaceutical and biotechnology investments, along with their vital roles in creating innovation, would be diminished if the United States were to adopt price controls. A heath care economist said “Pharmacogenomics would be adversely affected. Potential treatments for sub-populations won’t be developed, orphan drugs would be killed, and companies would only pursue therapies in which there was a substantial market.”

“A price-regulated environment will lead to loss of innovation,” said a pharmaceutical executive. “With a price control, we will set a more stringent bar in drug R&D and try to kill compounds early to save clinical cost. Half of our current projects might be terminated.”

“ I don’t believe price controls on drugs would improve the situation,” said a senior representative of a consumer/patient advocacy group. “Pharmaceutical companies would

have no incentives to invest in areas with low returns, such as orphan drugs, and innovation would be affected."

However, other interview participants argue that the "pricing/innovation" linkages/component relationships would not be affected by price regulations. They believe the industry is driven to innovate regardless of the pricing system (i.e., innovation would not be stalled due to decreased financial incentives). They don't believe that the secondary economic benefits, as measured by employment and GDP, would suffer in either the short or long-run, or even that those considerations should influence the debate. "This is an issue of public necessity that can't be left to the mercy of a free market," said a health care economist from academia. "There are no free market solutions to health care. It's a moral issue."

There were mixed reactions from stakeholder interview participants on the degree to which price intervention would encourage or discourage the development of "me-too" drugs. "I'm skeptical that price controls would adversely affect R&D or any related factors," said a senior representative of a consumer advocacy group. "The industry will continue to invest in innovation. Perhaps price controls would stop the copycats and the marketing of not particularly innovative products." However, from an economic and consumer perspective, it is important to have multiple drugs in a class for competition and the ability to select drugs. "Different patients respond to different products and brands, so formulary limitations may not always lead to the best outcomes," said another senior representative of a consumer advocacy group.

### *Returns*

The cost of capital[8] for risky investments is higher. Our analysis found that pharmaceutical sector returns[9] are aligned with risk and that U.S.-based firms would be most vulnerable to price intervention. Using the recognized investment-measurement tool, Jensen's alpha[10], the team evaluated the relationship between risk and return in the industry based on monthly stock return data by measuring return relative to the cost of capital adjusted for risk. The team found that:

a) Pharmaceutical sector returns continued to be aligned with risk during the 1990s.
b) The pharmaceutical sector's rate of return above the cost of capital is lower than that of some other R&D-intensive sectors.
c) Price intervention would have a greater effect on U.S.-based firms than on European-based companies.

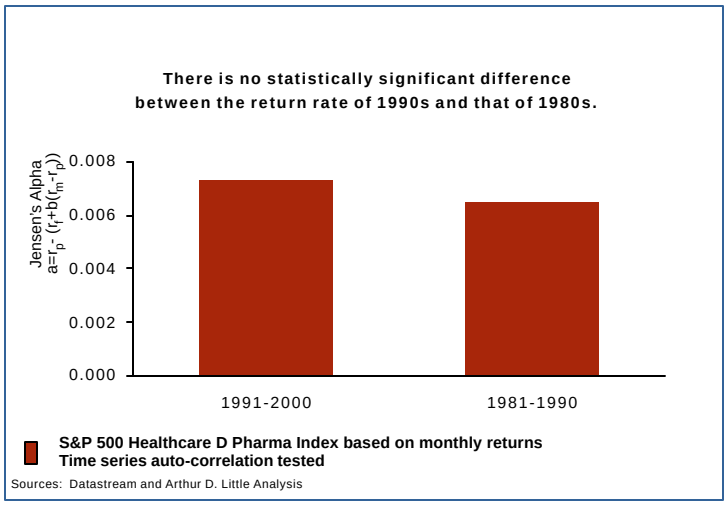
[8] "The concept of cost of capital is based on the Capital Asset Pricing Model (CAPM), which depends for its validity on the efficiency of capital markets. The CAPM approach remains one of the most widely used models of expected returns, and no better practical alternatives to estimating the cost of capital presently exist." (1993 OTA Report, p.276)

[9] Return was defined as the change in the S&P500 Health Care Major Drug Sector Index from period to period.

[10] Jensen's alpha has been widely used to measure whether returns on a portfolio of stocks exceed the expected cost of capital as measured by CAPM. A low Jensen's alpha suggests low differential return above the cost of capital. Based on monthly stock return data, the Jensen's alpha for the pharmaceutical industry in the 1980s was .65% and in the 1990s was .73%. Jensen's alpha is an important measurement of mutual fund and stock portfolio performance explained in many finance texts (Bodie; Elton; Sharpe).

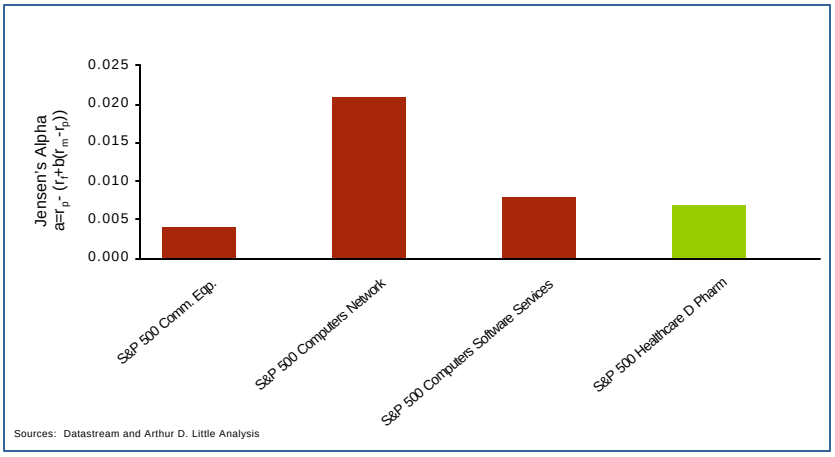
**a) The pharmaceutical sector's risk-adjusted rate of return remained steady from 1981-2000.** We analyzed the risk-adjusted returns from 1991-2000 and found them to be similar to the 1981-1999 period (see Figure 9). In 1993, the U.S. Office of Technology Assessment in a study entitled "Pharmaceutical R&D: Costs, Risks, Rewards" determined the 1981-1990 rate of return in the pharmaceutical sector and concluded that the rate was 2-3% above the cost of capital. In conjunction with this study, our findings confirm that the industry returns have continued to be aligned with risk during the 1990s.

**Figure 9: Risk and Return of the Pharmaceutical Sector**



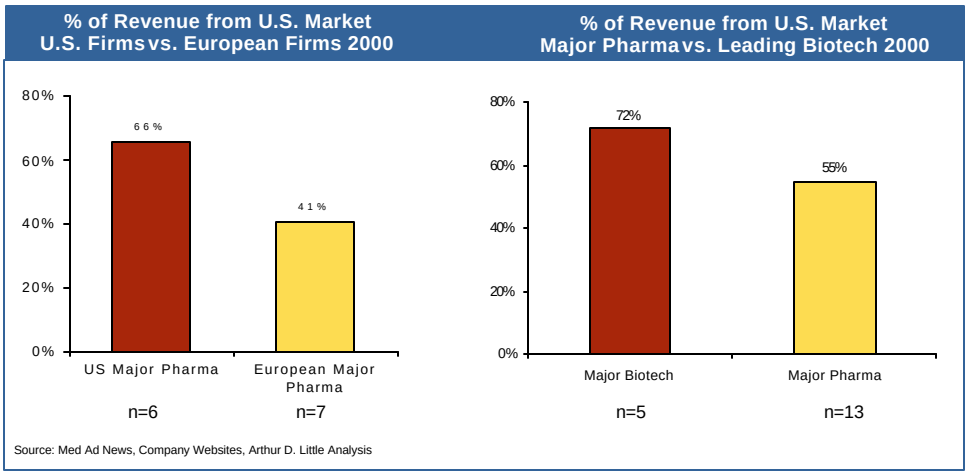

**b) The pharmaceutical sector's rate of return above the cost of capital is lower than that of other R&D-intensive sectors.** We compared Jensen's Alpha of S&P 500's pharmaceutical industry's index against that of other S&P 500 R&D-related industry indexes. We found that the pharmaceutical sector's differential return above the cost of capital, as measured by CAPM, is lower than that of computer network and software services sectors, but not the communication equipment sectors (see Figure10).

**Figure 10: Rate of Differential Return Across Selected R&D-Related Industries (1991-2000)**



c) **In terms of returns, price intervention in the U.S. market would have a greater affect on major U.S.-based pharmaceutical firms and biotechnology firms than it would on major European-based companies.** By comparing the U.S. revenues of six major U.S.-based pharmaceutical companies with seven major European-based pharmaceutical companies, we found that these major U.S. pharmaceutical firms derive approximately 66 percent of their total revenues from U.S. market while the major European firms derive about 41 percent from the U.S. market. The relative dependence on the U.S. market can be seen with the following example. A 20 percent reduction in U.S. revenues is associated with a 13 percent decrease in total revenues for major U.S. pharmaceutical firms *ceteris paribus*[11], as opposed to an eight-percent decline for major European firms *ceteris paribus*. By comparing the U.S. revenues of five major *biotechnology* companies with the 13 major pharmaceutical companies, we found that the major U.S. biotechnology firms derive approximately 72 percent of their total revenues from the U.S. market while the major pharmaceutical firms derive about 55 percent from the U.S. market. A 20 percent reduction in U.S. revenues is associated with a 14 percent decrease in total revenues for the major U.S. biotechnology firms *ceteris paribus*, and only an 11 percent decline in total revenues for the major U.S. and European pharmaceutical firms *ceteris paribus* (see Figure 11).

**Figure 11: Percent of Revenue From U.S. Market**

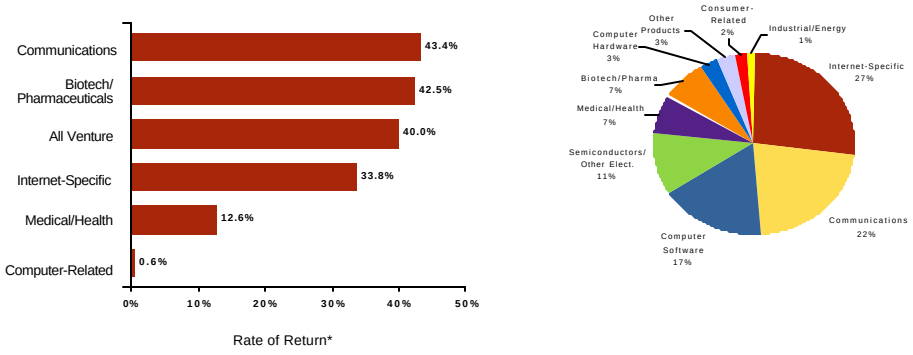



During our interviews, we identified diverging views on the level of returns required for continued innovation, as well as the impact of returns on R&D investments and hence innovation. Most pharmaceutical and biotechnology executives agree that price controls would decrease their profit margin, even if the top line remains the same. Some raised the experience in Europe, specifically Germany, as evidence of a decline in industry returns, innovation, and jobs under price regulation (in the early 1990s). The financial investors interviewed believe that investment will dry up in the short-term.

[11] The phrase *ceteris paribus* is Latin for "other things being equal."

The return rates of biotechnology-focused venture funds are similar to those of other funds, suggesting a decreased return on biotechnology could redirect venture capital investment to other industries (see Figure 12). "We will pull our money out," said a venture capitalist. "Price regulation will lower biotech's return rates and drive capital away to other industries." Another financial investor said: "There's no doubt that with lower returns, the risk-return profile will change completely. The risk of drug development would still be there, but the returns wouldn't, so there would be no way to justify the investment."

**Figure 12: Rate of Return and Venture Capital Investment by Industry (2001)**




Source: Venture Economics
*The internal rate of return, see www.ventureeconomics.com/vec/methodology.html for the method of calculation.

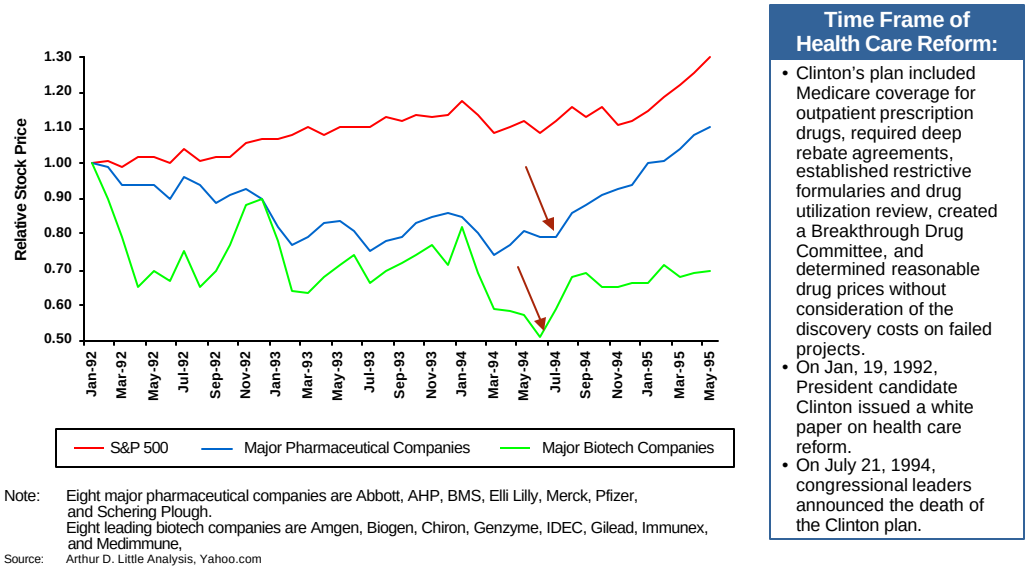
### *Investments*

Although difficult to predict the impact that changes in public policy would have on the level of pharmaceutical and biotech venture capital investments, modeling and past experience can serve as guides to estimate those effects. For example, President Bill Clinton's proposed government regulation in 1992-94 suggests that price intervention or regulation would negatively affect the level of investment—particularly in the biotech industry. During this period, we found there to be declines in:

a) Industry stock prices, with biotechnology stocks proving particularly sensitive,
b) R&D spending by major U.S. pharmaceutical companies, and
c) Venture capital investment in biotechnology.

**a) While both pharmaceutical and biotechnology sectors experienced declines in market value, biotechnology stock prices proved to be particularly sensitive to proposed government regulation.** While the S&P 500 steadily increased from January 1992 to May 1995, the major biotech companies dropped by 41% and major pharmaceutical companies dropped by 21% in the same period (see Figure 13).

**Figure 13: Pharmaceutical and Biotech Sector Stock Price Changes**

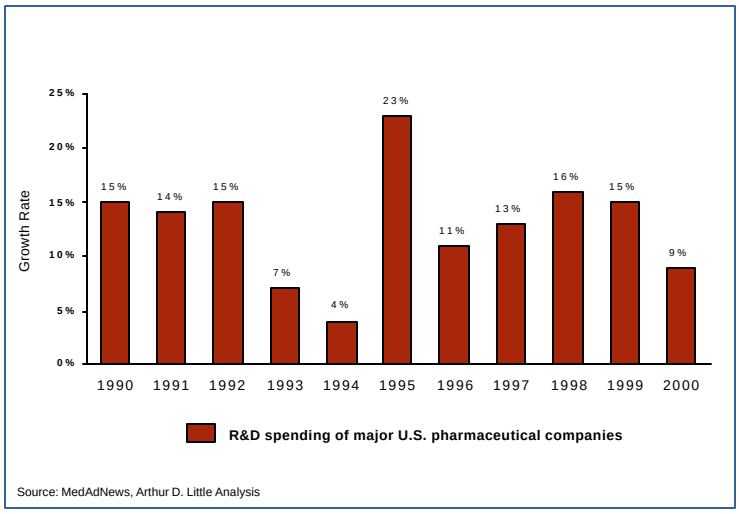



Note: Eight major pharmaceutical companies are Abbott, AHP, BMS, Elli Lilly, Merck, Pfizer, and Schering Plough.
Eight leading biotech companies are Amgen, Biogen, Chiron, Genzyme, IDEC, Gilead, Immunex, and Medimmune,

Source: Arthur D. Little Analysis, Yahoo.com

**b) During the 1993-1994 period, lower revenues due to the industry keeping price increases tied to the Consumer Price Index resulted in lower R&D investments.** After analyzing R&D spending and growth rates for seven U.S.-based pharmaceutical companies from 1990 to 2000, we found that R&D spending was at its lowest in 1993 and 1994 at seven percent and four percent respectively (see Figure 14). During this period, several major companies pledged before a Senate committee to continue to keep price increases of individual products tied to the Consumer Price Index[12]. This compares to a 15 percent growth in R&D spending in 1992 and a 23 percent growth in 1995.

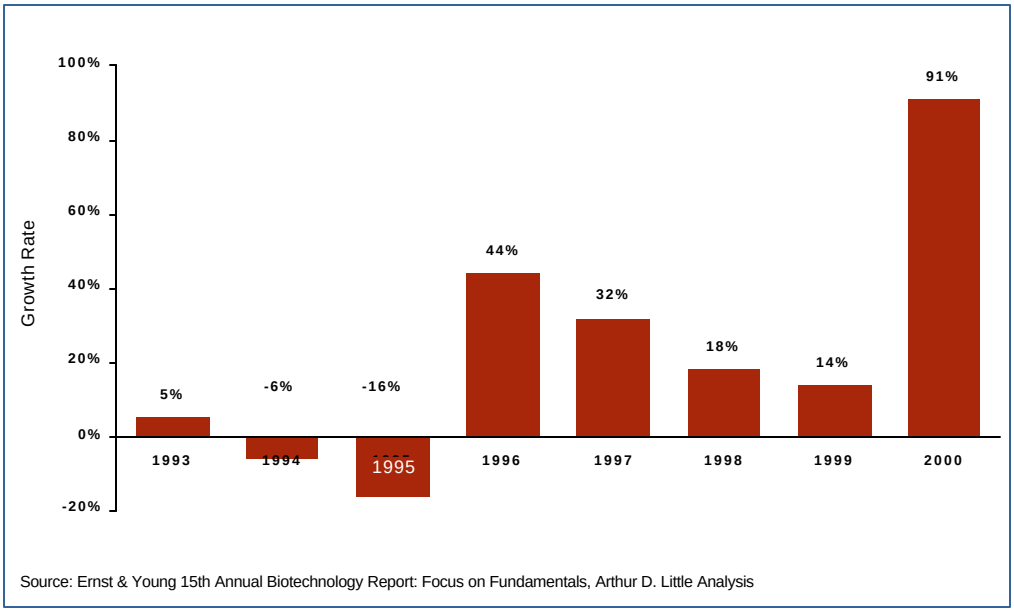
**Figure 14: Annual Growth Rates of R&D Spending (1990-2000)**




[12] Carey, M. "Glaxo, Merck Continue Pledge to Keep Drug Prices to CPI", 11/18/93, Dow Jones News Service Ticker

c) **Venture capital investment in biotechnology dropped precipitously in 1994 and 1995, reflecting concern about Clinton's proposed government regulation of health care spending.** A review of the annual growth in biotech venture capital funding from 1993 to 2000 indicates declines of 6 and 16 percent in 1994 and 1995 respectively. Investment levels grew by 44 percent in 1996 when it was clear that Clinton's plan would not be pursued (see Figure 15).

**Figure 15: Annual Growth of Biotechnology Venture Capital Financing (1993-2000)**




Source: Ernst & Young 15th Annual Biotechnology Report: Focus on Fundamentals, Arthur D. Little Analysis

Scherer (2001) noted that "pharmaceutical industry R&D investments tend to exceed risk-adjusted capital costs by only modest amounts"[13] and Lichtenberg (2001) further analyzed and argued that perception regarding expected future profits greatly influences current R&D spending. He concludes that, "policies that threaten to diminish future profits will reduce R&D investment today, even if they do not affect current profits."[14]

Our interview participants have mixed views on the potential impact of price controls on R&D investments and projects. Most of those interviewed believe that price controls will lead to decreased R&D investment, resulting in a focus on lower-risk projects, such as formulation improvement, line extension products, and life-cycle management, but less investment in orphan drugs. "If pharmaceutical prices are reduced, investments in genomics and other basic research could be more adversely affected than investments in product R&D and life cycle management," said a pharmaceutical executive. "Although there would be more access (more patients get existing drugs), there would also be less investment and fewer new drugs for the long run," said a health care economist. Just as R&D allocation and pipeline decision-making processes vary among pharmaceutical and biotechnology organizations, so do strategies to address price

[13] Scherer, F.M. "The Link Between Gross Profitability and Pharmaceutical R&D Spending" *Health Affairs*, (September/October 2001): 216-220.

[14] Lichtenberg, F.R. "Probing The Link Between Gross Profitability and R&D Spending" *Health Affairs*, (September/October 2001): 221-222.

controls. For instance, one pharmaceutical R&D executive said "The marketing versus R&D decisions in the wake of a price control depends on the product and competition. In the short-term, marketing and sales prevail over the longer-term R&D efforts. If you decrease marketing, you're going to kill the top line even faster."

Some interview participants believe that R&D would become more efficient and focused under a price-controlled scenario. They believe companies would develop products to address truly unmet needs and invest less in "me-too" drugs and incremental improvements. (Though the market works best with enough different "me-too" drugs to support competition.) "With price controls, we would be more radical in our prioritization in order to maximize innovation," said one pharmaceutical executive. "There's no question that it will be more risky with fewer projects." While some interview participants commented that innovation and the rate of development would be maintained if R&D productivity were improved, others commented on the challenges of achieving R&D efficiency without jeopardizing potential innovation. "It's difficult to gain efficiencies with the risks and uncertainties in pharmaceutical R&D. There would be a gap in investments to discover and develop innovative products," said a health care economist.

"Government should tolerate current inefficiencies for the sake of long-run benefits," said one biotechnology executive. "What could flow out of proteomics is really unimaginable." With regard to the potential loss of innovation, one pharmaceutical executive said: "With price controls, I believe we will set a more stringent bar in drug R&D and try to 'kill' compounds early to save clinical study cost. Half of our current projects might be terminated."

Through interviews with venture capitalists, we found that their investment decisions are based on the degree to which they perceive a product as innovative enough to compensate for the high risks associated with the industry. "We look for companies whose products and technologies are substantially better than current therapies," said one venture capitalist. "To invest in marginal improvement is not worth it. In today's market, an incremental improvement will not generate enough return for us."

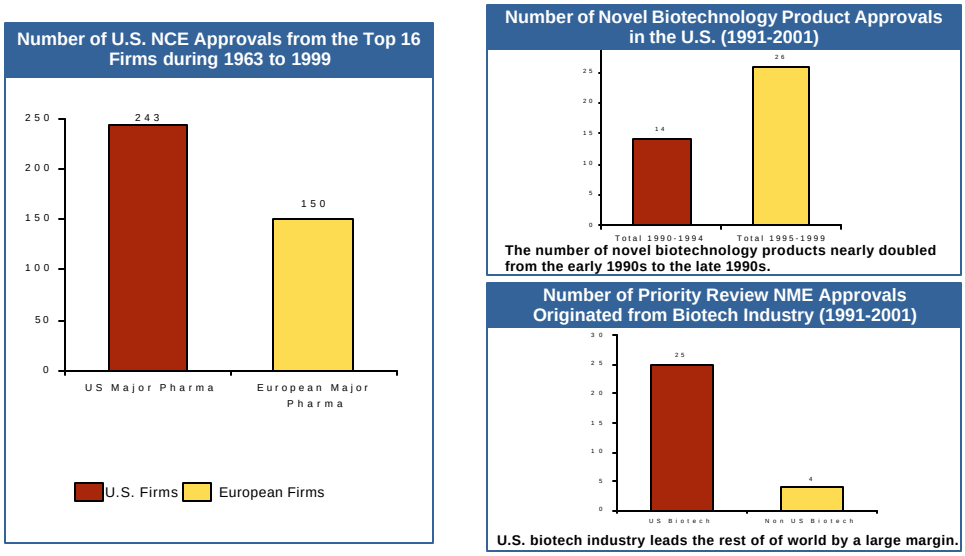
### *Degree of Innovation in the U.S. Market*

The U.S. market leads the world in bio-pharmaceutical innovations. We conducted analyses to measure the "progress of innovation" by type of companies (e.g., U.S. based versus European), by the biotechnology industry and by countries. We found that the U.S. excelled in the following:

a) Major U.S. pharmaceutical firms have contributed more new chemical entities (NCEs) to the U.S. market than have their European counterparts.
b) The United States has outpaced the rest of the world in the number of first launches and first launches of FDA priority review drugs.
c) The biotechnology industry has experienced triple-digit growth in the number of drugs in development and drugs in the market.

a) **From 1963 to 1999, major U.S. pharmaceutical firms contributed 62 percent more NCEs to the U.S. market than did their European counterparts**. Our analysis also showed that the number of novel biotechnology product approvals in the United States nearly doubled from the early 1990s to the later 1990s. During this same period, the number of priority review (NME) approvals originating from U.S. biotechnology companies was almost six times greater than that from non-U.S. biotechnology companies (see Figure 16).

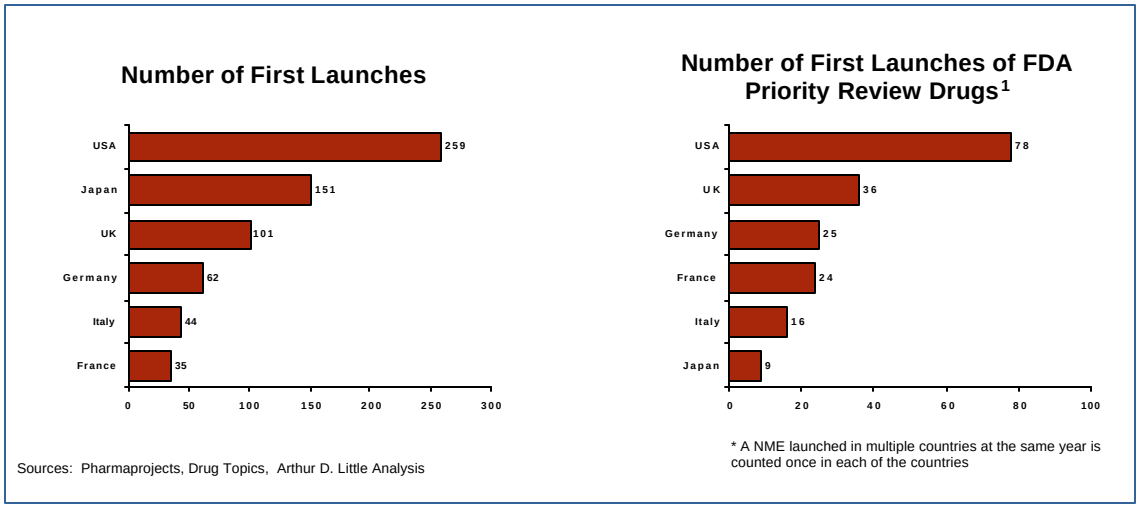
**Figure 16: Contributions of New Drugs by Major Pharmaceutical and Biotechnology Firms**




Source: DeMasi, Drug Information Journal Vol. 34, Tufts Center for the Study of Drug Development Arthur D. Little Analysis

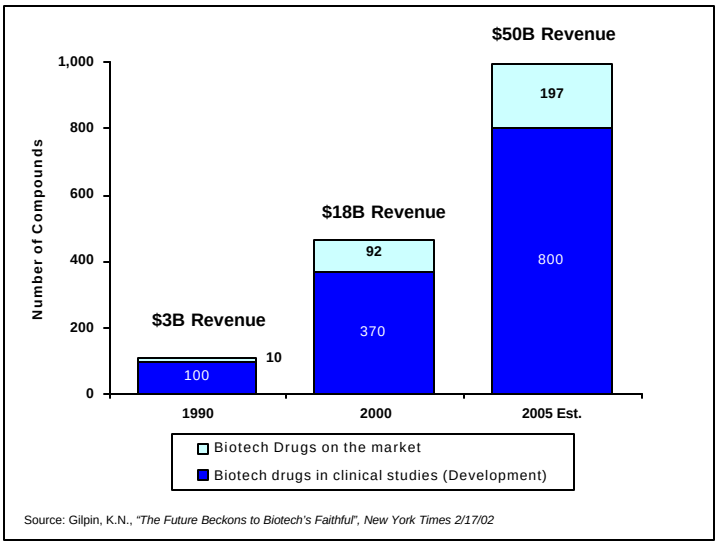
b) **American patients are the beneficiaries of more new drug approvals than patients in any other country in the world.** From 1990 to 2000, the United States launched 259 U.S. new drugs, compared to Japan's second-place showing of 151 new launches. The United States likewise launched 78 FDA priority-review drugs, compared to the United Kingdom, in second place with 36 (see Figure 17).

**Figure 17: Number of U.S. Launches of Innovative Medicines, 1990-2000**




c) **The biotechnology industry has experienced triple-digit growth in the number of drugs in development and drugs on the market.** The health care benefits of 1990s investments in biotechnology R&D can be seen in a 370 percent growth in the number of drugs in development, a 920 percent growth in the number of biotechnology drugs on the market, and a 600 percent growth in revenues (see Figure 18).

**Figure 18: Biotechnology Revenues, Drugs on Market, and Drugs in Clinical Trials**




### *Economic Contributions*

We examined the economic contributions that are derived from the pharmaceutical and biotechnology sectors under a market-based pricing system, and found that:

a) The pharmaceutical sector contributed significantly in terms of direct, indirect, and induced impact on sales, labor income, and employment.
b) The biotechnology sector provides employment and revenue generation.

c) Pharmaceutical and biotechnology sectors comprise a notable portion of the U.S. stock market value.

Is innovation responsible for economic benefits? The accumulation and application of new knowledge, cornerstones of innovation creation, are vital to economic growth. Consider the experiences of Korea and Mexico. Korea poured its energies into developing high-technology. But Mexico has largely avoided investing in innovative businesses, sticking instead to traditional agriculture and natural resources (e.g., silver and oil) and businesses employing less-skilled labor. The numbers tell the story. The average real wage in Korea grew ninefold from 1960 to 1990, while the real minimum wage in Mexico stayed almost the same during the same time period. Between 1990 and 1998, Korea's real economic-growth rate was eight times that of Mexico's."[15]

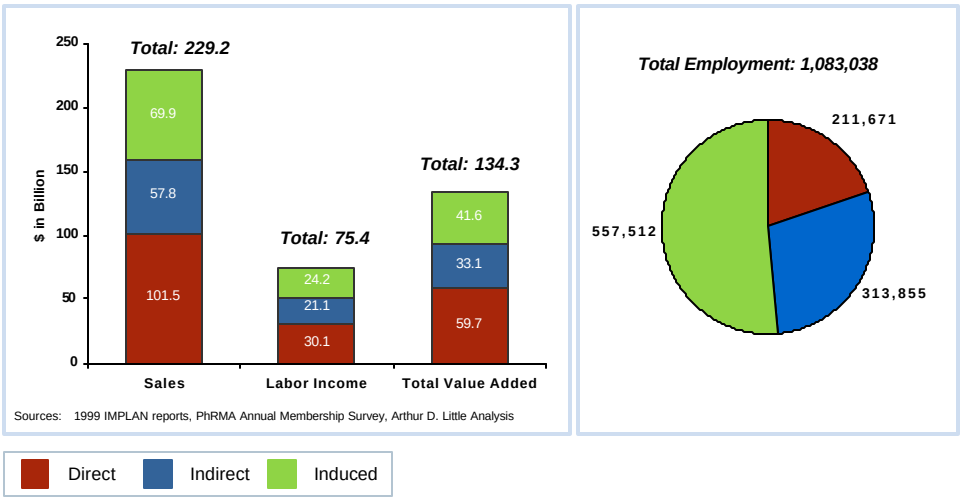
It is clear that investment in education, new knowledge, and innovation are fundamental to substantial economic well being. It is also clear how fast a country or region can lose the economic advantage associated with innovation. "In just a decade, the balance of research power and investment has shifted dramatically from Europe to the U.S., sending a frightening signal to the European Union. Those and hundreds of smaller investment decisions have deflated Europe's pre-eminence as a scientific powerhouse over the past decade. In 2000, Europe attracted only 70 percent of the $24.3 billion in pharmaceutical-research investment that the U.S. did, a direct reverse of their portions of research dollars in 1990[16]." The EU "High Level Group on Innovation and Provision of Medicines, G10 Medicines Report 26 Feb 2002" makes recommendations that "find the right balance between health objectives and industry competitiveness[17]". "Stimulating Innovation and Improving the EU Science Base[18]" is an important goal asserted by the report.

Like the high-technology industries of the 1980s and 90s, the pharmaceutical and biotechnology industries are perfectly positioned to be significant contributors to economic well being in the coming decades by leveraging the volumes of new genomic, transcriptomic, and proteomic knowledge created by current and future scientific achievements.

[15] Enriquez, J, As the Future Catches You, Crown Business/Random House, NY: NY, 2001, p.140.
[16] Fuhrmans and Zimmerman, "Swiss Drug Giant Joins Exodus To U.S. With New Global Lab," *The Wall Street Journal* (May 7, 2002)
[17] High Level Group on Innovation and Provision of Medicines, G10 Medicines Report 26 February 2002 page 5
[18] High Level Group on Innovation and Provision of Medicines, G10 Medicines Report 26 February 2002 page 11

a) **The pharmaceutical sector contributed $229.2 billion in sales and $75.4 billion in labor income, and employed nearly 1.1 million in 1999.** We examined the contributions to the economy derived from a market-based pricing environment in terms of direct, indirect, and induced impact on sales, labor income, and employment. (Direct impact consists of sales [revenue], labor income, employment, and total value-added contributions attributed directly to the sector; indirect impact refers to the goods and services that the sector purchases from other industries, such as equipment manufacturers; and induced impact measures the purchases made by employees in the industry.) Of that $229.2 billion, $101.5 billion was in direct sales, $57.8 billion was in indirect sales, and $69.9 billion was in induced sales. The pharmaceutical sector also employed a total of nearly 1.1 million people through direct, indirect and induced means, totaling over $75 billion in labor income (see Figure 19).

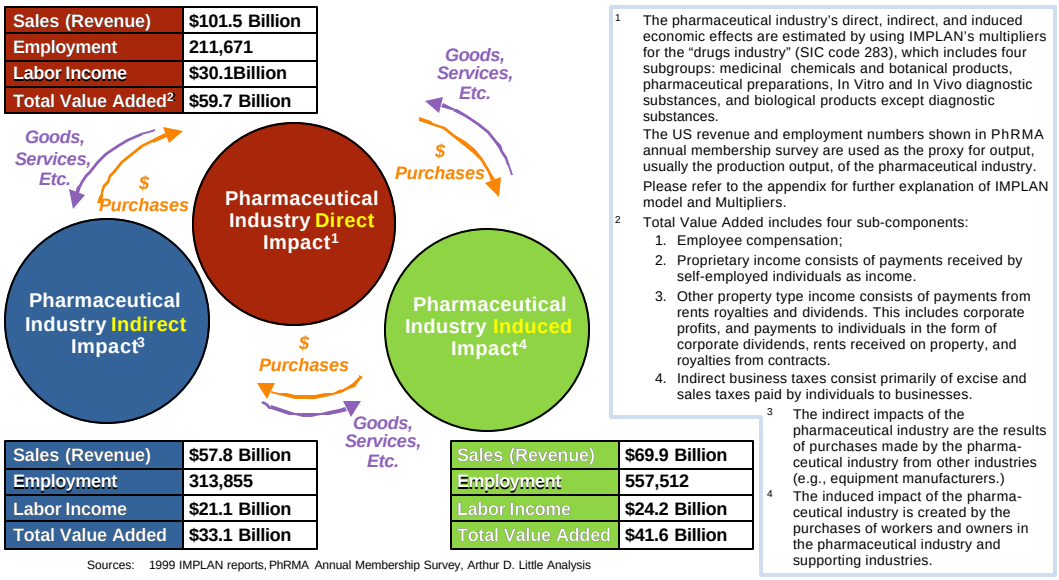
**Figure 19: Total Economic Impact by the Pharmaceutical Sector (1999)**




By using an input-output model, known as IMPLAN[19], to estimate the direct, indirect, and induced impacts in terms of sales, labor income and employment, we found that the pharmaceutical sector bought approximately $58 billion in goods and services from other industries during 1999 (indirect effect). In addition, people employed in the pharmaceutical sector purchased nearly $70 billion in goods and services (induced effect) (see Figure 20).

[19] IMPLAN is an Input/Output Model describing commodity flow from producers to intermediate and final consumers. In the input-output model, multipliers are mathematically derived which uniquely describe the change of output for each and every industry as a result of producing one dollar of final demand which are unique to each industry. The notion of a multiplier rests upon the difference between the initial (direct) effect of a change in final demand and the total effects (direct, indirect, and induced) of that change. (www.implan.com)

**Figure 20: Total Pharmaceutical Industry Economic Contributions by Type (1999)**




Sources: 1999 IMPLAN reports, PhRMA Annual Membership Survey, Arthur D. Little Analysis

**b) The U.S. biotechnology industry provides employment, as well as revenue generation.** State politicians and leaders throughout the United States are trying to boost their regional economies by attracting state-of-the art industries, such as biotechnology. New England and California have significant biotechnology hubs which return money and resources back into their economies (see Figure 21). These regions have well-educated labor forces and access to universities and hospitals.

**Figure 21: U.S. biotechnology Industry Characteristics by Selected Regions (2000)**

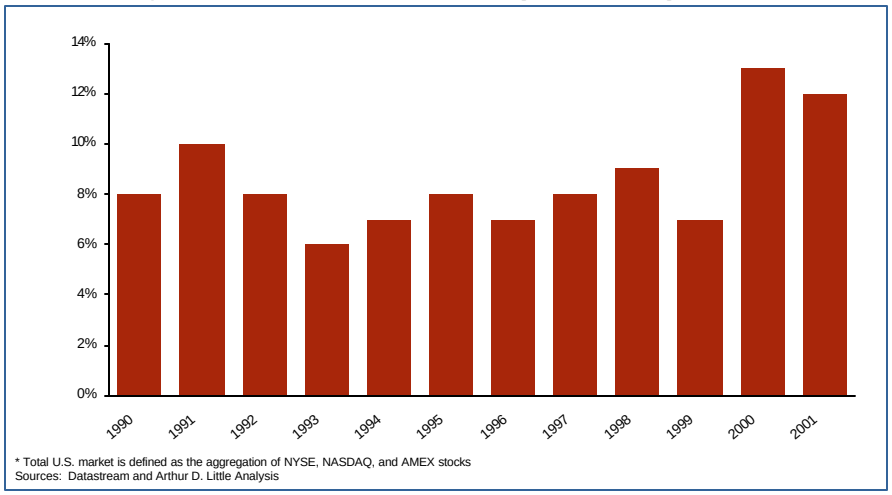
| Region | Number of Public Companies | Market Capitalization 6/30/01 (in millions) | Number of Employees | Revenue (in millions) | Market Cap per Employee (000's) | Revenue per Employee (000's) |
|---|---|---|---|---|---|---|
| San Francisco Bay | 76 | $92,168.20 | 26,464 | $5,851.40 | 3.48 | .22 |
| New England | 48 | $53,575.20 | 20,641 | $3,069.90 | 2.59 | .14 |
| San Diego | 31 | $23,272.10 | 7,976 | $874.00 | 2.91 | .10 |
| New Jersey | 21 | $10,591.70 | 3,556 | $549.90 | 2.97 | .15 |
| Mid-Atlantic | 19 | $22,240.20 | 3,871 | $769.00 | 5.74 | .19 |
| Pacific Northwest | 19 | $17,189.60 | 3,258 | $1,096.60 | 5.27 | .33 |

Source: Ernst & Young, 2000, Arthur D. Little Analysis

**c) Pharmaceutical and biotechnology sectors comprise a notable portion of the U.S. stock market value.** We calculated the market capitalization of the pharmaceutical and biotechnology sectors against the total U.S. market value as measured by the aggregation of NYSE, NASDAQ, and AMEX stocks. We found that from 1990 to 2000, the market capitalization of the pharma/biotech sectors

averaged nine percent of the total market value. By 2001, that share had risen to nearly 12 percent (see Figure 22).

**Figure 22: Market Capitalization of Pharmaceutical and Biotechnology Sectors as Percentages of Total Market Value* (1990-2000)**




* Total U.S. market is defined as the aggregation of NYSE, NASDAQ, and AMEX stocks
Sources: Datastream and Arthur D. Little Analysis

## Overall Conclusions

Contrary to the widespread belief that the pharmaceutical sector enjoys a high rate of return even when the substantial risks inherent to the industry are considered, our analysis found that returns are aligned with risk. Moreover, industry returns have remained steady since 1981. The industry's risk-adjusted return is lower than that of other R&D-based industries, such as computer network and software services sectors.

Using past experience to predict the impact that price intervention could have on the level of investment in pharmaceuticals and biotechnology, we believe there would be a decline in stock prices, R&D spending, and venture capital funding. Though both sectors would be affected, biotechnology would be particularly vulnerable to changes in pricing policy. Furthermore, the value of public R&D funding might be diminished if private R&D funding is weakened, which means that new, gene-based knowledge might not be translated into useful therapeutics.

As the world's largest and only remaining market-based pricing environment, the United States has emerged as the global leader in innovative drugs with more new product launches than all other countries combined. The U.S. biotech industry likewise surpasses the rest of the world in terms of drugs under development.

Significant economic benefits accrue in environments with strong pharmaceutical and biotechnology businesses. In our post-industrial economy, pharmaceutical and biotechnology sectors form a foundation for building and maintaining a strong economy.

## Areas for Further Exploration

Our efforts to analyze the question of the impact of U.S. market-based pricing on innovation creation identified some important areas for further primary research:

1. We have insufficient knowledge about bio-pharmaceutical R&D productivity and innovation creation. The rapidly evolving technologies, the proprietary advantages conferred by improved R&D productivity, and the long product development timelines make it very difficult to critically examine and publish R&D productivity studies. Nonetheless, the development of metrics and initiation of prospective research in the area could help us better understand this vital component of innovation creation.

2. Additional primary data regarding the economic spillover benefits need to be collected across countries so that we can better understand the economic contributions of companies which are striving to use the latest life sciences knowledge.

3. We need more comprehensive research on the benefits of pharmaceuticals across therapeutic areas and across classical health care delivery 'budget silos' which impede our ability to recognize total value (benefits and costs) of bio-pharmaceutical innovation.

4. Further evaluations of private and public efforts to address access and utilization (over-, under-, and mis- use) are needed.

5. Thorough multinational comparisons of bio-pharmaceutical pricing systems and innovation creation and diffusion are needed to evaluate how market-based pricing affects future bio-pharmaceutical innovation investment.

## Acknowledgements

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## Appendix A: Interview Program

To better gauge the policy issues around market-based pricing and bio-pharmaceutical innovation, we conducted interviews with 58 stakeholders representing broad-based, multi-disciplinary fields. Figure 1A illustrates the approach used for the interviews.

### Figure 1A: Interview Program Approach

**Design**

- The objective of the interview program was two-fold:
  - Engage participants in a discussion regarding the pricing/innovation relationship
  - Assess impact of pricing on innovation under pricing scenario
- General and customized interview guides were designed for each stakeholder

Interviewees with broad-based, multi-disciplinary perspectives were selected:
- 13 Experts/Economists from Academia
- 12 Pharmaceutical Executives (1 European)
- 8 Biotechnology Executives (1 European)
- 3 Industry Financial Investors
- 5 Advocacy Groups
- 5 Trade Associations and 6 Other Health Care Organizations
- 4 Pharmaceutical Buyers/Providers
- 1 Legislator/Health Policymaker
- 1 State Government Agency

**Implementation**

- Provided background material and interview guides in advance so interview participants could review questions and address those of key interest
- Two factors resulted in covering all general guide questions and stakeholder-specific questions:
  - Time availability with interview participants (e.g., 30 minutes versus 60 minutes)
  - Interview participants knowledge and interest in addressing the question
- Conducted total of 58 interviews (based on contacting approximately 150 prospective interviewees)

**Analysis**

- Interview program enabled us to identify various issues and perspectives of stakeholders
- Interview findings supplemented both the primary and secondary research analyses
- Selected findings were organized and reported in a "mentions analysis" format; however, since participants were selected for representation of diverse perspectives, only general trends (as opposed to quantitative summaries) can be inferred.

We identified in our interviews some converging and diverging themes related to market-based pricing and bio-pharmaceutical innovation. Highlights of these findings are demonstrated in Figure 2A.

### Figure 2A: Converging and Diverging Perspectives

**Converging Perspectives**

- The value of bio-pharmaceuticals, specifically in saving other medical resource costs (e.g., hospitalizations, MD visits, etc)
- The demand for continued research and development, including new tools to address unmet health care needs
- Maintaining a certain level of pharmaceutical profits to foster, accelerate and encourage innovation
- The need to address and improve access to health care and pharmaceuticals (but fragmented payer system and budget silos present a number of conundrums)
- Lack of holistic, multi-stakeholder approach in addressing health care issues

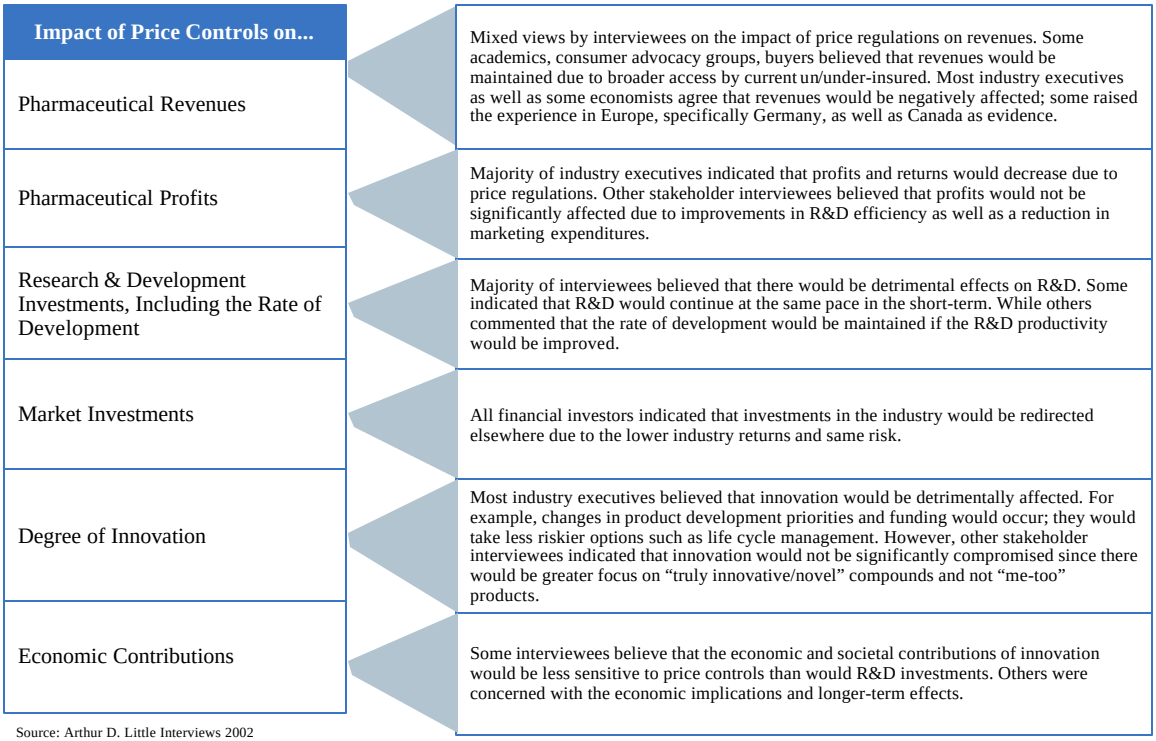
**Diverging Perspectives**

- Definition of bio-pharmaceutical innovation and perceptions about prices
- The level of R&D investments including R&D productivity and efficiency issues
- The level of pharmaceutical profits required for continued innovation
- Role of pharmaceutical industry relative to other health care system components in addressing access issue (e.g., value of pharmaceutical company prescription drug discount cards)
- Stakeholder (government, pharmaceutical firms, buyers) solutions and degree of involvement in addressing the health care issues

Source: Arthur D. Little Interviews 2002

Interview participants also provided diverse perspectives on the impact of price regulation on components of the pricing and innovation relationship (see Figure 3A).

**Figure 3A: Perspectives on the Impact of Price Controls**




Source: Arthur D. Little Interviews 2002

## Appendix B: Literature Review

### Highlights of Literature Review Related to Industry Returns and Risk

- **Regarding pharmaceutical pricing:**
  - Danzon et al. (2000), examined cross national price differences for pharmaceuticals and found that U.S. prices are not much higher than elsewhere, as commonly believed
  - Price elasticity is a key issue in the price regulation debate. Ellison et al. (1997). modeled the own and cross-elasticity for four cephalosporins and found high elasticities between generic substitutes and significant elasticities between some therapeutic substitutes. To date, there is little evidence showing prescription drugs' own elasticity is also high
- **Regarding whether the pharmaceutical sector's return is aligned with its risks:**
  - In 1993, the U.S. Office of Technology Assessment published a milestone report and concluded that returns to the pharmaceutical sector during 1970's and 1980's were about 2% to 3% higher than its cost of capital
  - Since 1993, few studies have examined returns to the pharmaceutical sector despite the fact that it has experienced changes, such as drastic increase of R&D cost, etc.
  - At the product level, Grabowski and Vernon (2000) have demonstrated that return to pharmaceutical products is highly skewed, suggesting that price regulation targeting high-revenue products is likely to negatively affect the pharmaceutical sector
- **Regarding the potential impact of price regulation on the industry return:**
  - Few articles directly examine how pharmaceutical price regulation affects the industry's rates of return
  - Several articles modeled how pharmaceutical companies will respond to price regulation by adopting different pricing strategies. Aslam et al. (1998) found that while price regulation may lead to lower introductory prices for new drugs, the existing drugs' prices may increase

### Highlights of Literature Review Related to Investments

- **Regarding the relationship between the pharmaceutical rates of return and industry and R&D investment:**
  - Scherer (2001) found that the investments on R&D is closely correlated to the gross margin of pharmaceutical companies
  - Grabowski et al. (2000) found that expected returns and cash in flows are important explanatory variables of the research and intensity. Gambardella etc.(1989), also found that shocks to sales explain 24%, 28%, and 6% of the variance of the firms' R&D, capital, and market value

- **Regarding price regulation's potential impact on industry investment:**
  - Ellison et al.(2001) identified a 52.3% decline in market adjusted stock prices of major pharmaceutical companies are associated with the prior proposed health care reform during 1992 to 1994
  - There are very few articles discussing whether biotech industry will be more vulnerable to price regulation than the large pharmaceutical companies, although Scherer (2001) found the UK's rate of return cap scheme will hurt the biotech industry more

### Highlights of Literature Review Related to Innovation

- **Regarding the relationship between R&D investments and innovation**
  - Tuft's (2001) study demonstrated that the average cost for a successful R&D project is about $803 million and the average time required is 12 years
- **Regarding the potential impact of price regulation on pharmaceutical innovation**
  - Many articles found that a hospitable environment and system are necessary for innovation. For example, Rogers (1995) wrote "these tracer studies generally show that a major technological advance in such fields as military weapons, medicine, or agriculture requires not just one innovation, but a cluster of innovations, often as many as a dozen...we should not forget this functional interdependence of innovations…"
  - Although not directly measuring the impact of pricing regulation on innovation, Danzon (1995) analyzed how European pharmaceutical regulation led to lower productivity in the European pharmaceutical industry

### Highlights of Literature Review Related to the Outcomes of Innovation

- **Regarding health care outcomes**
  - The National Economic Research Associates, Inc (2001) analyzed the current and expected prevalence, estimated costs to the U.S. health care system, and the research in progress for ten diseases
  - Albert and Mary Lasker Foundation recognized that "…little effort have been made to quantify the value of medical research in terms of its impact on the length or quality of life - and virtually none on how research-related reductions in mortality and morbidity should be translated into dollars-and-cents.
  - The study concluded that medical research has and will continue to produce exceptional high returns
    - Increases in life expectancy in just the decades of the 1970's and 1980's were worth $57 trillion to Americans
    - Improvements in health account for almost one-half of the actual gain in American living standards in the past 50 years.
    - Medical research that reduced deaths from cancer by just one-fifth would be worth $10 trillion to Americans - double the national debt

- **Regarding any measurable health returns associated with pharmaceutical consumption**
  - Miller and Frech (2000) concluded that increased pharmaceutical consumption helps improve mortality outcomes, especially for those at middle age and older
  - Lichtenberg (2001, "Are the Benefits of New Drugs Worth Their Costs?") quantifies the aggregate improvements in mortality and morbidity gained from added drug expenditures

### Highlights of Literature Review Related to Relationship Between Use of Drugs and Other Services Across Large Populations

- Limited number of articles with evidence of how drugs reduced overall health care expenses
- No aggregate study exists which examines the correlation between changes in drug use/cost and other medical services use/cost for all drug classes across the population
- Three studies explore the relationship between use of drugs and other services across large populations
  - All three are associative
  - Two focus on narrow clinical areas and
  - Two use proxies (formulary status and reimbursement as markers for drug utilization)
- Soumerai and Lipton (1995) found that restriction of three drugs increased the rates of institutionalization-all at costs far in excess of the drug savings
- Horn (1996) found that the more restrictive a drug formulary, the greater the total health care costs for five major, drug-intensive diseases
- Lichtenberg's studies (1996) found that hospital costs declined most rapidly for those diagnoses with the greatest change in the distribution of drugs, by molecule
- Kleinke (2001) found that the added cost associated with breakthrough medicines represents:
  - A major structural shift from the provision of traditional medical services to the consumption of medical products, resulting in a decade-long reduction in hospital admissions and length of stay. Data about use of physician services are mixed
  - The creation of economic, social, and public health utility that we value as a society

## Appendix C: References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