

INTRODUCTION

**Robert Dressing, President
Cystic Fibrosis Foundation**

Just a few decades ago, it was a rare family that had not been touched by the ravages of disease. Polio, smallpox, and tuberculosis took innocent child and breadwinner alike, and left their families in despair. Today we live in a society where these afflictions have been all but wiped out by affordable, easily administered vaccines and medicines.

But not everyone has been so fortunate. Hundreds of thousands still suffer from Alzheimer's, muscular dystrophy, ALS, multiple sclerosis, and AIDS, not to mention cancer and heart disease that are the most common causes of premature death.

My own son is a victim of cystic fibrosis, one of the most common fatal genetic diseases. Less than 20 years ago, infants with CF rarely lived past age six. Thanks to drugs developed to control lung infections associated with CF, my son is alive today. Along with thousands of victims of other diseases, we wait, hope and pray while progress is made toward a cure.

Unfortunately, at the very time when scientific knowledge is on the verge of finding cures for CF and a variety of other diseases, talk of price controls threatens to delay the research that promises to produce a cure.

Of course, in a perfect world we'd have all the wonder drugs we need at little or no cost. But in the real world, there is a tradeoff between low prices and innovative research. The price of a drug must allow the developer to recoup astronomical research costs. The moral dilemma facing America is how to responsibly price pharmaceuticals to maintain sufficient research and development funds. I commend the Institute for Policy Innovation for taking a realistic look at this emotional issue with both compassion and candor.

Saving lives, curing diseases, and eliminating disabilities is much less costly than living with the enormous costs of long-term care. If you think research is expensive, try disease.

Some critics charge that pharmaceutical companies are simply enriching themselves at the expense of the sick. We're all concerned about health care costs, but innovative drug and genetic therapies are among our biggest health care bargains. Pharmaceuticals are net savers of health care dollars, treating conditions that would otherwise require much more expensive surgery.

Let's not forget that America's history is based on our willingness to take risks, and on free-market support of innovation. Profits are necessary to fund the high risk research that is essential to developing innovative new drugs and therapies. But innovation has a price. If we control prices on pharmaceuticals, we limit the research budgets of these companies, and we delay or diminish the breathtaking possibilities that such research will yield. That's a price I'm not willing to pay, and I don't think America is, either.

EXECUTIVE SUMMARY

Commenting on the medical progress that pharmaceutical innovations will provide humanity, noted physician and author Lewis Thomas wrote that "for the first time it is now possible to begin thinking about a human society relatively free of disease." Cures for cancer, heart disease, Alzheimer's, AIDS and other life-threatening conditions are not only possible but likely, a result of scientific advancement of which we have seen only the beginning. Yet at a time when pharmaceutical and biotechnology firms are on the verge of transforming scientific knowledge into life-saving cures, medical progress is jeopardized by proposals to impose price controls on drugs and vaccines.

The appeal of price controls is self-evident. But the current debate over pharmaceutical pricing obscures a deeper dilemma: Can drug prices be controlled arbitrarily without reducing the research and development that must take place to propel medical progress?

Pharmaceutical therapy is the most efficient form of health care. Since 1965 drug costs have increased more slowly than any other type of medical care. Drugs costs are only eight percent of America's total health care bill, and the average per capita out-of-pocket cost of drugs is \$232 a year. That is less than people spend out-of-pocket for health insurance premiums, doctors' fees, or hospital care. Pharmaceuticals not only hold the greatest promise for medical advancement, they can also help control health care costs as new drugs reduce dependence on less effective and more costly medical treatments. For example,

- Drug therapy for coronary artery disease costs approximately \$1,000 a year compared to \$41,000 for bypass surgery.
- Drug therapy for ulcers costs \$900 a year compared to \$25,000 for surgery.
- Drug therapy for depression costs \$5,000 a year compared to \$73,000 to institutionalize an individual.

The pharmaceutical industry is in a period of turmoil and transition. Scientific advancement has led to a greater understanding of the causes of disease and potential cures. In the meantime, the pharmaceutical marketplace has become more competitive, creating pressure on both prices and earnings. New breakthrough drugs soon find competitors, and generic alternatives to existing drugs are commanding a growing share of the pharmaceutical market. Generics, like computer clones, force prices down to commodity levels and place tremendous pressure on drug company profits.

To survive, pharmaceutical companies have had to restructure and devote billions of dollars to innovative new drugs and biotechnology developments. The Office of Technology Assessment estimates it costs approximately \$359 million to develop a single new drug, and less than one drug in ten recovers this cost. Given these enormous costs, the risk drug companies are now assuming, at a time when earnings are less predictable, is tremendous.

Since the mid-1980s, the pharmaceutical industry has spent approximately \$10 billion a year on the discovery and development of new drugs, including many biotechnology products. And this investment is already paying off. Because of advances in gene therapy and other new drug developments, Americans can expect to see incredible developments over the next decade, including:

- A 20 to 30 percent reduction in inpatient hospital use among the general public, and a 40 to 50 percent reduction in inpatient hospital use rates among the elderly.
- A decline in surgical procedures, with 85 percent of all surgical patients becoming ambulatory promptly after the surgery.
- A significant decline in the death rate from cancer, heart disease and other diseases.

New pharmaceutical and biotechnology products will save lives and money. Recent studies project that:

- New pharmaceutical products will save nine million lives and \$500 billion over the next 25 years.
- New vaccines to prevent childhood diseases will save from six to ten million young lives worldwide each year.

This future is now at risk. If price controls had been implemented in the 1970s we would have saved only one-tenth of one percent in the total increase in health care costs. Yet billions invested in cures for debilitating and fatal diseases would not have materialized, and many advancements that are within our reach today would still be years, if not decades, away. Just talk of price controls has already had a disturbing impact on future investments in pharmaceutical research and development. For instance,

- Many biotechnology concerns can no longer raise money for important research. Much of the money raised to develop cures for Alzheimer's, ALS, cystic fibrosis and other diseases could not have been raised in the current political environment.
- Billions that could be spent on developing new drugs are now being spent on marketing alliances and generic drug manufacturing, trading investment in future cures for spending on efforts to sell higher volumes of "day old" drugs.

In the competitive pharmaceutical marketplace, research, development and medical progress go hand in hand with profits. The real victims of price controls will be those people for whom no cure exists, and for whom existing treatments cannot offer a full and productive life. Robert Dresing, president of the Cystic Fibrosis Foundation and father of a son with the disease, made the choice very clear: "In our free market society, the drug companies' innovation should be and has been rewarded with profits from breakthroughs. If you destroy or diminish this potential, you discourage investment and that will cost us our children's lives."

I. INTRODUCTION

Over the past year, there has been a growing discussion of the merits of government price controls on drugs and vaccines. There is no doubt that for Americans with limited incomes, many items such as food, heat, and housing as well as drugs are relatively expensive. Yet focusing only on the price of pharmaceuticals ignores their value. Many lives have been saved and many have avoided the pain and loss of independence associated with being ill. Yet price control advocates are often too quick to dismiss these benefits.

During a debate with a health care "expert" who has been leading the charge to impose price controls on pharmaceuticals, I mentioned that two years ago my wife had rheumatic fever. This disease, rare nowadays, causes crippling rheumatoid arthritis and creates perforations in the heart, raising the risk of a fatal heart attack in the years ahead. The quick eye of our doctor led to an accurate diagnosis. He prescribed, not one day too soon, a 10-day regimen of penicillin that cost \$14. Even if the prescription had cost \$1,400 or \$14,000, it would have been well worth it to have my wife healthy again and to reduce the chances of her dying from a heart attack. In purely economic terms, we saved thousands of dollars in surgical costs and lost productivity. Yet the "expert" said that the issue wasn't my wife's rheumatic fever, it was "responsible pricing."

Pharmaceuticals have provided an enormous benefit to Americans, saving billions of dollars and millions of lives. Polio, smallpox, and influenza have nearly been wiped out thanks to vaccines. Drugs for ulcers, high cholesterol and arthritis have prolonged millions of lives and reduced the need for expensive and painful surgery in the process. Cancer patients are living longer, and people that are HIV-positive can live more productive lives by taking a combination of AZT and new, more powerful antibiotics.

The pharmaceutical industry is in transition as the generic revolution and managed-care groups have led to price competition and cuts in the cost of pharmaceuticals. America spends less per capita on drugs than most other developed countries, and drug costs in the U.S. have increased more slowly than other medical expenses.

Moreover, under not-so-gentle prodding from consumers, pharmaceutical companies are being forced to forgo incremental drug developments in favor of drugs that significantly improve medical problems. As a result, drug companies are investing billions of dollars to develop cures for cancer, arthritis, Alzheimer's, cystic fibrosis, multiple sclerosis and AIDS. Vaccines that would prevent those illnesses as well as fatal childhood diseases are under development as well.

America's health care cost crisis is not a product of high drug costs, and government control of prices and profits is not the solution. Drug costs are only eight percent of all health care spending in this country¹. While 60 percent of Americans have no insurance coverage for drugs, for most the average out-of-pocket cost of pharmaceuticals is less than the cost of one year of cable television. And while no one likes to spend money on drugs, they are less expensive and more liberating than the alternative. For example, someone would have to buy 30 years of heart medicine to equal the cost of open-heart surgery.

Current research and development programs, funded out of drug company profits, are focusing on innovative and increasingly risky pharmaceutical advances. Would cutting drug profits really improve our health care system?

Eliminating all drug profits would mean saving less than two percent of the country's \$750 billion health care bill. But it would dramatically reduce the \$10 billion a year investment drug companies make in developing new vaccines, drugs and biotechnology products. Many of these new drugs can make the dream of a cure for now-fatal diseases finally come true. Diseases that are targeted by pharmaceutical and biotechnology R&D disable and kill hundreds of thousands annually, force many more out of work or into hospitals and nursing homes, and cost approximately \$500 billion a year. Price control advocates distort the truth when they say the industry can cut prices and lower profits while continuing innovative R&D.

Without the incentive to make a profit, there will be substantially less investment in pharmaceutical R&D. We may save money in the short run, but the bill will be paid by denying or delaying millions of people access to drugs that can save their lives. Robert Dressing, President of the Cystic Fibrosis Foundation and a parent of a young person with the fatal disease, frames the issue best:

Many are blinded by their zeal to go after an industry that turns a profit. It may be hard to swallow sometimes, but profit is not a dirty word.... In our quest to reduce health care costs, the search for solutions must be honest and complete.... Prescription drugs account for less than eight percent of every health care dollar spent. Even if we were successful in cutting this amount of profit in half, the total impact would be negligible. We would only be making a drop in the bucket and at what cost—our children's lives.... In contrast, we could have a great impact on improving the quality of life and significantly reducing cost by continuing to cure disease.... Cripple the drug industry and we will surely cripple the very people who need our help. Caution must prevail.²

This report examines the cost of drugs and their cost-effectiveness. It describes how scientific advancement, price competition and generic substitution have transformed the pharmaceutical marketplace. It details the progress being made on several fronts—with cancer, heart disease, Alzheimer's, cystic fibrosis and other life threatening diseases—and the promise these innovations hold. Finally, it examines the impact government price controls would have on pharmaceutical companies and medical progress.

II. THE COST OF DRUGS IN PERSPECTIVE

What America Spends on Drugs

For most Americans, drug costs are an unwanted expense but not a true burden. Per person, they are still the smallest and most efficient portion of total health care dollars. According to the Organization for European Cooperation and Development (OECD), which has compiled comparative health expenditure data from the U.S., Europe and elsewhere, Americans spend \$232 per capita on pharmaceuticals.³ As **Figure 1** indicates, U.S. per capita expenditures are lower than most industrialized countries once foreign purchasing power is taken into account. Moreover, per capita drug costs in the U.S have increased at about the same rate as countries with price controls.

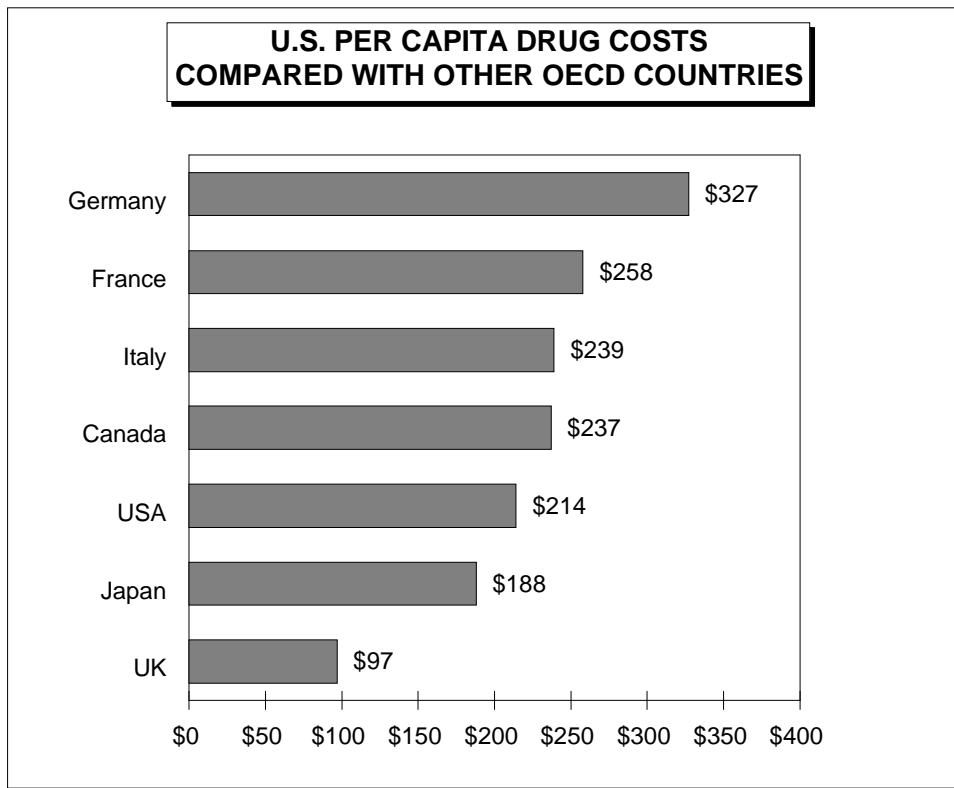


Figure 1

Source: OECD *Health Data 1993*⁴

While all health care costs are increasing, **Figure 2** shows that from 1980 to 1990 drug costs increased more slowly than hospital and other types of medical expenditures. In fact, the cost per patient for the eight most widely used drugs grew at an annual rate of 1.6 percent between 1985 and 1992, while the CPI increased at a rate of 3.9 percent.⁵

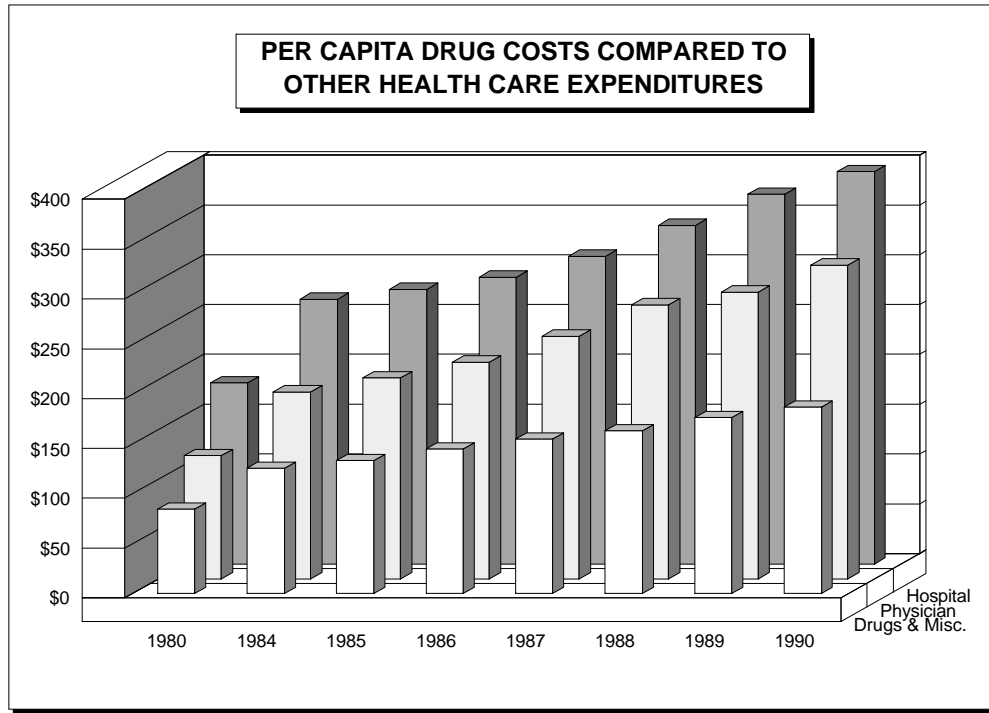


Figure 2

Source: US Health

Source: *Health Care Financing Review*, Fall 1991, U.S. Health Care Financing Administration⁶

Furthermore, if we look at what we spend as a nation on prescription drugs as a percent of our total health dollar we see, as **Figure 3** shows, that the cost of drugs relative to U.S. health spending has declined over the past 20 years from 12 percent to 8 percent.

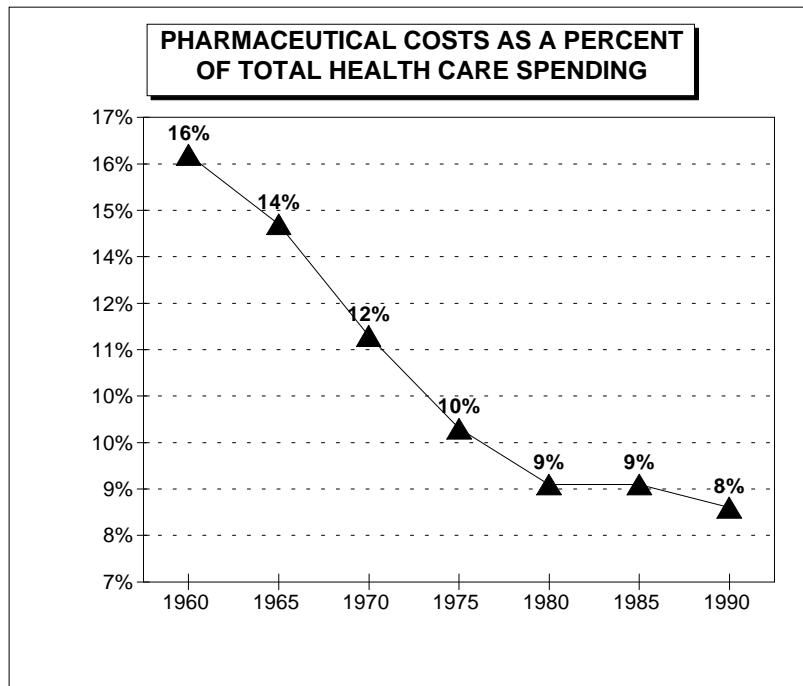


Figure 3

Source: OECD Health Data 1993

Even older Americans, who purchase 34 percent of all prescription drugs, are not unduly burdened by drug costs.⁷ According to a 1991 survey conducted by the American Association of Retired Persons (AARP), over half of all Americans 65 and older spend \$230 or less a year on drugs.⁸

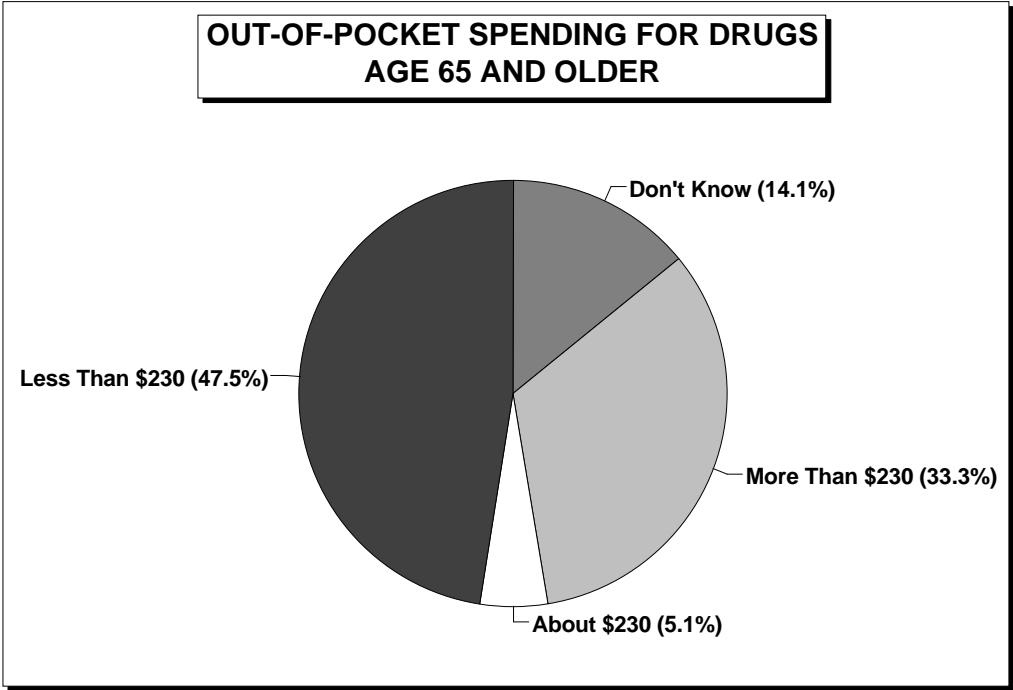


Figure 4

Source: American Association of Retired Persons

Pharmaceutical Cost-Effectiveness

While many drugs are expensive, their prices pale in comparison to other forms of medical treatment that are much more costly and less effective. Yet because health insurance covers 80 to 100 percent of hospital and physician costs, compared to 60 percent of drug costs, consumers feel the cost of the \$1,000 a year in heart medicine more than the \$50,000 heart surgery the medicine can avert. A thousand dollars is a lot of money, but even if it were \$840—which would be the price with all profits stripped out—that amount would still seem high compared to paying nothing out of pocket for surgery.

It is important therefore to bear in mind the cost-effectiveness of drugs compared to other medical treatment. Drug therapy for ulcers costs \$900 a year compared to \$25,000 for surgery. As a result, ulcer drugs have made surgery almost obsolete. On other fronts,

- Drug therapy for depression costs \$5,000 a year compared to \$73,000 a year for institutionalization.⁹
- A new drug that prevents the rejection of a kidney transplant costs \$4,500 but saves yearly dialysis costs of \$40,000.

- The net annual benefit of using beta blockers to help prevent second heart attacks is estimated to be between \$1.6 billion and \$3 billion.
- The total cost of childhood vaccines is \$188 and virtually guarantees that children will avoid crippling and costly diseases.
- Drugs for arthritis and osteoporosis have permitted the elderly to avoid more costly and restrictive institutionalization.
- Antibiotics that help prevent infections in caesarian section patients helps to avoid up to \$182,000 in costs for every 100 patients.
- Drug therapy for gallstones costs \$1000, while surgery costs \$12,000.

Just as new drugs and vaccines are saving health care dollars, later generation versions of old drugs can also be more cost-effective. Reducing the number of times someone has to take a drug increases the rate at which they will follow the prescribed drug regimen. Since up to 10 percent of all hospital admissions and 23 percent of all nursing home admissions result primarily from an inability to comply with drug regimens, the savings and well-being derived from more powerful and reduced-dose formulations of existing drugs are proving to be substantial.

Future savings from new drugs should be even greater. The Battelle Institute studied the impact of pharmaceuticals on eight major diseases in the U.S. by extrapolating trends of morbidity and mortality. It concluded that pharmaceuticals saved 671,000 lives between 1968 and 1989 and averted \$83.8 billion in indirect costs.¹⁰ Drugs in development for such diseases as Alzheimer's, heart disease, cancer, AIDS, and arthritis are expected to avert \$500 billion in costs, and save nearly 9 million lives over the next 25 years.

III. COMPETITION TRANSFORMS THE MARKETPLACE

The pharmaceutical industry is in a period of turmoil and transition. While encouraging scientific advancements are fueling the demand for even greater research dollars, market forces are putting pharmaceutical manufacturers under unprecedented price pressure. Therapeutic substitution and use of pricing formularies by both government and private health care providers limit the prices manufacturers can charge for their products, and pressure from generic alternatives is forcing prices down to commodity levels. To survive, pharmaceutical manufacturers have been forced to restructure and redirect resources into high risk drug and biotechnology innovation.

Lower Prices

A combination of factors including competition from generic drugs and the setting of "benchmark" prices by large purchasers such as Medicaid and HMOs has resulted in industry-wide price restraint. Moreover, price restraint is not only the rule for established drug products, but also for pricing many new drug products. Generally, "therapeutic areas with more than one product introduction showed an increase in list prices of little more than one percent in 1992, compared with over five percent in areas with no new products."¹¹ On average, product launch prices are now 14 percent below the market segment leader where there are competing therapeutic products.¹²

The pricing of two new significant drug products bears out this trend. Merck's Proscar and SmithKline Beecham's Paxil were priced below anticipated levels in order to kick-start sales, particularly to managed-care customers. In another area, the ACE inhibitor Lotensin was launched in 1991 after four other ACE inhibitors were on the market. It is priced 50 percent below Bristol-Myer/Squibb's Capoten and 25 percent lower than Merck's Vasotec.¹³ In 1990 these two drugs held 87 percent of their therapeutic market. They hold just 60 percent today.

The response to lower launch prices has been price discounting. Recently, Merck announced a 4 percent price decrease to compete with an aggressive promotion of Bristol-Myers' cholesterol drug, Pravachol. Generally, neither the analysts nor drug company executives surveyed expect pricing decisions to contribute more than a negligible amount to industry revenue growth for the future.

Substitution of Drug Products

The substitution of generic for name-brand drugs or one brand for another is a major factor pushing prices lower. **Figure 5** indicates how small parts of drug industry revenues are free from competition and how important innovation is to generate returns.

The Office of Technology Assessment (OTA) conservatively estimates that branded drugs will lose 12 percent of their revenues each year after a drug goes off patent and competes with a generic equivalent.¹⁴ Yet, as **Figure 6** demonstrates, generics are rapidly grabbing market share, and at a much faster pace than OTA estimated. Simultaneously, generics are marketed today at 80 to 90 percent less than a branded drug's list price, compared to 40 to 60 percent discounts during the time OTA reviewed.

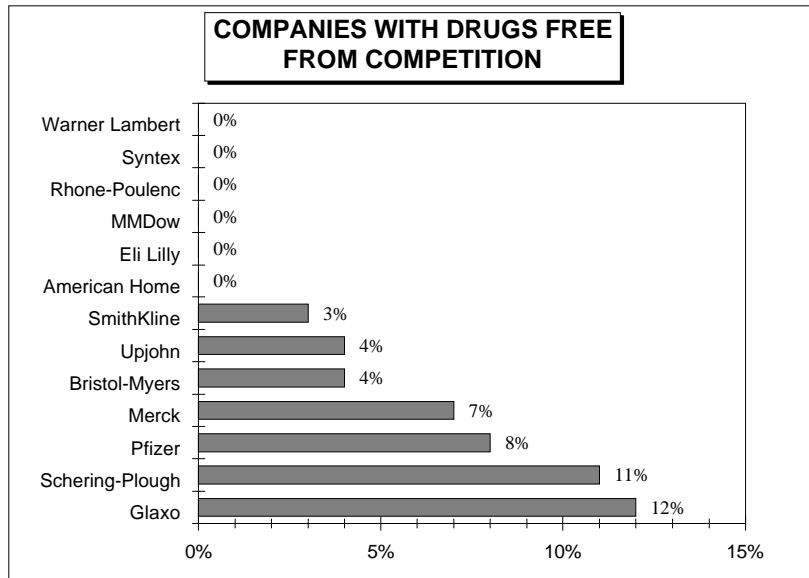


Figure 5

Source: Oppenheimer & Co. estimates

In fact, while the industry projected revenue losses of 30 to 50 percent within two years of patent expiration, actual revenue losses for some drugs are much higher. Naprosyn, for example, is projected to lose 50 percent of its revenues in the first year it goes off patent and Pfizer's anti-inflammatory drug, Feldene, lost nearly 45 percent of its unit sales and revenue in the first four months after patent expiration.

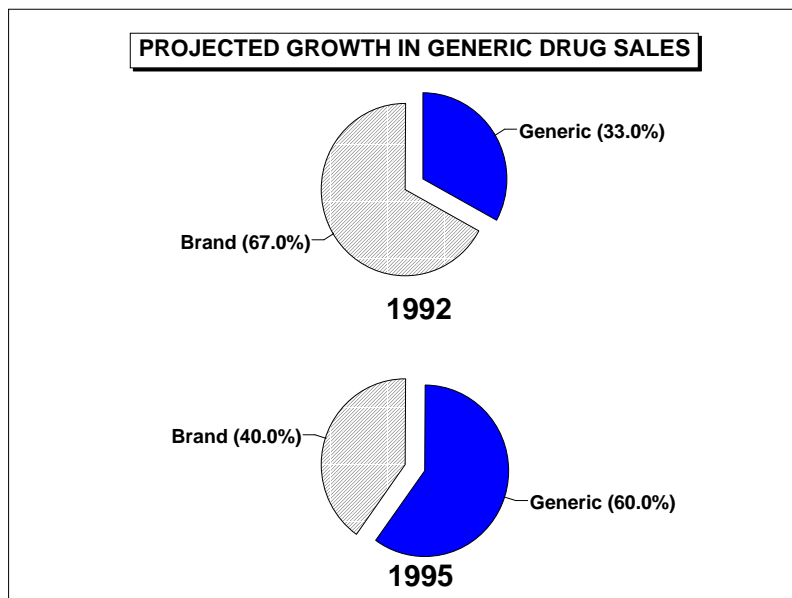


Figure 6

Source: IMS America Survey

Among products where there is no generic substitute, prior approval and drug utilization review increasingly limit physicians' choices within a therapeutic category to one or two products at most. Typically, these are products that have been offered at the lowest price.

Many companies are seeing the impact of these measures on the bottom line. Most recently, Marion Merrell Dow's top three drugs lost market share to less expensive competition. In announcing that its first quarter 1993 earnings would fall as much as 70 percent below estimates, the company cited "federal and private price restraints as a factor in this quarter's disappointing earnings."¹⁵

The use of therapeutic substitution and formularies is growing rapidly: Fully 70 percent of HMOs require some form of generic or therapeutic substitution in one or more therapeutic classes. For example, Medco Containment, a mail-order pharmacy that works with health insurance programs, aggressively pursues discounts from brand-name drug manufacturers. Zantac and Tagamet, two ulcer drugs, compete on price, with the latter drug's manufacturer, SmithKline, offering lower prices to companies such as Medco. A major insurer estimates that over 40 percent of all drugs will be dispensed from a restricted formulary list by 1995.¹⁶

In the final analysis, the introduction of many drugs, including generics, has promoted price competition in several therapeutic classes. As a result, competition has eaten away at the dominance of many older drugs. While critics commonly point to the rise in prices among the 200 most prescribed drugs, the fact is the "top 200" market share has declined over the past 15 years. As **Figure 7** shows, the number of prescriptions dispensed from the top 200 drugs has declined 32 percent since 1980.

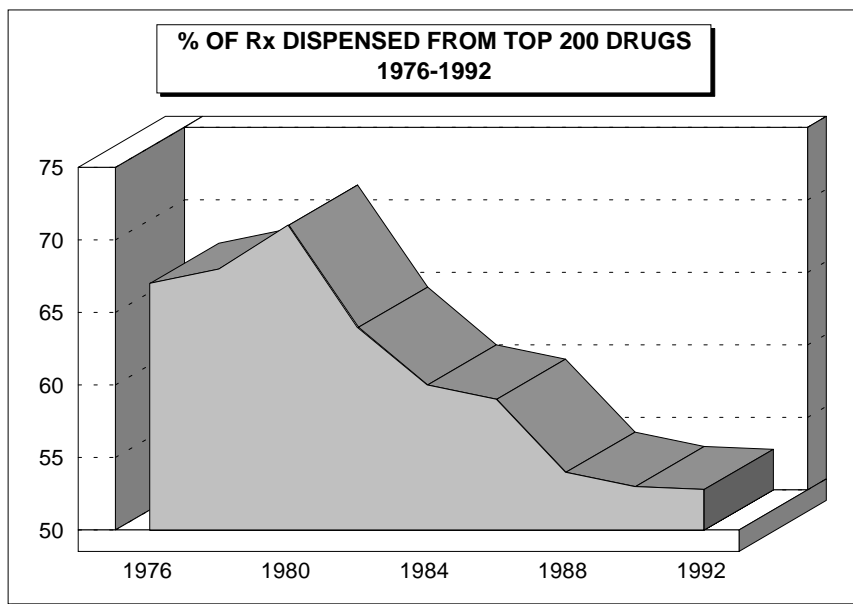


Figure 7

Source: IMS America Survey

Patents

The downward pressure on prices will accelerate over the next two years as nearly a third of prescription drug products with \$10 billion in revenues lose patent protection by 1995. By 2000, 200 drugs with \$22 billion in sales will be off patent. Certain companies such as Syntex, that depended upon one drug (Naprosyn) for most of their revenues, have seen patents expire this year. **Figure 8** demonstrates the peril many companies could or will be facing if they have no innovative drugs to take the place of products going off patent.

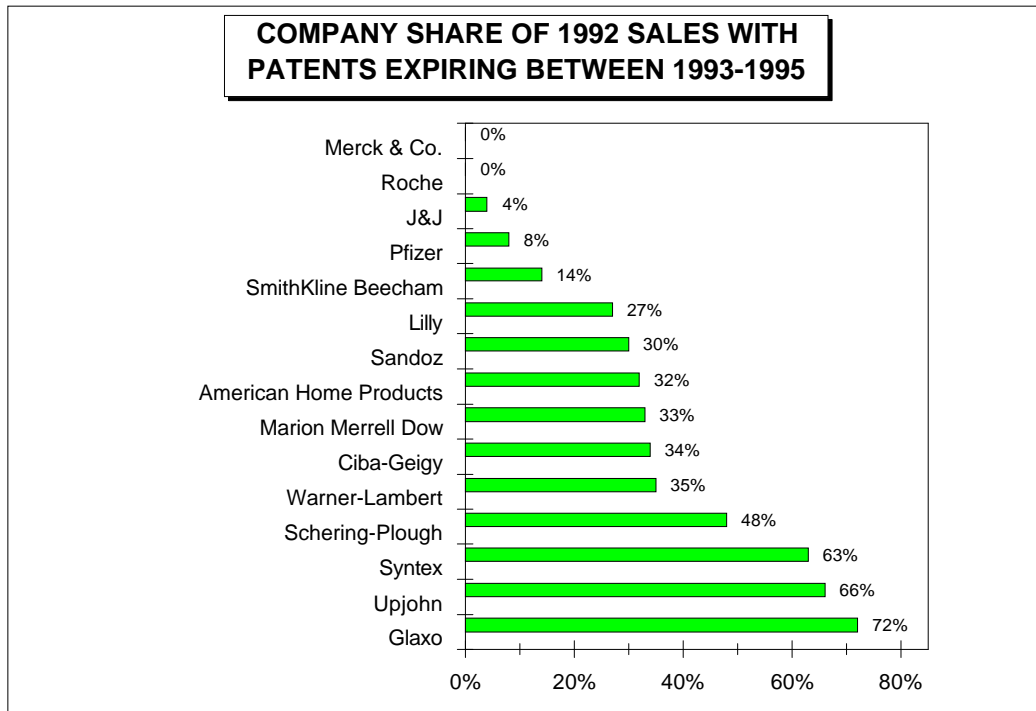


Figure 8

Source: *Scrip Magazine* April, 1993

Many companies such as Syntex, Merck, Bristol-Myers, Warner-Lambert and ICI have attempted to sustain price levels by going generic with drugs first or attempting to retain sales by introducing sustained-release versions of off-patent products. One industry expert has deemed such strategies—including the manufacture or licensing of generic products—examples of "playing a losing hand brilliantly."¹⁷ Any company seeking to maintain profitability through price increases and the introduction of therapeutically similar compounds is destined for extinction. The only reliable long-term offset to patent expirations is focused, well-funded research and development and the introduction of new products that can command entrepreneurial profits.

Competition Creates a New Pharmaceutical Industry

The prescription drug business has an average unit growth rate of only two to three percent a year. In the new pharmaceutical market, revenue growth by drug companies will have to come from significant new product introductions as well as from their presence in the above-average-growth therapeutic segments, such as anti-cancer and cholesterol-lowering drugs. The riskier environment has led companies to announce layoffs in an industry that was considered recession-proof. Job losses in such companies as Syntex, Merck, and Bristol-Myers Squibb total about 10,000. Concern about the future profitability of drug companies in a more competitive environment—with price controls looming on the horizon—has resulted in the loss of \$90 billion in the market value of pharmaceutical stocks since 1991.

Hence, in the new pharmaceutical marketplace, price controls are not only redundant, they could inhibit the tremendous restructuring and redirection of the industry into areas of high risk innovation. While pharmaceutical companies need to innovate to survive, they also need the incentives to innovate. In retrospect, without the profits generated by past drug sales, the industry would be hard put to make the move to better drugs and biotechnology.

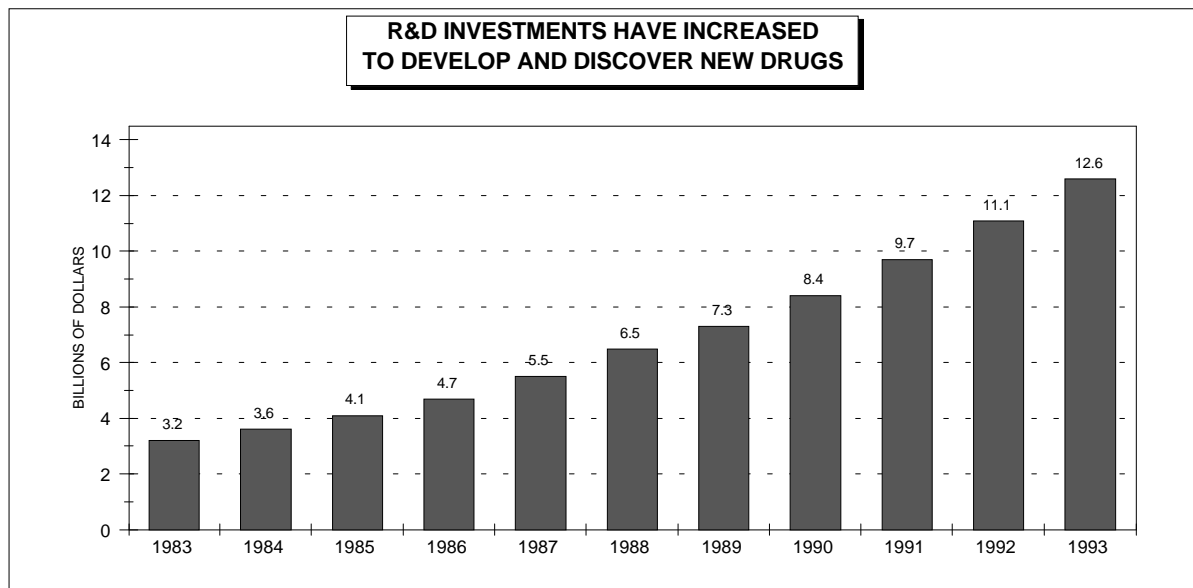


Figure 9

Source: Pharmaceutical Manufacturer's Association

At a time when the industry's future profitability is questionable, it has embarked on a costly and risky effort to capitalize on new technologies for discovering and developing new products (Figure 9). The Office of Technology Assessment estimates it costs approximately \$359 million to develop a single new drug, and less than one drug in ten recovers this cost. The average cost of drug development has been rising over the past 20 years, in large part because of the difficulty involved in finding cures or treatments for diseases such as AIDS, cancer, arthritis, Alzheimer's, and a variety of incurable genetic disorders such as multiple sclerosis. In addition, more rigorous Food and Drug Administration requirements, the need to establish dramatic therapeutic benefits, and the expensive process of developing biotechnology products have driven up the cost of development.

The stable, steady cash flow of past drug developments not only supported the transition to a more innovative industry, it also attracted investors at a substantially lower cost of capital because the industry offered high and predictable returns. Costlier capital would have meant avoiding the riskier but potentially more beneficial R&D of the type we will discuss in the following section. Without the high profits of the past, there would have been less market capitalization, more debt, fewer resources for R&D, and less pharmaceutical advancement.

This investment is going into buying the hardware and brain power that forms the biotechnology revolution. As one researcher has noted, "All the easy drugs are discovered. Now we are on to finding the needles in the haystack." Drugs companies are shifting out of traditional paths to drug discovery—testing compounds to see if they have any interesting effects—to using the genetic codes and behavior of cells to find out how diseases work and how to stop them. Every day a new gene is discovered and every day another door of understanding opens showing how illness unfolds and how to stop it. As a result, the number of biotechnology products in development has increased dramatically in recent years.

It is ironic that at the very moment when market pressures are forcing manufacturers to lower prices and be more innovative, price controls threaten to derail this progress. Driven by continued market pressure (that government price controls would eliminate), the pharmaceutical industry is on its way to delivering innovative therapies that prevent or treat a whole host of once-debilitating diseases.

IV. HOPE ON THE HORIZON: THE BATTLE AGAINST DISEASE

In a two-week period this past August, major pharmaceutical advancements were announced that hold great promise for Alzheimer's and cystic fibrosis sufferers. Ironically, these accomplishments received little press coverage, at least by way of comparison to the on-going debate over controlling pharmaceutical and other health care costs. Efforts must be made to make health care as efficient as possible. But policy makers must be careful not to squander the opportunity to eliminate the suffering and financial burden of millions of people in a short-sighted pursuit of price controls that will dry up the research and development that holds such great promise for the future.

The Emerging Pharmaceutical Revolution

Pharmaceutical advancement is driving a complete revolution in the quality and character of health care as we know it today. Because of advances in gene therapy and other new drug developments, Jeffrey Goldsmith of Health Futures, Inc., predicts that the following developments will occur by the year 2002:¹⁸

- A 20 to 30 percent further reduction in inpatient hospital use. Now at 800 days per 1,000 patients, it should drop to 550-600 days per 1,000 patients within 10 years.
- A 40 to 50 percent reduction in inpatient hospital-use rates among the elderly, thanks to the new technologies and improvements in the life expectancies of the elderly.
- A 70 percent reduction in length of stay for transplant surgery.
- A decline in surgical procedures with 85 percent of all surgical patients becoming ambulatory promptly after surgery.

Pharmaceutical advances have the potential of saving \$500 billion and 9 million lives over the next 25 years.¹⁹ And as the following sections describe, diseases and genetic disorders once considered untreatable are now under attack by new and exciting pharmaceutical therapies.

Cancer

"The future of cancer treatment is limited only by the discovery of the genetic sequences involved in a number of cancers," observes Dr. Bruce Chabner, Director of Drug Development at the National Cancer Institute. "Within 5 to 10 years we will have gene therapies to treat cancer." The following examples drawn from experimental gene therapy of other diseases suggest their potential:

In 1990, an NIH team took white blood cells from a six-year-old girl with a genetic deficiency that restricted the production of white blood cells, and put them in a culture with a mouse virus carrying a "new" gene and approximately one billion altered malignant cells. The cells with the properly functioning genes were put back into the girl. The doctors hoped

the new genes would reproduce the gene the girl lacked. They did. Her white blood cell count increased, and she began to fight off the tumors. A second girl was treated in 1991 and is also doing well. These two girls are now receiving infusions of healthy genes into stem cells (that manufacture new cells in bone marrow) in an effort to cure them permanently and eliminate the need for recurring infusions.

Recently, a similar experiment was tried with infants. The cells of newborns were taken from the umbilical cords, and the missing gene that produced white blood cells was inserted. The babies, born on May 10, 1993, will continue to receive infusions of engineered cells in order to repair their immune systems fully.

Another researcher directly injected his patient with genetic material that would tell cells to produce an immune response to tumor cells. The technique has been successful. The trials show that DNA can be used like a drug. Several drug companies and biotech firms are working on cancer vaccines that will stimulate an immune response. As new genes and their roles in cancer are discovered, companies and researchers will come closer and closer to finding genuine cures for cancer. Just recently, scientists located the gene that causes colon cancer. And in recent months genes that control over 30 percent of brain cancers were discovered.

At present many anti-cancer advances involve beating back cancer with chemotherapy and boosting the immune system in order to sustain patients receiving treatments. These advances, which include the new cancer drug Taxol, have been able to reduce tumors and prolong life. Recently Bristol-Myers Squibb announced the successful use of antibodies carrying anti-cancer drugs ("smart bombs") to destroy tumor-ridden cells without harming healthy ones. Trial using humans are beginning and results will be known within 2-3 years. Interferons—proteins that attack tumors—have proven effective in putting many cancers in remission. But the hope for the future rests with gene therapy. In 20 years it will be possible to take a cancer vaccine orally. Indeed, the dream of researchers at the M.D. Anderson Cancer Center in Houston is to be able to produce substances which can be put in table salt, as iodine is today, to suppress tumor growth.

Alzheimer's Disease

Alzheimer's disease is a progressive degenerative disease of the brain. Nearly four million Americans have Alzheimer's, and it is the fourth leading cause of death among adults, killing more than 100,000 each year. Without a cure or way of preventing Alzheimer's, 14 million Americans will be afflicted with the disease by the year 2050. Alzheimer's costs America \$90 billion a year in medical costs and lost productivity. Recently, however, the new drug Tacrine has been shown to slow the progression of memory loss and personality disorders. Sixty drugs are in development to mitigate Alzheimer's.

The search for a cure goes on. Researchers believe that Alzheimer's may be caused by the overproduction of a protein that forms plaques on the brains of its victims. They have identified the gene that controls the production of this protein, called beta-amyloid (BAP). Based on these findings, NIH scientists have found drugs that appear to block the development of BAP. Most recently, researchers have found the gene that may lead to half of all Alzheimer's cases. A "defective" version of this gene, which also controls the product of apolipoprotein E (a substance

that moves cholesterol through the blood stream), is also linked to a significantly higher risk of being afflicted with Alzheimer's. While this gene is only one of other factors that cause the disease, it points towards a possible preventive drug. Dr. Allen Roses, one of the discoverers of the genetic link, noted that "I'm optimistic enough to predict that in 10 to 15 years, we'll have a safe and effective medication that a 50 year old could take every day to prevent Alzheimer's disease." Three pharmaceutical companies are seeking to develop a gene therapy for the disease based upon this discovery.

Heart Disease

Heart disease remains the nation's leading cause of death. Nearly one million people died in 1990, and the disease accounts for 43 percent of all deaths each year. Treating heart disease patients costs \$117 billion annually. With proper diet, exercise, and medication, the risk of heart disease has been reduced considerably. In 1980, 33 percent of all heart patients died after a first heart attack. Thanks to a number of medicines, including beta-blockers, calcium channel blockers, and other innovations, the rate has been cut by 20 percent.

Until recently, people who had a first heart attack and survived died of a second one within five to ten years. New research on ACE inhibitors, a medication that stops the clogging of arteries and hypertension, has extended life for millions. Betty Nelson, a 64-year-old grandmother who suffered three heart attacks in less than a day, was put on an ACE inhibitor years ago. She is alive and active today. "My mother had a heart condition. Her doctor said she had a year to live and that was just about right. But I've gone three years and feel good. Without Capotril (an ACE inhibitor) I don't believe I'd have seen my grandson grow or watch my son get married. For me, every day is precious."

Beyond such medications lie even greater opportunities to control heart disease:

- A research team in France and the U.S. has discovered a genetic defect linked to hypertension, the leading cause of strokes and a major contributor to heart disease. People found with the defect could be given gene therapy or drugs that would counteract hypertension earlier in life.
- Dr. Jan Breslow of Rockefeller University has discovered the gene that causes low cholesterol and lipoprotein levels. "These low levels cause about 50-70 percent of cholesterol related heart problem," noted Breslow, "and we now know that 90 percent of these lipid levels are the result of a genetic defect. People with this condition don't respond to the usual cholesterol drugs. We are moving forward to develop a gene therapy, giving people the gene that makes more of the cholesterol. If we do, it could eliminate a lot of heart disease we can't do much about at this time."

AIDS

AIDS is a disease that threatens to kill over 200,000 Americans by the year 2000. It is an insidious illness. The HIV takes over the immune system and programs it to shut down. When people die of AIDS it usually means they die from a disease their immune system would destroy if it were operating properly. The pharmaceutical industry and the National Institute of Health (NIH) have poured billions into seeking treatments and a vaccine that will trigger an immune response against AIDS. Such a vaccine is proving difficult to develop.

In the meantime, much progress has been made in treating the illness. In 1984, a person with AIDS would die within 18 months of the diagnosis. Now, thanks to many small but important steps, including drugs for pneumonia and a Hepatitis B vaccine, the life expectancy of AIDS victims has been extended. Joel Thomas, a lawyer who found out he was HIV-positive 15 years ago, urged the development of more treatments while a search for a cure continues: "Early intervention is the single most cost-effective measure that you can take. If you keep people healthy for as long as possible, you don't have to spend \$150,000 for one episode of PCP (pneumocystis carinii pneumonia)."²⁰

The failure to come up with a "cure" for AIDS has been disappointing. Yet the relative lack of progress stems from the lack of knowledge about how the AIDS virus behaves and manages to elude most treatments. The battle against AIDS underscores how even full-blown drug trials are essentially basic research about the AIDS virus. In this respect, some preliminary trials of several potential AIDS vaccines have shown some promise. Viagene has just received NIH approval to begin human trials of a gene-transfer vaccine for AIDS, and both Immune Response Corporation and Genentech have developed vaccines that respond to the HIV antigen. Medimmune is developing a drug that will prevent eye infections that lead to blindness in HIV patients. In addition, researchers are learning more about the immune responses that control the HIV infection. Once these responses can be identified and understood, second and third generation vaccine therapies can be developed.

Schizophrenia

For years this most common of mental illnesses has robbed its victims of the ability to function in the world. Schizophrenics are haunted by inner voices, thoughts of violence, and a helplessness that degenerates into paranoia. There are nearly three million schizophrenics in America and only half respond to Thorazine, the standard drug treatment. Schizophrenia costs about \$50 billion a year, with \$29 billion of that spent on medical treatments and institutionalization.

Recently a drug called Clozapine was made available for schizophrenia. While the drug is expensive, it is cheaper than any other medical treatment, including the \$73,000 a year it costs to institutionalize a patient. The drug's ability to reverse the darkest ravages of the disease have been deemed miraculous. "In 15 years of practice, I've never seen anything like it," noted Dr. Samuel Risch, a psychiatrist at Emory University in Atlanta.

Of 20,000 American schizophrenics who were given the drug, more than half improved, becoming less withdrawn and free of the inner voices. Ten percent of all patients responded to the drug as if they were "reborn." One went back to teach public school part time after two years on Clozapine. For hundreds of thousands of schizophrenics and their families, this new breakthrough drug has ended a nightmare of mental anguish.

Cystic Fibrosis (CF)

Cystic fibrosis is the most common fatal recessive genetic disease among Caucasians of northern European descent. Approximately 30,000 Americans have CF and the disease occurs in about one in every 2,000 to 3,000 births. Most stricken with CF die before they are 30.

CF prevents glands that produce mucus, sweat and intestinal secretions from functioning properly. Mucus winds up clogging the lungs, causing respiratory infections and lung damage. The build-up of secretions prevents nutrients from being absorbed into the blood stream. As a result, children with CF may starve to death without timely diagnosis and treatment.

Less than 20 years ago, there was little one could do for a CF victim. Infants with CF rarely lived past age 6. Life expectancy is now up to 29 years of age. Robert Dresing, the President of the CF Foundation, has a son who was diagnosed with CF at 18 months. "The only reason he has survived," says Dresing, "is the fact that we have developed drugs over the last 20 years to control lung infections. These drugs have put him in a 'holding pattern' until we can develop the ultimate therapies that will either reverse, control, or cure this disease." Debbie Gibson, a participant at a recent National Health Council town meeting agrees: "I would not be alive today, but for the grace of God and the advances of research and technology throughout my lifetime."

Thankfully, the best appears yet to come. Recently, Genentech received preliminary FDA approval to market a drug that, for the first time, breaks down the proteins that form the thick mucus that is the grim hallmark of CF. This drug, called Pulmozyme, is most effective for people with moderate levels of mucus. In addition, the gene that causes the glandular malfunction has been discovered and two CF cures are currently in development. One approach is to replace the defective CF protein. Another approach is to add normal genes to the defective ones to permit a person's cells to produce the normal CF protein.

By the end of the decade a doctor will be able to diagnose CF and prescribe an inhaler that will contain a genetically engineered virus that will be sprayed into the lungs. The virus will carry the new genes that will go to work producing the normal proteins. These proteins will dissolve the mucus and over time will eliminate CF entirely. As Robert Beall, Director of Research for the Cystic Fibrosis Foundation notes, "we are closing in on a cure for cystic fibrosis."

Infectious Childhood Diseases

Each year, millions of children around the world die of such diseases as respiratory infections, acute diarrhea, meningitis, ear infections, and other illnesses. Despite the advent of vaccines, many infectious diseases remain without a preventive medicine. Today, however, there is hope that vaccines to eradicate these diseases will be available within a generation.

In the past, the vaccine business has been a listless and unprofitable activity. But biotechnology has made it easier to identify viruses and has opened up new markets through the development of products targeting specific diseases such as hepatitis B (a leading cause of liver cancer), respiratory syncytial virus, ear infections, and a virus causing acute diarrhea. In addition, technology exists to combine various vaccines into a single, time-released shot. Fewer vaccinations and fewer doses mean that children, particularly children in the Third World, will have vaccines that transcend scarce medical resource limitations and the poor distribution that has limited immunization in the past.

The lessons learned from biotechnology also hold the promise of vaccines for other illnesses that are the result of immune system malfunctioning. Gene-based vaccines for rheumatoid arthritis, some forms of cancer, AIDS and other diseases are being developed.

Because of biotechnology, vaccines could literally become an inexpensive preventive measure against diseases that take lives and cost huge sums of money. "Gene manipulation gives us the ability to identify genetic problems and find simple, cheap, available-to-everyone remedies for them," notes Dana Wensch, a geneticist at Ohio State University. "The day will come when no one has to die from a genetic disease."

Gaucher's Disease

Gaucher's disease is an extremely rare inherited disorder caused by a missing protein. The disease mostly affects children, and drains bone mass from the body. Breaking bones, internal bleeding, and bone diseases such as osteomyelitis are common. Normal activities such as walking cause excruciating pain, swollen glands, and perpetual black and blue marks. Recently a cure for Gaucher's disease was found. Genzyme, one of the early biotech companies, developed a product called Ceradase after following through on an NIH study of a product that was about to be shelved for lack of financing and medical interest. Ceradase replaces the missing protein and has restored people to health.

One of the first patients to use Ceradase was Abby Turner, an 8-year-old whose hopes of becoming a gymnast were crushed when Gaucher's disease erupted. She was anemic and exhausted and sometimes looked as if she were seven months pregnant. Abby was sick so often that her mother noted that "We weren't sure whether Abby would make it into her teens."

Upon taking Ceradase, her condition improved markedly. Within six months of treatment, she gained 24 pounds and grew four-and-a-half inches. Her enlarged spleen shrank to normal size. By year's end she was again riding her bicycle and taking dance lessons once a week. The constant trips to the emergency room ended as well. Abby will have to remain on Ceradase for quite some time, though in doses much smaller than those initially required to undo the accumulation of damage.

Moreover, Genzyme is now working on a gene-based therapy for Gaucher's disease that allows for even quicker recovery and longer lasting results. Gaucher's disease is an excellent example of how breakthroughs in pharmaceutical research have benefitted victims of rare diseases for which traditional drug discovery methods were too slow and cumbersome. As the entire human chromosome structure is mapped out by the end of the century, the sources of more rare diseases—as well as their cures—will be uncovered.

Huntington's Disease

The discovery of the elusive gene defect that causes Huntington's disease has given new hope to people who are robbed of all mental and physical powers before they die. Huntington's causes a degeneration of the brain and leads to loss of coordination, dementia, personality changes, memory loss, and finally death. Huntington's afflicts 30,000 Americans and another 150,000 people have a 50 percent chance of developing the illness.

Until the gene was discovered, there was no hope for a cure. But a cure is still in the future. Years of research and hundreds of millions of dollars will have to be spent. As geneticist Floyd McKusick has observed, "I can't help but believe that some sort of treatment will be devised now that the genetic defect is known."

Multiple Sclerosis (MS)

MS is a disease in which the nerve signals to the brain are disrupted and distorted by what amounts to short circuits. A fatty substance called myelin which protects nerve fibers of the brain and spinal cord is destroyed when the body's immune system mistakenly attacks the myelin instead of a real disease. The attack of the immune system eats away at the myelin and exposes these nerve fibers. MS victims have problems including numbness, slurred speech, double vision, muscle weakness, loss of bladder control, and confusion. Approximately 300,000 Americans have MS. The disease costs billions each year in medical care and lost productivity.

There are 12 biotech firms with products that have the promise of either slowing or reversing MS. One product recently approved by the FDA, Betaseron, has reduced the number of times MS flares up by 33 percent. Other companies are developing MS vaccines that would stimulate an immune response to the disease. One company, Autoimmune, is testing an MS vaccine that can be taken orally, with one's orange juice in the morning. In one case from this test, an MS patient on crutches threw them away and took up jogging! Hence, for the first time in history, MS patients will have a therapy that can reduce the impact of MS and actually slow its progression. And because the vaccine "repairs" the runaway immune system, it also holds promise for diseases such as rheumatoid arthritis, which are caused by similar immune malfunctions.

Amyotrophic Lateral Sclerosis (ALS)

ALS, commonly known as Lou Gehrig's disease, afflicts 25,000 Americans. ALS causes the deterioration of nerves that transmit messages to the brain. These nerves waste away and cut off the information the brain needs to instruct the muscles to carry out even the most basic of functions including swallowing and breathing. People with ALS rarely live longer than five years.

Yet even here, the hope for a treatment that could slow the progression of ALS now exists. A new biotechnology-developed protein called ciliary neurotrophic factor (or CNTF) has been found to support the growth of nerve cells, replacing those that die when attacked by ALS. Recently, the gene that causes ALS was found. Researchers are excited because this is a gene that was discovered years ago and is well-known. The genetic defect lowers the amount of a substance called SOD, exposing nerve cells to deadly molecules called "free radicals." SOD mops up free radicals so when SOD is in short supply, the nervous system can't fight back. Researchers now believe that injecting SOD into cells may slow or stop the onslaught of ALS.

Price Controls: At What Price?

Tremendous progress has already been made in treating what were only a few years ago untreatable diseases. But billions of dollars more of R&D is critical to continued progress. While others see pharmaceutical profits as "sins of the past" (this is language from a White House report on price controls), those that depend upon future funding for cures see them as a source of hope. As Brian Dickinson, a journalist who is part of a clinical trial of CNTF noted, "one thing already is sure in my mind: At a time when President Clinton is assailing the drug industry for excessive profits, it is encouraging to remember that drug companies are putting immense efforts into seeking products that could bring about life-saving breakthroughs. There are those of us who cannot help but admire their efforts."

V. PRICE CONTROLS COULD CRIPPLE MEDICAL PROGRESS

Noted physician and author Lewis Thomas believes that "it is now possible to begin thinking about a human society relatively free of disease." Two decades ago, such a vision would have been unimaginable. The fact that we are on the threshold of a new era in which diseases such as arthritis, diabetes, multiple sclerosis, and cystic fibrosis could be eliminated within 10 years; childhood diseases could be eliminated; and others such as cancer, ALS, and AIDS could be arrested and treated like high blood pressure is due almost exclusively to the advances that have emerged from the pharmaceutical industry over the past 15 years.

The ability to diagnose diseases earlier and to treat illnesses with drug and gene-based therapy will revolutionize medicine—changing its structure, reducing its costs, improving its ability to heal permanently, and increasing well-being and productivity throughout every stage of life. As *Scrip* magazine publisher Philip Brown has noted, significant medical progress will not come from any other quarter:

"AIDS is not the only disease that hits the headlines. There are also Alzheimer's disease, MS, ALS, not to mention the multiple forms of cancer and, of course, heart disease. From where do people think practical solutions will come? If they think that there is any answer other than the pharmaceutical industry, then they are seriously deluding themselves."

If significant medical progress is dependent upon pharmaceutical and biotechnology advancements, the profits that drive research and development cannot be ignored. Competition from generic drugs and a growing managed care network is already restraining earnings and the potential for reinvesting profits into R&D. Price controls would further discourage earnings-driven R&D and also discourage outside investment. Both would curtail the development of new drugs and postpone life-saving and life-enhancing cures.

History shows that price controls have never worked. People and companies spend time and resources trying end runs around the system rather than responding to consumer preferences and human needs. For example, during World War II, price controls led to the proliferation of "inferior off brands, some made by brand name producers who did not want to damage the long-run reputation of their regular label. In this way price controls change the character of products by degrading them."²¹

Price controls also stifle innovation by limiting returns people get when risking capital in new ventures. For example, when one considers that the risk of losing money exceeds 50 percent when drilling an oil well, it's clear that risk alone will not deter capital suppliers if the rate of return is sufficient to compensate the risk. It was no surprise that price controls on oil hurt oil exploration and drove investment in energy development elsewhere.

Price control advocates deride the notion that such controls will hurt pharmaceutical R&D. Yet all they have to do is look at current efforts to cut pharmaceutical prices and profits in Europe to see what impact it is having on the research infrastructure there. In the U.K., where price controls are in effect, 80 percent of all drugs prescribed are 20 years old or older. The three British pharmaceutical powerhouses, Glaxo, SmithKline Beecham and Burroughs Wellcome conduct a major portion of their new drug development in America.

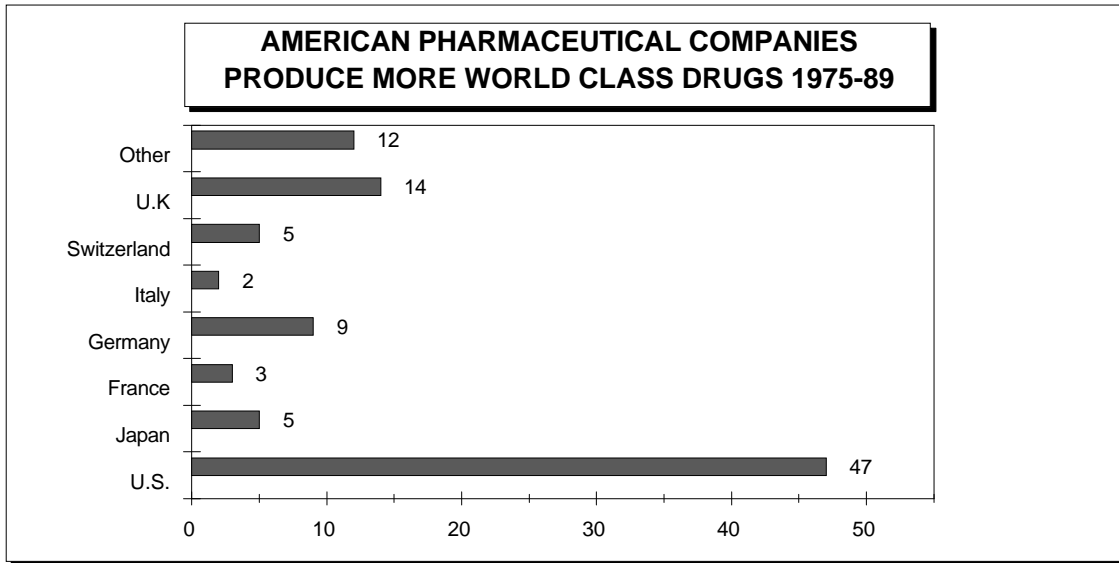


Figure 10

Source: E. Barrel, "Fifteen Years of Results of Pharmaceutical Researching the World," *Perspective et Saute Publique*, Paris 1985 and Update 1990.

The relatively open pharmaceutical market in the U.S. has been fertile ground for innovation and rapid developments in biotechnology. A 1991 report by the U.S. International Trade Commission (ITC) to the Senate Finance Committee found that "national cost containment policies and price controls were found to be the key determinant of the level of industry research and innovation since they can reduce the revenues which fund the R&D necessary to remain competitive."²²

That's why, as **Figures 10 and 11** indicate, U.S. pharmaceutical companies have established a clear dominance in pharmaceutical and biotechnology markets. As for innovation judged by new patents, America's biotechnology firms outpace many other country's:

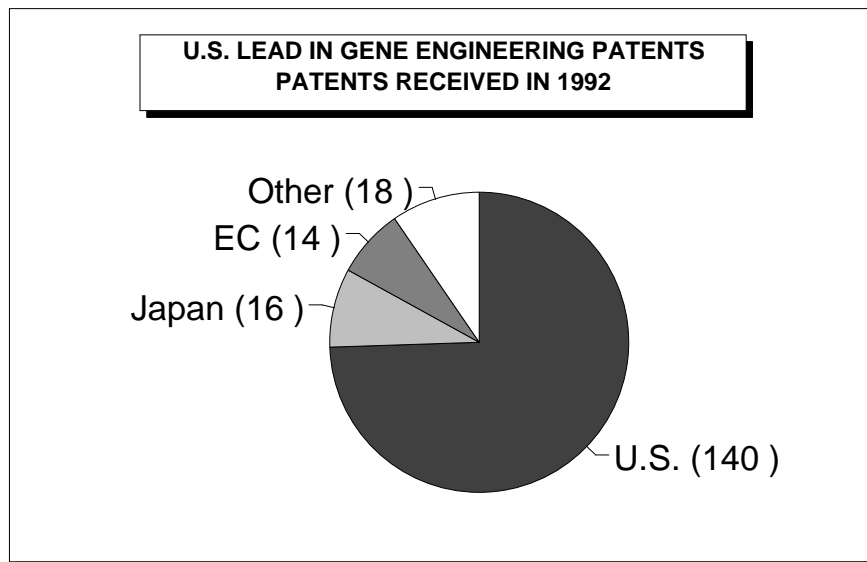


Figure 11

Source: PMA Survey

A British-trained researcher who now manages the clinical development of products for one of this country's leading biotechnology firms explains why America is the home of pharmaceutical and biotechnology innovation:

"I believe the science in America is better, but that doesn't explain why the country is so far ahead. The difference is that here there are capital markets willing to invest billions into biotechnology. There is nothing like it in Europe and Japan. Additionally, we have more entrepreneurs in America. Research scientists or professors leaving their labs and setting up a new company would be unheard of in Europe. In America people want to reap the rewards of their efforts and take the risk."²³

Dr. Steven Paul, who recently left his job as director of central nervous system research at the National Institutes of Health to assume similar responsibilities at Eli Lilly also noted the importance of entrepreneurial activity: "I have always marveled at the entrepreneurial ability of companies to throw everything they have into developing a new drug. It's why we lead the world in so many medical advances. There really is nothing like it in the world."²⁴

In fact, an example of what could happen to our pharmaceutical industry from government-imposed price controls is taking place right now in Germany. In an effort to control health care costs, the government has focused on freezing drug prices, cutting physician drug budgets, and even proposing to tax drug companies on revenues that exceed government set drug expenditure caps. Earlier versions of price controls in Germany led to a 25 to 40 percent decrease in pharmaceutical prices. The decrease in revenues had an immediate impact on R&D spending.

Dr. Rolf Schell, head of health economics at Hoescht AG, has stated that the first phase of this policy, implemented in 1989, has caused a 10 percent reduction in R&D expenditures by German drug companies.²⁵ Recent efforts to cut drug spending means that Bayer AG, once one of the largest and most innovative drug companies in the world, will lose about 15 percent of its sales in 1993. Bayer's Chairman Manfred Schneider warned that if Germany becomes a country of copycat generic drugs and cheap medicine, "the research-based pharmaceutical industry no longer has a future here."²⁶ It is important to note that measures taken in Germany such as mandatory generic substitution, drug budgets, and other indirect measures to control drug prices have been aggressively advocated by the Clinton Administration and other policy makers.

Early Warning Signs: It Can Happen Here

While the Clinton Administration has touted itself as an enthusiastic backer of advanced technology-based industries, biotechnology executives interviewed for this report had a different view. The chairman of one of the leading biotechnology firms in the world said bluntly, "We raised \$100 million for our new gene therapy product last year. If we had tried to hold an offering today we couldn't do it. The threat of price controls has done more to damage the biotechnology industry than anything else that has happened in the industry's history."²⁷

Earlier this year, after the President assailed vaccine companies for "unconscionable prices" the market value of all pharmaceutical stocks dropped by \$90 billion. That is equivalent to the total economy of a small country transferring investment out of pharmaceutical R&D and into less risky businesses. It is naive to think that this won't affect the money available for R&D for new drugs and is an indication of the far more serious impact that price controls would have.

Critics maintain that price controls will cut only "wasteful" research and that innovative drugs would be spared. In fact, the Clinton Administration and others have talked openly about having the government control the prices of new drugs by imposing taxes and cutting patent lives of new products that exceed a government-approved price. As discussed earlier, fully one-third of all pharmaceutical R&D is now in biotechnology. This is in addition to the billions raised and spent by biotechnology firms through public offerings and venture capital firms. This investment, unparalleled in the world, is tied up in searching for cures. It is those cures that price controls will prevent.

The industry has made deep financial commitments to innovative new drugs and biotechnology. But even now this commitment may be jeopardy. Investors, nervous about the ability of the companies to get a satisfactory return on R&D expenditures, have held back, as reflected in lower stock prices. In this environment, controls on prices and patents will mean even lower returns. Capital will flow out of the industry and become more expensive. In turn, R&D programs will have to be cut back. The therapies in development will be affected and millions will die or live in discomfort as the vision of a disease-free society will be postponed.

Biotechnology R&D Spending Is Being Scaled Back

Already drug companies have begun to hold the line on R&D expenditures in expectation of lower earnings. This is having a direct effect not only on their own development efforts, but on their commitment to biotechnology. As a recent *Wall Street Journal* article noted, leaks and policy "trial balloons" are helping to "wreck havoc on small biotechnology firms."²⁸ As a result, many promising therapies are being shelved because of a growing lack of resources and a concern about price controls. One executive put it this way:

"We know that our ACE inhibitor has promise in preventing hardening of the arteries but we can't commit the resources to prove its effectiveness. The fact is, generics are coming on the market and they will grab more business. We will never get our investment back on such a project."

Henri Temeer, Chairman of Genzyme and one the pioneers of the biotechnology business, believes that price controls will lead to "dumbing down" biotechnology R&D to safer projects. Temeer noted that "if you introduce price controls on new products, the result will be a lot of "me-too" research. It will be less risky and will pick on those therapies that can be reimbursed. You won't be able to raise the money otherwise. Proponents of government controls don't know what it takes to attract investment for projects that won't show a pay-off, if at all, for at least 10 years. They have no idea what investors need in return for investing \$100 million at a time when you can't even show them a project."²⁹

Lawrence Kurtz, a vice president at Chiron, believes that price controls will hurt biotech firms in another way: If price controls are imposed, drug companies will cut back on riskier, but potentially highly beneficial research. "Since many biotech companies depend upon drug companies for licensing fees, royalties and development assistance during clinical trials, they will take an indirect hit on innovation."

More generally, several large pharmaceutical companies have slowed or plan to reduce biotechnology investment because of the threat of price controls. Companies will continue to invest in biotechnology as a way of improving their R&D productivity, but as a recent survey reveals, "companies are generally looking to avoid higher-risk projects, and by definition,

biotech deals are high risk."³⁰ For every company that increases its biotechnology profile, several others seem to be paring back, watching and waiting, along with the rest of the investment community, for the final health care proposals out of the Clinton administration. One Eli Lilly executive predicts that total industry alliance activity "will be about half" of last year's.³¹

NIH-Private Industry Research Partnerships Have Been Stifled

Another casualty of the price control fever has been the productive and beneficial relationship between the National Institutes of Health, academic researchers, and private industry. The Administration and some members of Congress have accused the industry of unfairly profiting from the basic research and clinical trials that NIH conducts and sponsors. They want the government to have the right to set prices on drugs developed with reliance on federally supported research.

Companies such as Bristol-Myers Squibb that invested \$300 million developing Taxol, the new cancer drug that was initially discovered by NIH, would be required to get their prices approved before marketing the drug. Congressional hearings have been used as forums to put pressure on companies to enter into pricing arrangements, and legislation is pending that would make such price controls federal law.

NIH research directors are upset and frustrated by the divisive and destructive impact this "jawboning" has had on public-private collaboration in drug development. Indeed, the Clinton Administration is prepared to spend billions subsidizing other high tech industries and is encouraging partnerships in other areas through new incentives. Yet the pharmaceutical industry would be penalized for successfully utilizing opportunities other industries will essentially be paid to use!

Dr. Steven Paul, the former scientific director of the National Institute of Mental Health and now vice president of central nervous system research at Eli Lilly, is deeply troubled by the intrusion of price controls into a previously collaborative process. In an article he wrote for The Wall Street Journal he noted that "the adversarial relationship with the industry that the administration and other officials are promoting by characterizing its people as predators creates disincentives to creativity and its consequent innovation."³²

In an interview Dr. Paul talked specifically about the impact on innovation that has already taken place in the wake of such attacks:

"The mission of NIH is to determine how things work. This is its primary mission. We need the private companies because funds for research grants are tight. Drug development is an extremely high risk adventure that government can partake in. The opportunities we identified at NIH are too important to have industry and government fighting. Drug companies are now afraid to have their compounds tested because of the threat of price controls. As a result, we now have an absence of drugs for NIH clinical studies. All the truly interesting drugs are gone and they will never come back. As a result, the investment NIH makes in basic research is being wasted."³³

A senior research program director at the NIH has noted:

"Requiring companies to set a price at the time of licensing is nuts. We are trying to get companies like Bristol-Myers to make an investment in cancer research when they make more on one good arthritis drug than they do on all their cancer products. To change the stance and penalize companies will mean that there will be less risk and fewer products developed. That means that our mission, to get drugs into clinical use and see how effective they are, will be diminished. No one talks about all the money companies invested into products that we ultimately found had no benefit. That goes on all the time. We need a greater partnership between government and biotechnology. There is something fundamentally wrong with looking at successes like Taxol and penalizing that success."

Vaccine Development Has Been Jeopardized

The most direct example of the impact price controls will have on R&D and on the health and well-being of people around the globe is taking place now in the vaccine industry. Until recently the vaccine business languished as an unprofitable sideline of the pharmaceutical industry. Low prices, a largely public market, and high liability combined to drive all but two American companies out of the business. In 1986, Chiron came out with a biotechnology-based vaccine for Hepatitis B, a deadly and highly infectious disease that is also a leading cause of liver cancer. Chiron licensed the vaccine to Merck who developed and marketed the product. SmithKline Beecham soon followed with their own recombinant Hepatitis B vaccine. As noted earlier this led to a renaissance in childhood vaccine development.

Yet the Administration's proposal to replace the private market for vaccines with a program that buys up nearly all the shots and distributes them free of charge has forced companies to put many innovative R&D projects on hold. The President has attacked vaccine prices as "unconscionable," and in February at a public health clinic asserted that "we cannot possibly justify financing research and development in future vaccines based on prices that will assure that children will not receive the vaccines that are available today." Yet childhood vaccines cost only \$165 for the shots needed by age 2 (25 cents a day), one-half the fees doctors charge to administer shots.

As a result, vaccine companies are bracing for the worst and have begun to prepare a list of projects to be cut in the event the Administration has its way. A survey of the four companies operating in the U.S. market (SmithKline Beecham, Merck, Connaught, and Lederle-Praxis) found that in every case companies are preparing to cut *or have already cut* R&D in childhood vaccines. Biotech companies such as Chiron have stated that "price controls are a dagger aimed at the heart of vaccine development." The president of one vaccine operation noted that a 10 percent decrease in R&D spending could "delay, perhaps by as much as three years, several major projects we have underway."³⁴ A director of vaccine production explained why:

"Under the Clinton vaccine pricing plan we could keep making vaccines that are on the market. But we couldn't pay for R&D costs of vaccines in phase II trials or earlier in the development process. The reason being that we couldn't support the manufacturing and testing infrastructure required to support research. We'd have to end research in better delivery systems for vaccines, including oral administration, which is critical to the Third World situation. We would also have to cut down on costly field trials, which means fewer developments."³⁵

All four companies suggest that more complex combination vaccines and research on vaccines for otitis media, rotaviruses and RSV could be scrapped in favor of adult vaccines. "It takes 11 years to make a vaccine and three years to build a vaccine facility. You don't make that kind of investment with uncertainty in the marketplace."³⁶

As it is, many experts are concerned that the vaccine industry isn't doing enough research fast enough and worry that universal purchase could make a bad situation worse. Dr. Samuel Katz, chairman of the Public Health Services Advisory Committee on Immunization Practices, has noted that "a national purchase program could threaten future innovation in vaccine R&D." Anthony Robbins, one of the founders of CVI, has stated that "the evidence is that the current rate of profit is insufficient to drive them at an appropriate rate. We could be a lot further along than we are now."

Indeed, between 6 and 10 million children around the world are killed each year by diseases for which vaccines are being developed. Because of possible price controls that would give American families a subsidy of 25 cents a day for one year, research and development that could save many innocent lives may be lost.

VI. CONCLUSION: TURNING TOWARD THE FUTURE

Four years ago, Beth Ward had to deliver her baby Carly by emergency caesarean section. Carly was born six weeks early and contracted Respiratory Distress Syndrome, the leading cause of death and disability among premature infants. For infants with RDS each breath is a struggle for life. Ms. Ward remembers that "my daughter Carly was put on a ventilator in the Intensive Care Unit because her lungs were underdeveloped. She was born with RDS. Of course, we were very scared..."

Until recently, the ventilator was the only source of treatment—as well as a great source of danger. Extended use of the ventilator has been associated with lung damage, brain hemorrhage, retardation, and cerebral palsy. A new drug called Exosurf, introduced in 1988, was given to Carly and helped save her life. The drug cut her use of the ventilator and helped fight off infection. The drug cost \$800 but her hospital stay was cut by several days, saving her family more than \$1,000 a day. Exosurf reduces the number of deaths due to RDS by over 60 percent. Today 98 percent of all RDS infants will live.

As the public and policy makers deliberate the question of pharmaceutical price controls, we must keep the story of Carly Ward in mind. The drug that saved her life was made possible by the profits of drug products that preceded its development. Pharmaceutical profits have fueled a massive revolution in health care. As the investment in biotechnology and new drug development begins to bear fruit, new therapies will change the way we treat disease.

Today, doctors intervene after symptoms have occurred to try to forestall a life-threatening event. The current generation of drugs has strengthened our ability to do just that. What doctors will do tomorrow, however, is intervene earlier, soon after conception perhaps, to evaluate the inherited disease risks and periodically monitor those risks. This will enable clinicians and family members to work together to manage the emerging risks and eliminate them before they reach the stage of symptoms.

Predictive genetics will give us the ability to launch our assaults on diseases like heart disease, cancer, schizophrenia, and diabetes 10, 20, 30, even 50 years before the first symptoms appear. In many cases, the technology used to launch that attack will probably be the most exciting area of potential therapeutic advance in the next 20 years.³⁷

These advances are going to require continuous investment to be developed. If we impose price controls on all drugs, capping profits today and limiting prices and patent life for future drugs, we will save money today at the expense of future cures. But is this savings worth the price?

Price controls will cripple research and development and delay the realization of a disease-free society. Limiting price increases to the inflation rate plus one percent would yield \$1.2 billion a year in savings, or less than 75 cents a prescription. Price control advocates must be pressed to explain how they intend to limit prices and preserve the capital markets and entrepreneurial spirit that have fueled the research and development that has resulted in so many life-saving innovations.

ENDNOTES

1. O.E.C.D. *Health Data 1993*. Though authorities differ on this figure, eight percent is the highest number generally agreed upon.
2. Statement of Robert E. Dresing, President and CEO, Cystic Fibrosis Foundation, before the U.S. House of Representatives, Committee on Energy and Commerce, Subcommittee on Health and the Environment, Washington D.C., February 22, 1993.
3. This figure represents the total per-capita expenditure, including out-of-pocket and third-party expenditures. Recent Foster Higgins survey data of employee benefit programs reveal that some plans, particularly in Fortune 500 companies, have higher per capita drug expenditures than the national average: for current employees, \$330; for retired employees, \$500. Yet here too the survey found that the growth in expenditures was primarily a result of greater drug use and reliance on more expensive and innovative pharmaceuticals in lieu of even more costly surgical procedures and hospital stays, not on price increases.
4. O.E.C.D. *Health Data 1993*. The \$214 figure (as contrasted with the \$232 figure in note 3) represents O.E.C.D purchasing power adjustments for comparative purposes.
5. "U.S. Price Controls Unlikely?" *SCRIP World Pharmaceutical News*, March 16, 1993, No. 1803, page 16.
6. U.S. Health Care Financing Administration, *Health Care Financing Review*, Fall 1991. The \$187 figure represents per-capita expenses for prescriptions and prescription premiums.
7. *Older Americans and Prescription Drugs: Utilization, Expenditures and Coverage*. American Association of Retired Persons Public Policy Institute, Number 9, September 1991, page 2.
8. *Prescription Drug Survey*, conducted by Chilton Research Services for the American Association of Retired Persons, Fall 1991 (unpublished).
9. *Facts at a Glance*, Pharmaceutical Manufacturers Association, Washington D.C., 1992. These cost comparisons were gathered from various health insurers and health care advocacy groups.
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17. Phillip Brown, "A Caribbean Banana Lesson for the Pharmaceutical Industry," *SCRIP Magazine*, December 1992/January 1993, pages 3-4.

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23. Personal interview, Alison Tauton-Rigby, Sr. Vice President for Clinical Research Development, Genzyme Corp., April 10, 1993.
24. Personal interview, Dr. Stephen Paul, April 6, 1993
25. Drs. Richard Levy and Kerstin Menander, *Research in the Pharmaceutical Industry: Major Contributions to Biomedical Science and Implications for Public Policy*. National Pharmaceutical Council, 1992, page 49.
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28. "Clinton Health Plan Hurts Biotech Firms," *Wall Street Journal*, May 24, 1993, page B1.
29. Personal interview, Henri Temeer, Chairman of Genzyme Corp., April 14, 1993.
30. "Deal Making Ice Age," *In Vivo*, March 1992, page 5.
31. "Deal Making Ice Age," page 5.
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33. Personal interview, Dr. Stephen Paul, April 6, 1993.
34. Personal interview, Arthur Elliott, Director of Vaccine Production, Merck & Co.
35. Personal interview, Elliott.
36. Personal interview, Dave Williams, President of Connaught Laboratories.
37. Val Cardinale, page 47.

It's easy to understand the appeal of price controls. But such shortsightedness is equivalent to killing the goose that lays the golden eggs. A small savings in the cost of drugs today would leave thousands with no hope and millions more with a reduced quality of life. However well-intentioned, this is too high a price to pay.

Note: Nothing written here should be construed as necessarily reflecting the views of the Institute for Policy Innovation, or as an attempt to aid or hinder the passage of any bill before Congress.

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