Issue Brief

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The Biotechnology Revolution and Clinton-Care

by Dr. Robert Goldberg
with a Special Report on Voluntary Health Associations
by Christianna Shortridge

Introduction

Boomer Esiason, Quarterback, New York Jets

All my life I've prepared for the challenges of a professional football career. It has taken many long hours of focus, work and discipline for me to succeed as a pro quarterback. And like everyone, I've had the occasional setback and adversity that challenged my dedication and commitment. But nothing in my career could have prepared me for the challenge that came with the birth of my son. You see, my 3 year old son Gunnar has cystic fibrosis.

Now I face a new challenge, and a new priority. Each day my wife and I give Gunnar all the attention we can muster, all the physical therapy that he needs, and all the medicines that are available. My wife and I volunteer our time, talents and money to the biggest challenge we've ever faced. But mostly we dream of a cure for CF.

We know the cure we dream of will eventually be found. The CF gene has been isolated, and genetic therapies that will actually replace the defective gene are now being worked on. But until that day arrives, we as CF parents can only have faith, and support the work of those who are developing treatments and seeking cures.

Many diseases like CF affect relatively small amounts of people. Cystic fibrosis affects only 30,000 people a year. In a world of managed care and centralized allocation of medical resources, I fear that early-stage research on diseases like CF will be a luxury, not a priority. The resources to take gene therapy from the labs into the lives of people can only come from companies willing to risk billions of dollars. This study by the Institute for Policy Innovation clearly demonstrates the importance of private sector research funds, and how proposed changes in current laws governing the development and sale of new drugs could dash our dreams of a cure.

To many, the debate over health care is an interesting policy issue. But to thousands of families like mine, it is much more than that. My wife and I dream of the day when the only reason for our little boy's death will be from old age at the end of a long and full life. But until that day arrives, we as CF parents can only have faith in the therapies being invented by the dedicated researchers who now work so diligently at biotech companies and research universities. I hope policymakers will remember Gunnar and children with other fatal diseases as they consider legislative changes that might curb the incentive of scientists to invest, create and help.

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The Biotechnology Revolution and Clinton-Care

The New Architecture of Medical Progress

Biotechnology has not only revolutionized medicine, but it has also dramatically changed how the biomedical enterprise operates. The assembly line model of innovation — where basic science leads to applied research which in turn is used to develop and then market new products — is outdated, if it actually ever existed. Gone too is the image of companies racing against each other to find a cure. Today, the incredible potential of biotechnology — where a breakthrough genetic discovery for one disease can evolve into a potential cure for many others — has forged a more collaborative and integrated relationship between scientists and capitalists.

The organization and growth of private capital around early stage biotechnology is the single most important shift in the funding of medical research since the establishment of the National Institutes of Health (NIH) after World War II.

Intellectual and capital resources have shifted rapidly to adapt to this new architecture of medical progress. As a result, the organization and growth of private capital around early stage biotechnology is the single most important shift in the funding of medical research since the establishment of the National Institutes of Health (NIH) after World War II.

Nothing would derail this progress faster than the price controls on drugs and vaccines proposed in Clinton-Care. Price controls may seem an easy answer — after all, everyone wants to pay less for drugs. But while price controls may keep prices lower on existing drugs, they would greatly reduce private funding of biotechnology and pharmaceutical research. In short, biotechnology and pharmaceutical progress would be severely compromised.

The value pharmaceuticals and biotechnology offer today and promise tomorrow is often lost in the debate over whether they are too expensive. But even though the cost of new drugs and biomedical breakthroughs may be high, they are often more effective and less costly than other medical treatments. For example,

- Drug therapy for coronary artery disease costs approximately $1,000 a year compared with $41,000 for bypass surgery.
- Drug therapy for ulcers costs $900 a year compared with $25,000 for surgery.

Today, it's easy to take these and many other remarkable drug therapies for granted. But if price controls are adopted, the relationship between biotechnology and venture capitalists, and many promising pharmaceutical breakthroughs, will be lost.

The Context: Privatization of Medical Progress

Many thought that pharmaceutical and biotechnology firms would mature through consolidation, i.e., through the typical merger and acquisition route. That has not occurred. Instead, alliances have formed and been reformed around rapidly emerging scientific opportunities. This has been possible largely because of the flexibility and entrepreneurial orientation of venture capitalists who have played a major role in funding the biotech revolution.

The private sector is increasingly important to funding and assembling the pieces of the biological puzzle, and in the future this trend will only accelerate. In fact, to keep a pipeline full of new products, drug companies and venture capitalists are increasingly forced to invest in early, basic scientific research.

Jeffrey Casdin, a managing director of Oppenheimer and Co., Inc., observes:

> *"technology is advancing so rapidly that the few experts on the leading edge will continue to be attracted to . . . small start up companies where the lack of bureaucracy and a premium on achievement allow for the realization of their ideas and knowledge."*[1]

Hence, the drive to discover new drugs now focuses more intensively on the development of basic research. This has led to the creation of a more **symbiotic model** of medical progress reflected in the following developments:

1. Integration of Biotechnology and Pharmaceutical Companies

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While some policymakers love to love biotechnology and love to hate drug firms, the fact is that the two enterprises are virtually and nearly completely integrated. A recent Ernst and Young report on biotechnology notes:

> *"By aligning between and within their sectors — strength-to-strength and need-to-need — pharmaceutical and biotechnology companies are equipping themselves to pursue their long-term goals . . . state-of-the-art development and delivery of high quality, cost-beneficial products. The restructuring of the two industries is simultaneous and symbiotic."*[2]

As a result, the link between the two industries is enduring and complex. According to the North Carolina Biotechnology Center, there are nearly 400 alliances between biotechnology and pharmaceutical firms.[3] And a recent *IN VIVO* article estimates that pharmaceutical firms invested $2.3 billion in biotech companies in 1993.

2. Increased Collaboration Between Private Firms, NIH and Academic Researchers.

The development of knowledge about cystic fibrosis, for example, has been achieved through close NIH-industry-academic cooperation. Many people know that Genzyme Corporation has invested hundreds of millions of dollars in developing gene therapy for CF. Less well known is the fact that basic research essential to developing a cure has been conducted on a collaborative basis by NIH researchers, Genzyme Corporation, the University of Iowa, the Whitehead Institute, Children's Hospital in Cincinnati and the University of Michigan.

Similarly, NIH researchers and academic scientists play a critical role in taking molecules identified by private companies and determining appropriate disease targets. In some cases, such as with the cancer drugs Interleukin-2 and Interleukin-12, this discovery work is carried out simultaneously in cooperative fashion. The spill-over benefit to basic research is significant because it reinforces the value of discovery work to product development.

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3. Greater Concentration of Capital in Early Stage Biology

As advances in molecular science and genetics have revolutionized pharmaceutical research, a heavier concentration of R&D capital in fundamental research is required. This critical need for capital is being met by an amalgam of industrial and venture partners. In some cases — with gene sequencing firms for example — pharmaceutical firms, venture capitalists and biotechnology firms fund and contract with academic researchers to probe the genome for disease targets and sequence the human chromosome structure. Genzyme developed adenovirus facilities, supported animal studies and paid for primate studies to support discovery efforts of academic researchers working on cystic fibrosis.

Increasingly, venture capitalists are financing the basic biology that supports wide-ranging research activities. Genentech has a 20% stake in GenVec Inc., a gene

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therapy company funded by a venture capital firm, to develop cystic fibrosis therapies around the work of former NIH scientist Ronald Crystal. Similarly, the partnership between SmithKline Beecham, Human Genome Sciences, venture capitalists and a nonprofit is an example of how the basic biology behind medical progress will be financed and developed through the 21st century.

4. Clinical Research is a Critical Link Between the Lab and People's Lives

Finally and inseparably, the clinical research of thousands of physicians in community settings and teaching hospitals provides patients and researchers with insights on the versatility and efficacy of different drugs. Without clinical research, the lag time between the development of innovative technologies and its adoption would grow significantly. Examples of the crucial role clinical research plays in applying new drugs include the benefits of Pulmozyme, Genentech's cystic fibrosis drug for people with bronchitis, the use of calcium channel blockers in delaying kidney disease, the use of antibiotics in treating bacteria-induced ulcers, and the use of AZT in stopping HIV transmission between a mother and fetus.

Voluntary Health Associations: A Case Study of the Pro's and Con's of Price Controls

While all Americans have a stake in health care reform, among those most interested are those who suffer (or who have family members who suffer) from diseases like cystic fibrosis, muscular dystrophy, AIDs, Alzheimer's, heart disease, and cancer. Bonded by a common goal, many have joined with medical personnel, scientists and others to form voluntary health associations (VHAs).

In addition to advocacy, VHAs have come to play an important role in medical research. VHAs help to sustain the cooperation among academic researchers, private firms, venture capitalists and government scientists. They not only help fund research, they are actively disseminating discoveries throughout the research and financial communities. They also provide support in the conduct of clinical trials, serve as a prod to rapid FDA review and approval, and encourage close cooperation between patients and private companies in making new products widely available.

VHAs are important players in the health care debate, particularly with regard to proposed price controls, because they are forced to struggle with a wide variety of health care issues daily. VHAs are, understandably, selfish. They want it all: better and more comprehensive treatment, increased insurance coverage that can't be taken away if they change jobs, cheaper drug prices and, most of all, a cure. And who can blame them?

While concerned about long-range research prospects, some VHAs seem to regard health care costs, not the diseases that cause them, as their most dangerous enemy. As such, they see price controls not in terms of discouraging research, but in improving access. Many VHAs therefore like what Clinton-Care promises. These groups have focused on securing short- term savings in drug prices and more comprehensive insurance coverage, and either do not see price controls as a threat, or are willing to accept the trade-off of a cure that may be a decade or longer away for the promise of increased access to health care and insurance. By their emphasis, they share the Clinton administration view that controlling drug prices is more important than fostering the development of breakthrough drugs.

Other VHAs, however, see Clinton-Care's price controls on pharmaceuticals and biotechnology as a threat to innovation, and in a more personal way, as denying them a cure for their disease. They are not willing to trade the long-term benefit of a cure for the promise of lower drug prices and universal coverage.

Cystic Fibrosis

While the Cystic Fibrosis Foundation puts its own concerns before the pharmaceutical industry, it is concerned about protecting its investment in CF research. As a result, the CF Foundation believes it is important to protect the partnerships and flow of private capital supporting gene therapy. Robert Beall, the President and CEO of the CF Foundation, recently explained his views:

> *"For many years, we have waited for pharmaceutical companies to invest in cystic fibrosis, a disease representing a small population size. Cystic fibrosis patients have been forced to wait for"spill-over" products developed for other diseases. But times are changing. The biotechnology industry has increased its efforts to find a niche for diseases like CF and created a ground swell of interest. For instance, as we speak, Genzyme Corporation, Targeted Genetics, Genetic Therapy, Inc. and GenVen Corporation are developing strategies to, hopefully, cure cystic fibrosis by gene therapy . . . . Now, at the most precarious time in this industry's growth, certain officials choose to bash the biotech industry, questioning the prices charged for new products. These are the very products that could provide a better quality of life for CF patients and many others . . . . The free enterprise system must be protected, especially in the new realm of biotechnology . . . we cannot pull out the underpinnings of this industry by threatening to change the pricing structure by price controls.*[4]

Cancer

Many cancer groups see limits on drug prices and access to drugs as undermining medical progress against cancer. Dr. Lee Mortenson, the executive director of the Association of Community Cancer Centers asserts: "the infrastructure for innovation is being shaken to its core by health care reform. Price controls are discouraging drug development. The Clinton plan and managed care limits the amount of money covering payment for clinical trials and restricts off-label drug uses. That means that the use of new technologies could be stalled for a generation."[5]

Effects of Price Controls on Medical Research

The wrong kind of health care reform could shake the foundation of America's biomedical research enterprise to its core. Some policymakers believe they can impose price controls and, by funding NIH, still support basic research and sustain medical progress. But because the pathway of medical progress is interdependent, price controls and sure-to-follow cuts in clinical research will reduce the amount of important medical research being conducted in the United States.

Will the Clinton price controls really dry up pharmaceutical R&D? They already have. A recent survey of biotech firms found that in 1993 nearly 70 percent of all companies developing new products for treating AIDs, cancer and Alzheimer's had trouble raising R&D capital because of investor concerns about future price controls.

In fact, in 1993 the number of new biotechnology drugs in development failed to increase for the first time in five years. Companies with products in the biotech pipeline are not moving forward with expensive clinical trials because they are unsure of funding.

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Mortenson's observation is echoed by Dr. Harmon Eyre, deputy director of Research and Medical Affairs for the American Cancer Society: Dr. Eyre believes that

> *"price controls might increase the availability of medicine for current cancer patients. However, price controls will decrease the incentive for the pharmaceutical industry to invest in new drugs. Price controls could also affect the quantity of research into new cancer drugs, delay finding a cure for cancer and delay new research."*[6]

The public policy director for Cancer Care, a patient advocacy group, says her organization is telling the White House and Congress to not impose price controls on breakthrough drugs or limit access to new medicines because of cost considerations. She notes that while "there are plenty of anti-cancer drugs on the market, approximately 50% of all patients still die of cancer. New and improved pharmaceuticals are vital to treating diseases such as cancer and raising the quality of life for many patients."[7]

Eugene Schoenfeld, president of the National Kidney Cancer Foundation, recently stated at a National Health Council forum:

> *"I have kidney cancer. There is no cure for my disease. So the fact that someone with a drug for their illness will get it 5% less means that there might be less money to fund research that would benefit me and other people with kidney cancer. Price controls will destroy incentives to support continued research. To me, its a matter of life or death."*[8]

AIDS

Price controls are a positive prescription to many in the AIDS community. For example, Derek Hodel of the AIDs Action Council believes price controls will improve patient access to drugs. Other AIDS activists such as Brenda Lein of Project Inform trust the government to insure that price controls will not affect innovation.

While most AIDS organizations still regard patient access to medicines and clinical trials as the most important part of their agenda, there is concern about the impact of price controls on AIDS drug development. Martin Delaney, the founder and executive director of Project Inform, helped lead the effort to reduce the price and increase the access to AZT, the first AIDS drug. Delaney stated at the last AIDS Drug Development Roundtable that "we have reached a crisis in government-private sector cooperation because of price controls . . . on any drugs developed jointly by NIH and private company scientists. We have worked hard on improving cooperation but the congressional staff (who support stricter price controls on cooperatively developed drugs) never pay attention to what we are trying to do."

Similarly Jim Driscoll, director of the Direct Treatment Action Group, asserts that "price controls will reduce the chances of finding a cure for AIDs." Driscoll has campaigned vigorously against price controls in the Clinton health plan and frequently lobbies Congress and other AIDS organizations.

Other Groups

Abby Meyers, the director of the National Organization for Rare Diseases, favors strong price controls on breakthrough drugs because she believes that drug companies make excessive profits. In fact, she has lobbied in support of the administration's Advisory Council on Breakthrough Drugs.

Finally, some VHA's say they support the Clinton plan because it eliminates insurance regulations that limit coverage for pre-existing conditions. Steven McConnell, Senior Vice President for Public Policy at the Alzheimer's Association, believes that universal coverage is more important than fighting price controls. "There may not be a lot research can do immediately," says McConnell. "But the concrete things Clinton offers are excellent."

Conclusion

VHAs are a microcosm of the larger battle over health care reform and the narrower effects of price controls. Many VHAs are betting that the capital and commitment of the private sector will endure despite price controls. But if it doesn't, new medicines will take longer to emerge, or will be stifled altogether. Ultimately, price controls could hurt those individuals at the heart of the VHAs noble mission. The irony is that the only reason the administration's price controls have a chance of passing is because many disease groups are not opposing them.

- Christianna Shortridge

The current debate within voluntary health organizations (VHAs) reflects the tradeoffs inherent in current proposals for health care reform (see pages 4-5). Many VHAs reject price controls, believing they will dry up investment dollars and postpone a cure. Others so desire universal coverage and lower drug prices for their constituents that they aggressively support proposals that contain price controls.

Drug and biotech companies spend $14 billion a year on research and development — twice what the National Institutes of Health spends yearly.

What explains the apparent apathy of many VHAs about the impact of price controls on R&D? In part, these organizations mistakenly believe that the National Institutes of Health (NIH) are the sole sources of funding and drug discoveries. Yet, drug and biotech companies spend $14 billion a year on research and development — twice what NIH spends yearly.

If price controls are approved, drying up investment and R&D, who is going to make up the difference? Government? Not likely, and the bottom line is fewer dollars invested and fewer breakthroughs.

Furthermore, only 2 percent of all drugs have been discovered and patented by NIH. The vast majority were discovered by private firms. The NIH does play an important role in supporting basic, non-targeted research. But only pharmaceutical and biotechnology firms can assume the risks and costs of translating discoveries from the lab to the lives of people.

What has the specter of price controls done so far, and what will happen in the future if they are passed?

- According to a recent study by Duke University economists Henry Grabowski and John Vernon, the Clinton price controls would reduce the cash flow of the most commercially successful ("breakthrough") drugs by nearly 100%.[9] Not only would this reduce the amount of money available to pay for future R&D, it threatens the flow of venture capital into biotechnology.

A survey of 107 biotechnology firms, including 73 public companies found that nearly 83% of all companies, said that price control concerns made it more difficult to raise capital in 1993.

- Recent surveys of biotechnology firms and venture capitalists confirm that the threat of price controls has increased the risk and difficulty associated with raising capital for basic research. A survey of 107 biotechnology firms, including 73 public companies, found that nearly 83% of all companies said that price control concerns made it more difficult to raise capital in 1993.[10] Nearly 90% would seek out foreign partners or would make themselves acquisition targets. Nearly 70% of all firms would have to cut fundamental research and delay R&D if price controls were adopted.
- Similarly, 67% of all companies would be less likely to develop drugs for the Medicare population because proposed price controls would make more difficult to obtain investment capital.
- Venture capitalists — who as noted are funding an increasingly significant amount of discovery research — also expressed serious concerns about the negative impact of price controls. In 1993, 65% of all venture capitalists had invested less money in fewer biotech firms due to price control concerns.
- In 1994, 67% of all venture capitalists plan to reduce their investment in biotech because of concerns over price controls. The survey of 62 venture capital firms shows 90% of all venture capitalists would reduce their biotech investment activity if price controls are adopted.

In sum, the effect of price controls would be to chase money away from the discovery research that is the source of new products. As one venture capitalist notes, "We are increasingly uncertain that we can we find the cash to go all the way to bring a drug to market. Our ability to do so would be diminished in a dramatic way if controls are adopted."[11]

Gov't-Industry Collaboration is Being Discouraged

Recently, the price of drugs developed even partially under cooperative research and development agreements (CRADA's) between the National Institutes of Health and private industry has become a focus of congressional scrutiny. While NIH has the right to ask that drug prices under CRADA's be reasonably priced, some policymakers want NIH to take a more aggressive stance in setting drug prices.

The effect of "reasonable pricing" becoming an important policy consideration provides a natural foreshadowing of what would happen to collaboration generally. Since Congress began discussing the pricing of drugs cooperatively developed, the number of CRADAs has declined by 80%: Only 27 new CRADAs were established and many others were withdrawn.

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Current legislative proposals to subject products developed by researchers that obtain NIH funding to reasonable pricing clauses threatens to weaken collaboration further. For example, university-based gene therapy centers receive funding from NIH. None of the centers have sufficient resources to launch clinical trials, where it costs $30,000 per patient for gene therapy as compared with $5,000 per patient for other forms of biotechnology clinical trials. These centers lack the manufacturing facilities, research infrastructure and capital to carry out full-fledged gene therapy trials.

Private support in terms of building production facilities, carrying out preclinical work and animal studies and providing ample quantities of vectors and viruses is essential. Yet concern about NIH price controls are forcing companies such as Genzyme to rule out including top investigators. This defeats the whole purpose of gene therapy centers, which is to facilitate the commercialization of gene therapy, by taking the leading investigators out of the market.

Research directors at the NIH are deeply concerned about the effect price controls have had on their research programs. Dr. Bruce Chabner, director of the National Cancer Institute's Drug Development Program, observed that "we cannot move forward on three interesting cancer compounds because companies are reluctant to move forward under (CRADA) price controls. Companies are withdrawing drugs or refusing to work with us." And Anthony Fauci, the scientific director of the National Institute on Allergies and Infectious Diseases, asserted that "government and industry cannot come up with better drugs for AIDS alone. Price controls are overshadowing all collaboration. If industry is not a partner, the mechanism will not work."

Conclusion

The best long-term cure for skyrocketing health care costs is a cure for diseases, and pharmaceutical and biomedical breakthroughs are the only source of cures. Private capital has become increasingly important to early-stage science in biomedical and pharmaceutical research. The pathway between advances in molecular biology and the rapid development of breakthrough drugs for difficult diseases has been created through the combination of NIH-supported research, private capital and private companies. The enormous potential for innovation and discovery generated by this new partnership is in danger, since even the threat of price controls has already greatly reduced the flow of venture capital, the mother's milk of biomedical innovation.

Endnotes

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6. Personal interview, Harmon Eyre, M.D., Deputy director of Research and Medical Affairs, American Cancer Society, January 20, 1994.
7. Personal interview, Director of Public Policy, CancerCare, February 10, 1994.
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11. Robert M. Goldberg, *Price Controls and the Future of Biotechnology: The View of Venture Capitalists*, Gordon Public Policy Center, Waltham, MA, 1994, p. 6.

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